German Guideline Program in Oncology (GGPO)

Evidence-based Guideline on Prevention of Skin Cancer

Version 2.1 - August 2021
AWMF-Registernummer: 032/052OL

Guideline (Long Version)

DKG KREBSGESELLSCHAFT
Deutsche Krebshilfe HELFEN. FORSCHEN. INFORMIEREN.
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Important Updates

In the course of the update of the guideline (version 2), multiple changes were made in all sections of the guideline. A total of 164 recommendations and statements were consented. 74 of these recommendations/statements were newly developed in the course of the update and 47 were modified. It is not possible to list all of the new additions here, so only the most comprehensive update areas are highlighted. Documentation and descriptions of all adjustments to the recommendations and statements can be found in Chapter 10. The extent to which changes have been made to the recommendations is shown in the individual recommendations (for an explanation, see Chapter 1.10).

The following changes should be highlighted

- In order to eliminate conceptual ambiguities in the area of prevention, early detection and screening, a conceptual classification has been added to Chapter 3. This classifies and distinguishes between relevant definitions and concepts of prevention.
- In the area of primary prevention (see Chapter 5), new target group- and setting-specific recommendations for behavioral and situational prevention have been developed, and statements on specific topic areas have been upgraded through evidence-based approaches (see, e.g., Section 1.1.5 "Avoidance of UV exposure from artificial sources").
- The chapter on "Climate Change and UV Radiation" (see Chapter 6) has been completely redeveloped. It provides a presentation of the current state of knowledge on "Climate Change and UV Radiation" (Section 1), "Perceptions of Heat and UV Radiation" (Section 6.2), and "Climate Change and Urban Development" (Section 6.3).
- The chapter on "Occupational skin cancer" (see Section 7) is new to the guideline and focuses on the "Status quo outdoor workers" (see Section 1), "Behavioural and situational prevention measures for outdoor workers" (see Section 7.2), "Communicating information and motivating workers to take protective measures" (see Section 7.3), and "Occupational health screening for outdoor workers" (see Section 7.4).
- The section on "Secondary prevention" (see Section 8) has been fundamentally revised. This includes an up-to-date review of the evidence on statutory skin cancer screening (see Section 2) as well as a review of the communicative strategies and communication channels of secondary prevention (see Section 8.3).
- The section "Health economic evaluation" (see chapter 9) was fundamentally revised and now contains a comprehensive reappraisal of health economic evaluations of primary prevention measures for sunbed use (see 1.2), population-based primary prevention measures (see 9.1.3) as well as specific primary prevention measures (see 9.1.4) . In addition, a systematic literature review on cost-effectiveness analyses of secondary prevention of skin cancer was conducted (see 9.2).

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1. Information about this Guideline

1.1. Editors

German Guideline Program in Oncology of the Association of the Scientific Medical Societies in Germany (AWMF), German Cancer Society (DKG), and the German Cancer Aid Foundation (DKH).

1.2. Leading Scientific Societies

Deutsche Dermatologische Gesellschaft (DDG) e.V. represented by the Arbeitsgemeinschaft für Berufs- und Umweltdermatologie e.V.

Deutsche Krebsgesellschaft e.V. represented by the Arbeitsgemeinschaft Dermatologische Prävention e.V.

1.3. Funding of the Guideline

This guideline was supported by the German Cancer Aid within the framework of the guideline program oncology.

1.4. Contact

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1.5. How to cite

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1.6. Previous Changes

September 2021: Version 2.1: The editing mode (reviewed in modified) in Recommendations 4.3., 8.5., 8.9., 8.22., 8.44. was corrected and the listing of changes in Chapter 10 was adjusted accordingly. No substantive changes were made to the recommendations.

1.7. Special Comment

Medicine is subject to a continuous process of development, so that all information, in particular on diagnostic and therapeutic procedures, can only ever correspond to the state of knowledge at the time of printing of the guideline. The greatest possible care has been taken withregard to the recommendations given for therapy and the selection and dosage of medications. Nevertheless, users are urged to consult the manufacturers' package inserts and expert information and, in case of doubt, to consult a specialist. In the general interest, any discrepancies should be reported to the OL editorial office.

The user himself remains responsible for any diagnostic and therapeutic application, medication and dosage.

1.8. Objectives of the Guideline Program for Oncology

The Association of the Scientific Medical Societies in Germany (AWMF), the German Cancer Society (DKG) and the German Cancer Aid (Deutsche Krebshilfe) have set themselves the goal of jointly promoting and supporting the development, updating and use of scientifically based and practicable guidelines in oncology with the Oncology Guidelines Programme (OL). The basis of this program is based on the medical-scientific findings of the professional societies and the DKG, the consensus of medical experts, users and patients, as well as the set of rules for the development of guidelines by the AWMF and the professional support and funding by the German Cancer Aid. In order to reflect the current state of medical knowledge and to take medical progress into account, guidelines must be regularly reviewed and updated. The application of the AWMF regulations should be the basis for the development of high-quality oncological guidelines. As guidelines are an important instrument of quality assurance and quality management in oncology, they should be introduced into the daily care routine in a targeted and sustainable manner. Thus, active implementation measures and also evaluation programmes are an important part of the promotion of the Oncology Guidelines Programme. The aim of the programme is to create professional and medium-term financially secure conditions for the development and provision of high-quality guidelines in Germany. This is because these high-quality guidelines not only serve the structured transfer of knowledge, but can also find their place in the design of the structures of the health care system. Mention should be made here of evidence-based guidelines as a basis for creating and updating disease management programmes or the use of quality indicators extracted from guidelines in the context of the certification of organ tumour centres.

1.9. Additional Documents relating to this Guideline

This document is the long version of the S3 guideline Prevention of skin cancer. In addition to the long version, there are the following supplementary documents to this guideline:

- Abridged version of the guideline
- Patient guideline
- Guideline report on the guideline development process
- Evidence tables

This guideline and all supplementary documents can be accessed via the following pages.

- Guideline Programme in Oncology(https://www.leitlinienprogramm-onkologie.de/leitlinien/hautkrebs-praevention/)
- AWMF(http://www.leitlinien.net)
- Homepages of the participating professional societies, e.g. Arbeitsgemeinschaft Dermatologische Prävention(http://www.unserehaut.de, http://www.hautkrebs-screening.de)
- Guidelines International Network(http://www.g-i-n.net)

There is a separate S3 guideline on the diagnosis, therapy and aftercare of melanoma within the guideline programme oncology(https://www.leitlinienprogramm-onkologie.de/leitlinien/melanom/), which is also accessible via the websites of the guideline programme oncology and its sponsors.

1.10. Composition of the Guideline Group

1.10.1. Guideline Coordination

Prof. Dr. med. E.W. Breitbart and Prof. Dr. Thomas Diepgen (deceased on 27.03.2020), Prof. Dr. Andrea Bauer (since 28.03.2020)

Project team

Dr. Inga-Marie Hübner (project lead)

Yvonne de Buhr

Henriette Bunde

Dr. Rüdiger Greinert

Dr. Beate Volkmer

Anne Dost

Elisa Großmann

Jessica Achter

1.10.2. Involved Professional Societies and Organisations

Table 1: Involved Professional Societies and Organisations

Participating professional associations and organizations (alphabetical)	Representative(s)
Arbeitsgemeinschaft Dermatologische Histologie (ADH)	Prof. Dr. Michael Flaig
Arbeitsgemeinschaft Dermatologische Onkologie der DKG und DDG (ADO)	Prof. Dr. Carola Berking Dr. Peter Mohr (1)
Arbeitsgemeinschaft für Berufs- und Umweltdermatologie e.V.	Prof. Dr. Andrea Bauer
Arbeitsgemeinschaft Psychoonkologie der Deutschen Krebsgesellschaft (PSO)	Prof. Dr. Susanne Singer
Berufsverband der Augenärzte Deutschlands (BVA)	Prof. Dr. Ludwig Heindl PD Dr. med. Vinodh Kakkassery (1)
Berufsverband der Deutschen Urologen e.V. (BvDU)	Dr. Bernt Göckel-Beining
Berufsverband der Frauenärzte (BVF)	Dr. Wolfgang Cremer
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Berufsverband Deutscher Dermatologen (BVDD)	Dr. med. Martin Schlaeger
Bundesamt für Strahlenschutz (BfS)	Dr. M. Asmuß
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1: Vertreter

2: ausgeschieden

3: Vertreterin

Table 2: Composition of Guideline Workgroups

Workgroup	Composition of Workgroup
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WG 6: Sekundäre Prävention	**Lead: Prof. Dr. Eckhard W. Breitbart** Antje Backes Prof. Dr. Carola Berking Prof. Dr. Erhard Bierhoff Prof. Dr. Jean-François Chenot Dr. Wolfgang Cremer Dipl.-Med. Ingrid Dänschel Prof. Dr. Thomas Eigentler Prof. Dr. Moritz Felcht Prof. Dr. Michael Flaig Prof. Dr. Dr. Bernhard Frerich PD Dr. Andreas Gerstner Dr. Bernt Göckel-Beining Dr. Dr. Joachim Hübner PD Dr. med. Grit Mehlhorn Dr. Peter Mohr Dr. Rolf Ostendorf PD Dr. Christian Rose Prof. Dr. Andreas Stang Dr. Annika Waldmann

1.10.3. Additional Parties without voting Power

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Institution	Expert
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Universitätsklinikum Jena	Prof. Dr. Peter Elsner

1.10.4. Patient Involvement

The guideline was prepared with the direct participation of patient representatives (see table below)

Institution	Person
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1.10.5. Methodological Support

By the German Guideline Program in Oncology (GGPO):

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- Dipl.-Soz.Wiss Thomas Langer (DKG), Office of the GGPO c/o Deutsche Krebsgesellschaft e. V.

By external contractors:

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1.11. Abbreviations Used

Table 3: Abbreviations Used

Abbreviation	Explanation
ADP	Arbeitsgemeinschaft Dermatologische Prävention e. V.
AJCC	American Joint Committee on Cancer
AK	Actinic Keratosis
ALM	Acrolentiginous Melanoma
ArbSchG	„Gesetz über die Durchführung von Maßnahmen des Arbeitsschutzes zur Verbesserung der Sicherheit und des Gesundheitsschutzes der Beschäftigten bei der Arbeit“
AWMF	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften
BCC	Basal Cell Carcinoma
BER	Base Excision Repair
BfS	Bundesamt für Strahlenschutz
BG ETEM	Berufsgenossenschaft Energie Textil Elektro Medienerzeugnisse

Abbreviation	Explanation
CG	Control Group
CMN	Congenital Melanocytic Nevi
CPD	Cis-Syn-Cyclobutane Pyrimidine Dimers
CRBC	CPD-retaining basal cells
DBD	DNA Binding Domain
DDG	Deutsche Dermatologische Gesellschaft (DDG)
DKG	Deutsche Krebsgesellschaft e.V.
DKH	Stiftung Deutsche Krebshilfe
DRG (G-DRG)	Diagnosis Related Groups (German Diagnosis Related Groups)
EASR	European Age Standardised Rate
EC	Expert Consensus
EIS	Electrical Impedance Spectroscopy
ENT	Ear, Nose, and Throat
EORTC	European Organisation for Research and Treatment of Cancer
G-BA	Gemeinsamer Bundesausschuss
GEKID	Gesellschaft der epidemiologischen Krebsregister in Deutschland
HCA	Human Capital Approach
HPV	Human Papilloma Virus
IARC	International Agency for Reserch on Cancer, internationales Institut für Krebsforschung
ICD	International Classification of Diseases
ICNIRP	International Commission on Non-Ionizing Radiation Protection
IG	Intervention Group
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
KBV	Kassenärztliche Bundesvereinigung
KDIGO	Kidney Disease: Improving Global Outcomes

Abbreviation	Explanation
LDH	Lactate Dehydrogenase
LMM	lentigo-maligna-melanom
LOH	Loss Of Heterozygosity
MAs	Medical Assistants
MM	Malignant Melanoma
MLT	Multiphoton Laser Tomography
NBCCS	Nevoid Basal Cell Carcinoma Syndrome
NCP	National Cancer Plan
NER	Nucleotide Excision Repair
NiSG	Gesetz zum Schutz vor nichtionisierender Strahlung bei der Anwendung am Menschen
NM	Nodular Melanoma
NMSC	Non-Melanocytic Skin Cancer
OstrV	„Verordnung zum Schutz der Beschäftigten vor Gefährdungen durch künstliche optische Strahlung“
PPV	Positive Predictive Value
QoL	Quality of Life
RCT	Randomized Controlled Trial
ROS	Reactive Oxygen Species
RR	Relative Risk
SAB	Scientific Advisory Board
SCC	Squamous Cell Carcinoma
SCREEN	Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany
SCS	Skin Cancer Screening
SHH-Gen	Sonic Hedgehog
SHI	Statutory Health Insurance

Abbreviation	Explanation
SIGN	Scottish Intercollegiate Guidelines Network
SMO	Smoothened-Protein
SSE	Skin Self-Examination
SSK	Strahlenschutzkommission
SSM	Superficially Spreading Melanoma
UAS	Uniform Assessment Standard
UPF	Ultraviolet Protection Factor
ZI	Zentralinstitut für die kassenärztliche Versorgung in Deutschland

2. Introduction

2.1. Scope and Purpose

2.1.1. Objective and Key Questions

The development of the S3 guideline „Prevention of skin cancer“ is intended to adapt the primary and secondary prevention of skin cancer to the current international scientific status. In doing so, the guideline should contribute both to an improvement in health and to a higher quality of life of the population. This goal is to be achieved primarily by reducing the incidence, morbidity and mortality of skin cancer.

In order for the S3 guideline „Prevention of skin cancer“ to achieve this goal, {LINK_0ca37aa2fe4c4fc89b0995f4ac928868} describes the current international scientific and medical status quo on skin cancer required for this purpose. These explanations form the basis for the development of the questions and recommendations listed below. Specifically, the authors and editors of the S3 guideline „Prevention of skin cancer“ hope for broad consideration of the recommendations on the following points:

- Primary prevention
- Climate change and UV radiation
- Occupational skin cancer
- Secondary prevention
- Screening/ Screening test
- Suspicious diagnosis/ Confirmatory diagnosis
- Doctor-patient communication
- Communicative strategies and competences
- Informing the population
- Implementation of screening and quality assurance

In this context, the S3 guideline comments on the following questions, among others:

- Which behaviours reduce the risk of developing skin cancer?
- Which behaviours are recommended for certain groups of persons (e.g. persons at risk, children / adolescents and adults)?
- Which behavioural and relational preventive measures are suitable for imparting knowledge and sustainably changing the behaviour of the population?
- What changes in UV radiation can be expected as a result of climate change and what influence will this have on the risk of skin cancer?
- Which urban planning measures should be taken into account in future UV prevention due to climate change?
- What occupational cancer-related primary prevention measures should be recommended?
- Are there effective population-based and individual measures for early skin cancer detection?
- How should screening be conducted?
- What recommendations can be made for screening at-risk individuals?
- What diagnostic measures are available?
- Which diagnostic measure (or which combination of measures) is suitable for screening?
- What are the confirmatory diagnostic methods?
- How should histopathological diagnostics be performed?

- How should a doctor-patient discussion be set up (structure) and what content should be conveyed and in what form?
- What information is necessary so that the citizen can make an informed decision for or against participation in a screening examination?
- Which professional prerequisites are necessary or must be created for physicians & (health professionals) in order to be able to carry out screening?

2.1.2. Target Audience

The recommendations of the S3 guideline „Prevention of skin cancer“ are aimed at all health professionals and members of professional groups involved in the prevention and early detection of skin cancer. This includes practicing, preventively active physicians (dermatologists, general practitioners, general practitioners, physicians without a regional designation, general practitioners, gynecologists, urologists, surgeons, pediatricians, ENT physicians, oral and maxillofacial surgeons, histopathologists, dentists) as well as nurses and medical assistants (MFA). Further addressees are medical-scientific professional societies and professional associations, patient representatives and self-help groups of skin cancer, employers of outdoor workers as well as quality assurance institutions and institutions on federal and state level, such as the Federal Office for Radiation Protection (BfS), the Central Institute for Health Insurance Physicians in Germany (ZI), the Federal Joint Committee (G-BA), the National Prevention Conference (https://www.npk-info.de) as well as the Society of Epidemiological Cancer Registries in Germany (GEKID). (GEKID).

Finally, the S3 guideline „Prevention of skin cancer“ addresses the general population of the Federal Republic of Germany. A separate evidence-based patient guideline / health care guideline was created to directly address the population.

Interfaces to other guidelines

In Germany, three other guidelines exist that have interfaces with the guideline „Prevention of skin cancer“:

- Guideline Program Oncology (German Cancer Society, German Cancer Aid, AWMF): Diagnosis, Therapy and Aftercare of Melanoma: https://www.leitlinienprogramm-onkologie.de/leitlinien/melanom/
- Guideline Program Oncology (German Cancer Society, German Cancer Aid, AWMF): S3 Guideline Actinic Keratosis and Squamous Cell Carcinoma of the Skin: https://www.leitlinienprogramm-onkologie.de/leitlinien/aktinische-keratose-und-plattenepithelkarzinom-der-haut/
- German Dermatological Society: S2k guideline Basal cell carcinoma of the skin: https://www.awmf.org/leitlinien/detail/ll/032-021.html

During the update process of version 2.01, these interfaces were systematically taken into account and identified.

2.1.3. Validity and Update Process

However, this version of the guideline is not valid for longer than 5 years until the next update. The current version of the guideline can be viewed on the website of the guideline program oncology: https://www.leitlinienprogramm-onkologie.de/leitlinien/hautkrebs-praevention/.

The current focus in the German health care system on prevention is leading to continuous realignments in a wide variety of decision-making bodies, institutions and professional societies, on the basis of projects carried out and corresponding publications.

The necessary consideration in this updating process, not only of the evidence-based literature, but also of the corresponding orientations in the National Cancer Plan (NKP), the National Decade against Cancer, the DKH Expert Committee on Cancer Prevention, the Alliance for Health Literacy and many others, leads to the realization that this prevention guideline can only achieve its goal – of providing up-to-date recommendations/information for the care of the population – by means of a continuous dynamic updating process. It is therefore the aim to transform the guideline into a „Living Guideline" with regular (currently planned annual) updates.

Comments and advice are explicitly welcome and can be sent to the following address: hautkrebs-praevention@leitlinienprogramm-onkologie.de

2.2. Methodology

A detailed description of the methodological approach can be found in the guideline report of the S3-guideline Prevention of Skin Cancer(https://www.leitlinienprogramm-onkologie.de/leitlinien/hautkrebs-praevention/).

2.2.1. Levels of Evidence (LoE)

To classify the risk of bias of the identified studies, a modified system (see following table) based on the system of the Scottish Intercollegiate Guidelines Network (SIGN, see table below) was used in this guideline. In the system presented, cross-sectional studies on diagnostic issues and before-and-after comparisons were added at level 2, as these were not previously explicitly listed there.

Scheme of the modified evidence classification according to SIGN:

Evidence class	Description (modifications in italics)
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of systematic error (bias).
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with low risk of systematic error (bias)
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with high risk of systematic error (bias)
2++	High-quality systematic reviews of case-control or cohort studies*(including before-after comparisons*) orHigh-quality case-control or cohort studies (*including before-after comparisons*) with very low risk of systematic bias (confounding, bias, „chance") and high probability that the relationship is causal orHigh-quality *study with cross-sectional design to investigate diagnostic quality with very low risk of systematic bias*.
2+	Well-conducted case-control studies or cohort studies*(including before-after comparisons*) with low risk of systematic bias (confounding, bias, „chance") and moderate probability that the relationship is causal orStudy with

Evidence class	Description (modifications in italics)
	cross-sectional design investigating diagnostic accuracy with moderate risk of systematic bias.
2-	Case-control studies or cohort studies*(including before-after comparisons*) with a high risk of systematic bias (confounding, bias, „chance“) and significant risk that the relationship is not causal or study *with cross-sectional design to investigate diagnostic goodness with high risk of systematic bias.*
3	Non-analytic studies, e.g. case reports, case series, studies with *cross-sectional design without investigations of diagnostic goodness*.
4	Expert opinion

2.2.2. Grades of Recommendation (GoR)

The OL methodology provides for the assignment of grades of recommendation by the guideline authors within the framework of a formal consensus process. Accordingly, a multi-part nominal group process moderated by the AWMF was conducted.

In the guideline, the level of evidence (see 2.3.1) of the underlying studies and, in the case of recommendations, the strength of the recommendation (degree of recommendation) are reported for all evidence-based statements (see Chapter 2.3.3) and recommendations.

With regard to the strength of the recommendation, this guideline distinguishes between three grades of recommendation (see the following table), which are also reflected in the wording of the recommendations in each case.

Grades of recommendation used:

Degree of Recommendation	Description	Form of expression
A	Strong recommendation	shall/shall not
B	Recommendation	should/should not
0	Recommendation open	may/can

2.2.3. Statements

Apart from the recommendations, the guideline contains evidence- or consensus-based statements. Statements are statements or explanations of specific facts or questions without an immediate call to action. They are adopted in accordance with the procedure for recommendations within the framework of a formal consensus process. The

evidence-based statements are also assigned the modified evidence grading according to SIGN (see Section 2.3.1) described above.

2.2.4. Expert Consensus (EC)

Recommendations that were decided on the basis of expert consensus and not on the basis of a systematic search or guideline adaptation are shown as such with the graduation „EK“. Symbols to represent the strength of recommendation are not listed for expert consensus. The strength of the recommendation is implicitly derived from the wording in the sentence (should/should/could) according to the grading in the table "Grades of recommendation used" (see Section 2.3.2).

2.2.5. Independence and Management of Conflicts of Interest

German Cancer Aid provided the financial resources through the German Guideline Program in Oncology (GGPO). These funds were used for personnel costs, office supplies, literature procurement, and the consensus conferences (room rental, technology, catering, moderator fees, travel expenses of participants). The guideline was developed in editorial independence from the funding organization. All members provided a written declaration of any conflicts of interest during the guideline process. The disclosed conflicts of interest are listed in the guideline report accompanying this guideline. The conflict of interest declarations were reviewed and evaluated by a working group established for this purpose with the assistance of a patient representative. The results of this review are also available in the guideline report.

3. Concepts of Prevention

H. Bunde, E. Breitbart, I.-M. Hübner

The use of different terms, such as prophylaxis, prevention, precaution, and prevention, are in principle used for one and the same orientation, namely the avoidance of diseases or their progression. However, in our health care system they lead to different understandings according to their interpretation and use.

3.1. Conceptual Classification

Prevention is an umbrella term for measures aimed at reducing the occurrence and spread of diseases and the associated impact on morbidity and mortality in a society [1]. Prevention is directly related to a target disease and implies that it has specific causes that can be prevented by specific measures [2]. The main starting point is therefore the reduction or elimination of the causes of disease or the prevention of hazardous exposures [3].

The concept of prevention (originally disease prevention) developed in the 19th century from the debate on hygiene and public health.

One of the most commonly used terms, along with prevention, is “precaution.” This is an undefined legal term. It is not defined by law but can only be determined by interpretation. The term can be found in the coverage of daily needs (“Daseinsvorsorge": services of general economic interest provided by the state as “Gewährleistender"), financial security for old age (“Altersvorsorge,” § 33 SGB XII; contributions for a more equitable old-age provision, lifelong life annuity) and in insurance against the risks of illness as a safeguard in the event of illness. Precautionary expenditure is therefore the expenditure for insurance against future risks (insurance principle).

In the field of medical care, preventive measures are also often found under the term “Vorsorge.” In occupational medicine in particular, this term is enshrined in law in the Ordinance on Preventive Occupational Medicine (ArbMedVV). In the ArbMedVV, among other things, occupational medical preventive examinations are also used for cancer, as a paraphrase of various early cancer detection examinations.

The cancer screening programme introduced nationwide in 1971 was introduced at that time as “screening programme,” with the aim of bringing forward the time of diagnosis and the associated improvement in quality of life. The users often interpreted these preventive examinations in the sense of the above-mentioned insurance principle, so that the Federal Joint Committee (G-BA) has since then only spoken of prevention in its guidelines.

According to Rosenbrock and Michel (2007), the relevant goals of prevention include the avoidance, mitigation, or postponement of:

- Morbidity and mortality and the resulting losses in quality of life and restrictions in participation in social life.
- Direct medical costs of curation, rehabilitation, and social insurance.
- Indirect costs of illness due to reduced productivity, limited civic engagement, or welfare losses for society as a whole.

The prerequisite for the targeted prevention of a disease is knowledge of its pathogenetic dynamics, i.e. knowledge of the different stages of development and

progression of the disease process, both in terms of the population and at the individual level, taking risk profiles into account [3].

Service providers in the field of prevention, whether in the health care system or in kindergartens, schools, or other living environments of children and adolescents, at the workplace, and in other areas, should be aware of the fundamentals of preventive action. A prerequisite for this is the definition of the term “health.” Health is defined following the World Health Organisation (WHO) 1946 and Hurrelmann [4] (Hurrelmann, 2003, p3. in [4]), page 8, as a

“state of the objective and subjective condition of a person, which is given when this person is in the physical, psychological and social areas of their development in harmony with their own possibilities and goals and the given external living conditions."

TThis includes all health-relevant areas of life, such as education, work, housing, nutrition, transport, environment, family, leisure, etc., as they are also described in the Prevention Act. Health and illness are not to be understood as absolute and unchangeable stages, but as continuous and dynamic processes, in which the balance of risk and protective factors is reexamined at every point in life history ([4], p. 147).

It follows from this understanding of health that patients and users of the health care system are not to be classified as objects of health care, but rather that they are to be understood above all in their role as perceiving and acting subjects or as experts of themselves, whose individual life contexts and needs shape their health-related ideas and decisions.

This perspective requires a target group- and lifeworld-oriented approach from the actors involved in prevention work. In the personal preventive counselling situation particularly, this means identifying people's personal and social resources in discussion and jointly finding ways to adopt preventive behaviour in order to maintain health or minimise risk factors.

In this patient-centered approach, it is incumbent upon health professionals to establish a genuine appreciative encounter, taking into account medical-ethical principles (right to self-determination; do no harm; care, assistance; equality and justice ([Beauchamp, C. et al. 2019]),

in which neutral evidence-based and comprehensible information about prevention content and related information sources are conveyed.

Health promotion is often referred to in the context of prevention, especially in the primary prevention field. The term is historically younger than prevention and has developed with the health policy debates of the World Health Organization (WHO, Ottawa Charter) and under the influence of population and social science disciplines. The focus is on maintaining health by strengthening resources [5]. Health promotion aims to improve the individual's ability to cope with life and to promote the economic, cultural, social, and educational conditions for shaping life [3]. The prerequisite for this is knowledge of salutogenetic dynamics, i.e. the development and maintenance of health (as opposed to the avoidance of illness) at the individual level and in the collective [1].

Health promotion and disease prevention are complementary forms of intervention [6]. Both terms describe forms of interventions, i.e. targeted interventions or measures. However, they are based on different theoretical foundations and historical

contexts. The aim of interventions in both prevention and health promotion is to achieve health gains for both the individual and the population. This involves influencing process dynamics, i.e. future events. Differences exist in the forms of intervention and their principles of action [3]. Prevention follows an avoidance strategy based on the reduction of risk factors, whereas health promotion follows a promotion strategy, i.e. the strengthening of resources and protective factors [1]. Health promotion precedes prevention in time, whereby a clear separation of health-promoting and preventive measures is not always possible and a stronger integration of both forms of intervention is sometimes called for [1].

Depending on the initial situation, prevention measures can be classified along different dimensions. The various starting points, dimensions, and the classification within them are fluid and should be regarded as complementary.

3.2. Types of Prevention along the Course of the Disease

Prevention pursues staged goals, which can be differentiated into primordial, primary, secondary, and tertiary prevention along the developmental stages of a target disease.

Primordial Prevention

Primordial prevention begins even before primary prevention and is intended to prevent the development of social risk factors by influencing the healthy population with regard to living conditions and lifestyles in such a way that it is possible to maintain health [4].

Primary Prevention

Primary prevention targets healthy individuals or (sub)populations, or individuals without manifest symptoms [3]; [11]. It aims to prevent the recurrence of a (chronic) disease and to reduce the incidence of disease or accidents [12]; [11]. Different levels can be addressed, such as individuals, settings, or the population as a whole, and different starting points can be chosen, such as working towards the prevention or reduction of risk factors through individual behaviour or changing environmental factors that are causally involved in the development of disease.

Secondary Prevention

Secondary prevention aims at detecting the initial stage of a disease, the progression of which can be prevented or mitigated by diagnostic/therapeutic measures [3]; [11]. In terms of health policy, secondary prevention aims to reduce the incidence of manifest or advanced disease [6].

Temporally, secondary prevention starts even before symptoms or complaints appear. For this purpose, health checks, disease-specific early detection examinations or filter examinations (screenings) are carried out among defined population groups. The prerequisite is the clinically or epidemiologically proven additional benefit of early treatment (ibid.). In addition to early detection and early treatment, counselling on lifestyle changes can also be part of secondary prevention.

A key component of secondary prevention is screening. Screening includes recruiting apparently healthy participants, taking a medical history, and administering the

screening test for early detection of the condition in question. Usually, advice on risk factors and prevention can also be given in this context. According to Morrison (1993), screening divides participants into “individuals with a low probability of having the disease" and “individuals with a high probability of having the disease,” with the second group undergoing confirmatory diagnostics to confirm the diagnosis.

Tertiary Prevention

Tertiary prevention is aimed at people with a manifest disease or condition and aims to prevent or alleviate any resulting loss of function [11]. Appropriate diagnostic and therapeutic measures are intended to prevent complications and consequential damage and to prevent relapses [7]; [3]. The distinction between medical-therapeutic treatment and a tertiary preventive measure can rarely be drawn clearly. It is a question of the goal of the intervention whether an intervention is understood as curative or preventive [3]. In this context, both curative and preventive orientation of the intervention can be counseled to avoid continued disease-causing behaviours/risk factors, etc.

Quaternary Prevention

Quaternary prevention (first described by Jamoulle, 1968) is the avoidance of unnecessary medical intervention or the prevention of overmedicalisation, but can also mean the prevention of unnecessary prevention [8]. It is aimed at people who feel ill, but doctors would describe an overwhelming proportion of these complaints as symptoms that cannot be medically explained. In the “four-field table" model (Figure Figure 1), quaternary prevention is therefore placed at the point where a health disorder is present from the patient's point of view, but no disease is present from the doctor's point of view. Undoubtedly, the conscious and justified decision to forego further diagnostics and therapy is a difficult task for both sides. In this context, it is particularly important not to leave the patient alone with his or her illness, but to use communicative means in a trusting and appreciative atmosphere to find ways out of the illness together, based on the patient's personality or life history [9]; [10].

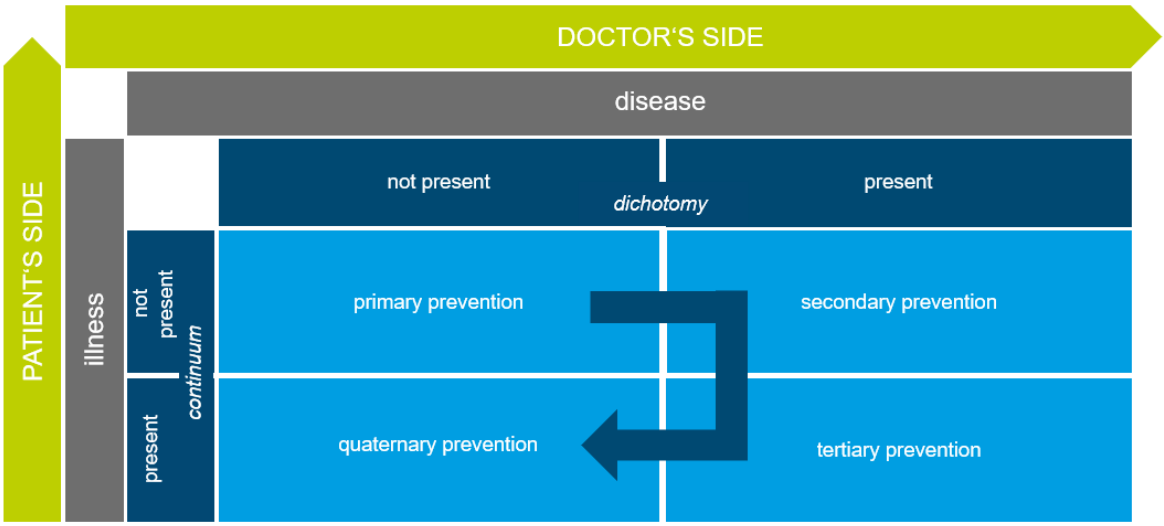

Figure 1: Four-field panel model of the different forms of prevention according to Kühnlein et al., 2010

The Choosing Wisely campaign, also adopted by the Association of the Scientific Medical Societies (AWMF) e.V., here under the motto: “Choosing Wisely Together,” is one way of implementing the requirements of quaternary prevention in the system. The “Choosing Wisely" campaign was launched in 2012 by the American Board of Internal Medicine (ABIM) Foundation and aims to avoid unnecessary medical services and to use existing healthcare resources responsibly. Thus, the campaign aims to reduce unnecessary services, i.e., overuse, through shared and evidence-based decisions by physicians and patients. To date, however, the effectiveness of Choosing Wisely campaigns has not been studied.

3.3. Forms of Prevention According to Context

In addition to forms of medical prevention (e.g. early detection measures, vaccinations), a distinction can be made between two other approaches to preventive measures that involve the context in different ways: behavioural prevention and situational prevention.

Behavioural Prevention

Behavioural prevention is concerned with influencing individual behaviour and consumption patterns in such a way that health risks are reduced [11]. This is done through education and information, but also by strengthening health literacy so that people are empowered and motivated to avoid or positively influence potential risk factors in their personal lifestyle (von Kardorff, 1995; Graf, Starke and Nellen, 2008). Behavioural prevention should be combined with relationship prevention interventions if it is to be popular and effective [12].

Relational Prevention

Relational prevention is used to influence people's living, working and environmental conditions, thereby improving the framework conditions for risk avoidance or health maintenance [11]. Although this influence tends to be indirect, it often has lasting effects [3]. Numerous measures of health protection are part of the prevention of social risks, such as consumer health protection or occupational health and safety in companies [11]. Urban development that takes account of the health needs of local residents, such as the provision of shaded areas, is also considered to be a form of preventive action.

3.4. Forms of Prevention According to Specification

Another focus is set according to the risk of disease or the degree of danger. Traditionally anchored primarily in the field of community psychiatry, addiction support and addiction prevention, the "triadic specificity model" is also gaining importance in prevention in general. A distinction is made between universal, selective, and indicated prevention.

Triadic Specificity Model

Universal prevention targets the entire population or large subpopulations with measures that are generally considered useful or necessary. Target group-specific or selective prevention is aimed at specific segments of the population with a suspected or above-average risk of disease, whereby selection can be based on various criteria such as socio-demographic characteristics, contextual characteristics or membership of a risk group [5]; [3]. The higher the disease risk of the affected group of people,

the more necessary the selective approach [5]. If the affected persons with whom a preventive measure is carried out already have the preliminary stage or early form of a disease, or if they have confirmed and individual risk factors of a disease, this is called targeted or indicated prevention [5]; [3]. It is sometimes difficult to distinguish between indicated prevention and curative measures.

3.5. Prevention by Level of Intervention

In the current debate on primary prevention, not only defined diseases but also the intervention area or context are increasingly coming into focus. The starting point for the choice of certain measures, especially primary prevention measures, is primarily the respective initial situation rather than a specific disease; this is also against the background that preventive strategies cannot always be assigned to a specific disease [13]. Three levels of intervention are distinguished: Individual, setting/lifeworld, and total population or large population groups. "Settings" refers to the spatial or social, everyday context of people, in which environmental, organisational, and personal resources (as well as other factors) act and thus influence health and well-being, e.g. schools, kindergartens, companies, old people's homes, and city districts [5]; [14]. As a second level, the contextual reference can be added, in which it is taken into account whether contexts are influenced by the measures and thus, among other things, a change in conditions occurs or whether these remain unconsidered. Thus, an intervention in a setting in which the living environment is used as access to the target group (e.g. for information) but is not itself changed (no contextual reference, behavioural prevention) can be distinguished from measures for the development of a health-promoting setting (contextual reference, relationship prevention), which are to be classified as higher in their sustainability. The goal of greater influence in settings forms the basis of the Prevention Act (PrävG §20 (1)), which was passed by the German Bundestag in June 2015.

3.6. Impact of Prevention on Health (Public Health Impact)

The implementation of prevention measures can be understood as the provision of prevention services to the population (or a subpopulation). Four elements can be distinguished (John et al. 2015):

- (Oncological) **target of** the intervention
- **Population** included
- **Performance of** the prevention
- **Outcome** (successful motivation and implementation of preventive behaviour)

In order to examine whether (and if so, what effect) prevention measures have on the population, five dimensions can be measured.

- **Reach**: the proportion of the target population reached by the intervention
- **Efficacy**: effectiveness of the intervention under the study conditions
- **Adoption:** implementation of the intervention by prevention actors
- **Implementation**: degree to which the intervention is implemented according to its original idea
- **Maintenance:** the maintenance of the intervention under routine conditions

Against this background, it is important to avoid ineffective and unnecessary measures. In order to achieve this goal, the Association of the Scientific Medical Societies (AWMF) has adopted the “Choosing Wisely" campaign, launched by the American Board of Internal Medicine (ABIM) Foundation in 2012, for the avoidance of unnecessary medical services and a more responsible use of existing resources in the health care system, under the motto “Choosing Wisely Together" (https://www.awmf.org/fileadmin/user_upload/Medizinische_Versorgung/GKE/Manual_GKE_AWMF_V1-1.pdf) [15].

3.7. Forms of Prevention at a Glance

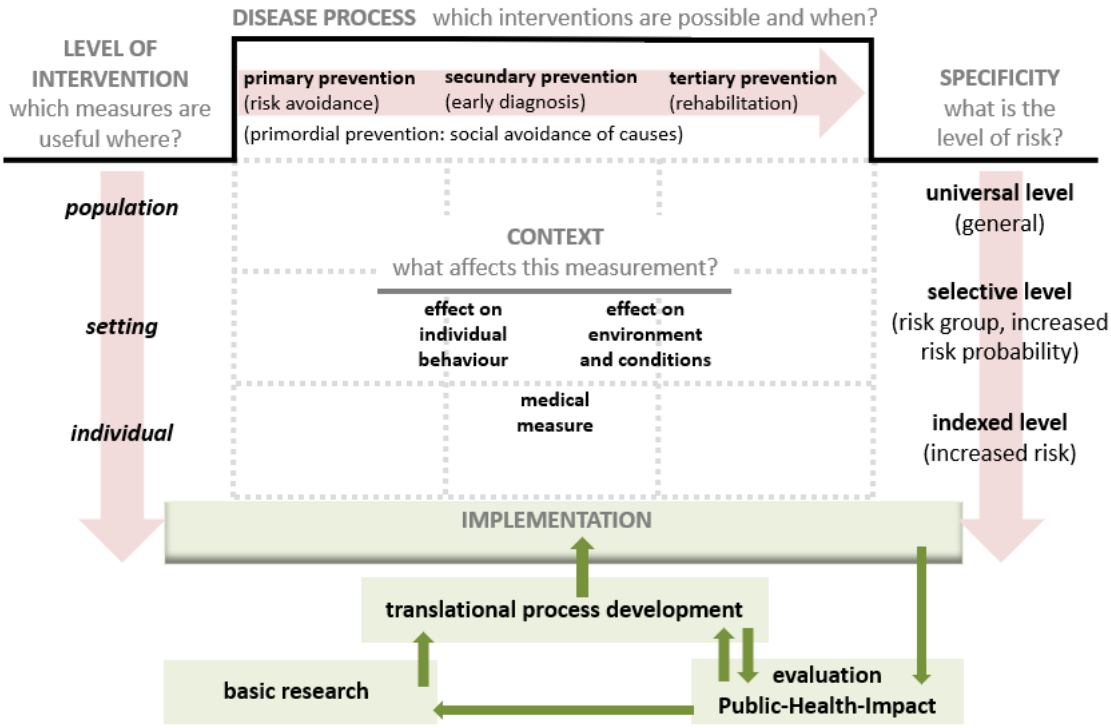

Figure 2: Prevention matrix: Different dimensions of prevention measures (ADP, 2020)

The figure "Prevention Matrix" summarizes the different dimensions of prevention. The planning of prevention measures can be oriented towards the course of the disease, the level of specification, or the level of intervention, or towards several of these dimensions simultaneously. In addition, a distinction can be made at all levels between medical behavioural prevention and relationship-based prevention (or a mixture of both). It is essential to pay attention to the effective implementation of and exchange with research results (translational process development) as well as the monitoring of the success of prevention measures (public health impact).

The concepts and approaches of prevention are shaped by their environment and are subject to constant change. In the field of primary prevention, for example, reference is often made to the historically more recent concept of health promotion, which is used in a sociological context and can be regarded as a complementary form of intervention. Health promotion follows a resource-oriented approach and aims to improve individual abilities to cope with life and to promote the economic, cultural, social, and educational conditions for shaping life [3].

3.8. Conclusion and Transfer to the Guideline

The terminological classification presented here and the concepts listed form the theoretical framework for the contents elaborated in the following chapters. The basic structure of the guideline is based on the different types of prevention and is oriented along the course of the disease. Within the individual chapters, the focus is on specification (see e.g. Chapter 5.1.2), contextualisation (see e.g. Chapter 5.4.4), and intervention levels. Living environments such as the professional setting (see Chapter 7) , the medical setting (see e.g. Chapters Chapter 5.4.2.3 and Chapter 8.4), and educational institutions (see e.g. Chapter 5.4) are given special emphasis. The same applies to vulnerable target groups such as persons at risk and children and adolescents (see e.g. Chapter 5.1).

In order to promote a stronger patient orientation in the health care system and to contribute to a higher health literacy of its users, the guideline contains recommendations for the promotion of doctor-patient communication in the context of skin cancer prevention counselling (see Chapter 5.4.2.3), early skin cancer detection, as well as information about the population and communicative strategies and communication channels in the field of primary and secondary prevention (see Chapter 8.3).

Furthermore, against the background of the definitions and concepts listed, guiding themes can be formulated which are continuously taken into account in this guideline and will be of high importance in the future. These include:

- Basic research
- Focusing on the effectiveness of prevention measures
- Prioritisation of measures/interventions with target group specificity, setting orientation, sustainability, and contextualisation
- Project development with target groups and improving communication with target groups to promote acceptance and uptake
- Promotion of health literacy through evidence-based information and training materials as well as the development of corresponding curricula, improvement of doctor-patient communication, and creation of health-competent organisations/relationships.
- Quality-driven promotion of digital transformation and new technologies.

This should sustainably increase the scope and quality of prevention research and practice and make a significant impact on health care. The boundaries between different disciplines are to be overcome, interfaces defined and used, and work carried out in an interdisciplinary and integrative manner with the involvement of a wide range of expertise. In this context, it is important to integrate all activities into the existing prevention landscape in Germany and to counteract the currently existing “patchwork" system by increasing networking and network formation.

4. Status Quo Skin Cancer

4.1. The Etiology of Skin Cancer

4.1.1. The Causes of Basal Cell Carcinoma, Squamous Cell Carcinoma, and Malignant Melanoma

Revision by R. Greinert, B. Volkmer

4.1	Consensus-based Statement	checked 2020
EC	On the basis of current knowledge, ultraviolet (UV) radiation is considered to be the most significant risk factor in the etiology of skin cancer, even if not all details of the induction, promotion and progression of skin cancer in humans have been elucidated.	
	Strong Consensus (100%)	

In 2009, the International Agency for Research on Cancer (IARC) classified solar and artificial ultraviolet radiation (UV radiation) used in tanning beds as a class 1 carcinogen (“carcinogenic to humans") [118]. This categorization was made without restriction to specific wavelength ranges (UVA, UVB) on the basis of the proven epidemiological and basic scientific evidence.

Fundamentals of the Biological Effects of UV Radiation

UV radiation covers the region of the electromagnetic spectrum that spans the wavelength range 100-400 nm. Historically, this wavelength range has been divided into UVC (100-200 nm), UVB (200-315 nm), and UVA radiation (315–400 nm) [96]. Solar UV radiation has a biological effect only through the UVB and UVA components, since UVC is absorbed by molecular oxygen in the Earth's stratosphere [96].

UV radiation can interact with a variety of cellular components (including membrane lipids, proteins, and intracellular photosensitive molecules such as flavins or porphyrins) [139], but mainly through the absorption of UV photons by nucleic acids [98].

UVB radiation can be absorbed directly by the DNA molecule. Photochemical processes then lead to dimerization reactions of adjacent pyrimidines on a DNA strand (cis-syn-cyclobutane pyrimidine dimers (CPD), or (6-4)-pyrimidone photoproducts ((6-4)-PP)) [100].

UVB and UVA radiation can further contribute to the formation of reactive oxygen species (ROS) via indirect reaction pathways in which the radiation energy is first absorbed by photosensitive molecules in the cell. ROS can then cause oxidative base damage, such as 8-oxo-7,8-dihydro-2‘-deoxyguanosine (8-oxo-dG) in DNA [101]; [100]. However, it has also been clear for some time that UVA radiation is also capable of producing CPDs in DNA [103]; [102]; [104]; [105].

DNA damage, such as CPDs and 8-oxo-dG, can be removed by efficient cellular repair systems (e.g. nucleotide excision repair (NER), base excision repair (BER)). If these repair pathways are defective or deficient (such as the NER in xeroderma pigmentosum

patients, who have a greatly increased risk of skin cancer), mutations may occur in the genome. In this context, CPDs mainly lead to C→T or CC→TT mutations known as “UV-signature mutations,” whereas UVA-induced oxidative base damage can lead to less significant G G-T “fingerprint" mutations. In general, two models of UV-induced mutagenesis are proposed to explain the major occurrence of C-T mutations in UV-irradiated cells. One reaction pathway involves a defective lesion bypass involving translhesion polymerases (polζ, polκ) [106]; [66]. In the other reaction pathway, deamination of (methylated) CPDs occurs first, which is then followed by a defect-free lesion bypass by polη [109] ; [110]; [107]; [108].

The study of mutation profiles in skin tumours, especially those occurring in XP patients, has, in the past, proven the importance of UV-induced bipyrimidine photoproducts and oxidative DNA damage in skin cancer development. In addition, genes have been identified whose UV-dependent mutations affect elementary cellular response pathways associated with the development and progression of basal cell carcinoma (BCC), squamous cell carcinoma (spinocellular carcinoma), and malignant melanoma (MM).

The relationship between UV radiation and the development of skin cancers has been demonstrated in many epidemiological studies, in animal experiments, and in a large number of basic experimental studies [98]. New studies in the field of sequencing human tumour genomes additionally prove the connection between UV-induced DNA damage and MM on the molecular genetic level. For example, Pleasance et al. (2010) showed that the mutations found in the sequencing of a melanoma metastasis genome belonged predominantly to UV signatures [111].

Basal Cell Carcinoma (BCC)

BCC is the most common skin cancer worldwide. It develops primarily on so-called “sun terraces,” such as the nose and forehead, among other places. For this reason, it was initially assumed that its occurrence depends on the cumulative UV dose. However, a number of BCCs that should not be underestimated also occur on “sun-protected" parts of the body, e.g. the upper body. Recently, it has been assumed that intermittent UV exposure, such as sunburns in childhood and adolescence, is also (partly) responsible for BCC, similar to MM [97]; [99]; [113], [115], [114]; [116]; [117]; [119].

Intensive worldwide research results now also point to a significant genetic determinant for the development of BCC. For example, it has been shown that patients suffering from naevoid basal cell carcinoma syndrome (NBCC), who often develop multiple BCC at an early age [120]; [121], frequently have losses of chromosome 9q. These findings led to the identification of the localization of a possible tumour suppressor gene in the 9q22-q32 region, the PTCH gene [122]; [124]; [123]. They also led to further characterization of the important Sonic-Hedgehog-Patched-Smoothened response pathway, which is reported to be disrupted in up to 100% of sporadic BCCs [125].

In the skin, a signaling cascade dependent on the Sonic Hedgehog (SHH) gene is implicated in hair follicle growth and morphogenesis. The protein product encoded by the PTCH gene, PATCHED1, serves as a cell surface receptor for the secreted signaling molecule SHH. In the absence of SHH, Patched1 inhibits Smoothened protein (SMO), a G-protein coupled receptor. Upon binding of SHH to PATCHED1, SMO is released and initiates a signal transduction cascade that causes activation of the transcription factor Gli. Dysregulation of the Hedgehog-Patched-Smoothened response pathway can result from loss of function of PTCH or increased expression of SMO, which lead to

increased levels of the transcription factor Gli and as a consequence induce BCC associated by inhibiting cell cycle arrest and differentiation [126] hair follicles [127]; [128]; [129]; [130]. In mouse models, disruption of the SHH-PTCH-SMO response pathway in hair follicle stem cells has been shown to be responsible for the development of BCC [131]; [132]. Mutations in PTCH or SMO have been found in the majority of all sporadic BCC [133]; [135]; [136]; [134]. Recent work has also reported the influence of WNT, NOTCH, mTOR, and Hippo, as well as the molecular response pathways involving these genes and altered miRNA expression profiles regulating [137].

UV-specific “signature mutations" (C→T, transition mutations) were found in the p53, PTCH and smoothened genes [127]; [138]; [142]; [141]; [140]; [143]; [144]; [145]; [146]; [136]. This finding must be taken as another important indication of the importance of UV exposure in the development of BCC. UV-induced p53 mutations in cells of the skin accumulate in “hot spots,” which differ from those in internal tumours. There is evidence that UV-specific mutations of the p53 gene may be specific for BCC [147].

A large body of recent work indicates that stem cells in the “bulge-region" of the hair follicle or interfollicular epidermal stem cells are important in the development of non-melanocytic skin cancers (NMSC, i.e., BCC, squamous cell carcinoma). Since stem cells and their differentiation or neoplastic transformation are essentially dependent on regulation by their microenvironment, intercellular communication and its signal-mediated response pathways are of great importance. In animal models and in vitro studies (also on human skin cells), the WNT, SHH, NOTCH and EGFR signal transduction pathways are particularly important in connection with BCC and squamous cell carcinoma (see review [148]).

In addition to the changes in the Hedgehog-Patched-Smoothened pathway described above, a striking feature of BCC genetics is that few numerical chromosomal aberrations can be detected in tumour cells [149]. However, BCC are characterized by marked intra-tumoural heterogeneity. In a cytogenetic analysis of 44 BCC, genetically unrelated subclones were found in 21 tumours and genetically related subclones in only 10 tumours [150]. The authors concluded that a large number of BCC are of multiclonal origin. They further demonstrated that a larger proportion of BCC were characterized by gain of chromosomes 18, X, 7, and 9, and that chromosomal losses frequently affected the distal regions of chromosomes 6q, 13q, 4q, 1q, 8q and 9p [150].

Squamous Cell Carcinoma (SCC)

SCC is the only skin cancer that has a known precursor: actinic keratosis (AK, also known as solar keratosis). AK represents a discrete, intraepidermal lesion that occurs on chronically sun (UV)-exposed areas, such as the face, scalp, lips, forearms, and hands, in fair-skinned middle-aged and older individuals. Cumulative UV exposure from the sun is considered to be the main reason for the occurrence of AK [151]; [152]. The incidence of AK therefore increases with age.

AK represents a precursor of squamous cell carcinoma [153]. In the literature, conversion probabilities, i.e. transition probabilities of AKs into invasive squamous cell carcinoma, can be found in a range from <1% up to 16% [155]; [156]; [157]; [158]. In individual cases, even up to 70% has been reported [159]. In a recent work by Criscione et al. (2009), which was prospectively designed and included more than 6,000 individuals with actinic keratosis, the transition probability AK to SCC is reported to be only 0.06%. However, six years after initial diagnosis of actinic keratosis, all occurring SCC were based on AK [160]. The presence of multiple actinic keratoses over a 10-

year period has been reported to have a lifetime risk of developing SCC in the range of 6-10% [155]. AK, as a feature of increased UV exposure, is an important risk factor for the development of SCC.

The risk of developing NMSC or MM is six times greater for patients with AK than for those without this lesion

[161]. However, the underlying mechanisms for this increased risk of skin cancer are currently not fully understood.

Neither is it sufficiently well understood for AK how high the transition probability from AK to SCC or other skin cancer entities is (see above) [163]; [162], nor do robust molecular biological or molecular genetic findings exist so far that could prove which genetic alterations might drive the transition AK to SCC [165]; [164]. However, evidence that appears to support that malignant progression of AK into SCC occurs [166]; [167]; [168] is interpreted by some dermatologists and dermato-histopathologists in such a way as to classify AK per se as squamous cell carcinoma confined to an epidermal extension (carcinoma in-situ) [169]; [170]; [154]; [167]; [171]. However, in a recent paper, Feldmann and Fleischer, after reviewing the data in the literature, conclude that “presently there is insufficient evidence to support the concept that AK is frank squamous cell carcinoma" [163].

However, recent work demonstrates that this view needs to be preceded. AK itself can be divided into three successive, histologically differentiable stages: AK I, AK II and AK III. It has been shown that the majority of SCC arises from AK I cells (proliferating atypical keratinocytes in the basal cell layer of the epidermis). However, the gradual emergence of SCC via AK I, AK II and AK III (“classical reaction pathway") is also still relevant for a substantial fraction of SCC [172]. In this regard, reference is also made to the S3 guideline Actinic keratosis and squamous cell carcinoma of the skin (https://www.leitlinienprogramm-onkologie.de/leitlinien/aktinische-keratose-und-plattenepithelkarzinom-der-haut/).

Due to this uncertain categorization, there is currently no reason to include AK in the group of skin cancer entities to be screened in skin cancer screening.

For the etiology of SCC, a relatively well-described model exists in which early-occurring UV-specific mutations in the p53 gene during the tumour initiation phase favor the development of a precursor of squamous cell carcinoma, AK. It is assumed that in AK initially only one allele of the p53 gene is mutated. This prevents the p53-dependent apoptosis of UV-damaged cells (so-called “sunburn cells") of some of the cells. Since at the same time “neighboring" cells show normal apoptosis, p53 mutated cells have a “selection advantage" and can expand clonally to AK. If the second p53 allele mutates in these cells during the tumour promotion phase, the p53-dependent cell cycle checkpoint function is switched off. Uncontrolled cell growth occurs and invasive squamous cell carcinomas are formed by induction of further (possibly UV-related) mutations in other genes (e.g. ras) during the tumour progression phase [173]; [174]; [175].

p53 mutations occur in 75-80% of patients with AK in the white population (30-40% in Japanese and Koreans) [176] and in more than 90% of patients with in situ squamous cell carcinoma (i.e., squamous cell carcinoma still growing noninvasively) [177]. For the latter and also for the p53 mutations in AK, it has been shown that they are mainly caused by UV-induced dimerizations of adjacent DNA pyrimidines and lead to C-T and CC-TT base substitutions (tandem mutations) [177], which are accepted as

“UV-signature-mutations" [178]. These mutations arise as a consequence of the misrepair/misreplication of UVB- and UVA-induced DNA damage, such as the cyclobutane-pyrimidine dimer and the pyrimidine(6-4)pyrimidone dimer [179]; [16]; [178]; [17]; [18]. This clearly supports the involvement of UV radiation in the etiology of squamous cell carcinoma. In the p53 gene, these mutations occur in specific “mutation hot-spots“ in the gene, located in regions where enzymatic repair of DNA damage by nucleotide excision repair (NER) is prevented or inhibited (“repair cold-spots“) [20]; [19].

A pioneering p53-dependent model for the development of SCC was established by studies in the hairless mouse and its variants in which the p53 DNA-binding domain (DBD) was replaced by the homologous human segment (Hupki mouse) [21]; [22]. UV-induced p53 mutations can be detected in this model by immuno-fluorescence detection of clonal “cell patches" (up to several thousand cells) in the epidermis. The origin of this clonal expansion of p53-mutated cells could be seen in the induction of single severely UV-damaged, non-apoptotic, persistent “CPD-retaining basal cells" (CRBCs), which have been detected in both mouse models and human epidermis [24]; [23]. CRBCs are likely interfollicular epidermal stem cells whose UV-induced damage is thought to be responsible for the development of squamous cell carcinoma [148]; [25]; [177]. Interfollicular epidermal stem cells, whose characterization and possible isolation is currently best described for the mouse epidermis, are characterized by the fact that they proliferate only rarely and therefore accumulate UV-derived DNA damage (“label-retaining cells,” such as CRBCs) [26]; [148]; [27]. Epidermal stem cells thus represent the “most suitable" target for the carcinogenic effects of UV radiation, as they can furthermore accumulate mutations due to their long residence time in the otherwise continuously renewing epidermis. This is consistent with early findings [28] and, with respect to skin cancer, new models for carcinogenesis [148]; [29]; [30].

Consistent with the dependence of squamous cell carcinoma on cumulative UV dose and the multistep nature of squamous cell carcinoma development (see above), squamous cell carcinoma, e.g. compared to BCC, exhibits much greater karyotypic complexity and cytogenetically documented heterogeneity. Nevertheless, some presumably squamous cell carcinoma-specific chromosomal aberrations could be detected in SCC. For example, loss of heterozygosity (LOH) of a “9q marker" was shown to occur frequently in SCC [32]; [31]. Moreover, LOHs in 3p, 13p, 17p, and 17q appear to be specific for SCC and its precursor, AK [33]. Using multiplex fluorescence in situ hybridization (m-FISH), it was further shown that complex chromosomal translocations are increased in cell lines derived from SCC [34], indicating a particular importance of genetic instability in the development of squamous cell carcinoma. In this context, it is important to point out that UVA radiation is able to induce DNA double-strand breaks via the induction of reactive oxygen species, which are known to be a necessary precursor lesion for the development of chromosomal aberrations [36]; [35]. Since 2015, multiple AKs (at least six individual AK lesions per year or confluent over an area of more than 4 cm² (field carcinogenization)) or a SCC are recognized as an occupational disease (OCD).

Malignant Melanoma (MM)

There is ample strong evidence that malignant melanoma (MM) occurs due to intermittent UV exposure and severe sunburns during childhood and adolescence [112]; [37]. MMs occur very frequently in fair-skinned individuals with red or blond hair (skin type I), who are prone to freckling, do not tan, and sunburn very easily (see Chapter 4.3). There is a link between the risk of developing MM and specific mutations in the

melanocortin-1 receptor [39]; [38]. This receptor is responsible for the type of melanin produced in melanocytes after UV exposure. It is hypothesized that individuals with such receptor mutations are unable to form the photoprotective eumelanin and instead produce the photosensitizing (and therefore potentially mutagenic) pheomelanin [40].

There is strong evidence that MM is autosomal dominant heritable, as 5-12% of affected patients have one or more first degree relatives who also have MM. In these individuals with familial melanoma, the cancer appears early. It is often accompanied by multiple other (skin) tumours [41]; [42]; [46]; [45]; [43]. Genetic analysis of families with high incidence of melanoma led to the identification of susceptibility genes such as the cyclin-dependent kinase inhibitor CDKN2A (p16INK4A) and the genes for the cyclin-dependent kinases CDK4 and CDK6. It has been shown that p16INK4A, genetically encoded on chromosome segment 9p21, is mutated in 25-40% of familial melanomas. It is now considered certain that this gene represents a predisposition gene for MM [47]; [48]; [49]. p16INK4A inhibits the progression of cells through the G1 phase of the cell cycle by suppressing the binding of cyclin D1 to CDK4/6. This is required for phosphorylation of the retinoblastoma protein, which controls the regulated transition of cells from G1 phase to replication (S phase). Mutations in the INK4A gene, which encodes the inhibitor CDKN2A (p16), abolish this regulation and lead to uncontrolled cell division. Furthermore, germ cell mutations and sporadic mutations in the tumour CDK4 gene have been shown to prevent the binding of p16INK4A to CDK4 and thus abrogate the inhibitory function of p16INK4A [50].

The INK4A locus also encodes a structurally and functionally distinct protein, p14ARF, which acts as another tumour suppressor [51]. p14ARF activates the p53 response pathway as a result of oncogene-mediated signaling (such as by c-Myc or ras oncogene) by binding to the p53 negative regulator Mdm2. This prevents the degradation of p53 and allows the induction of cell cycle arrest or apoptosis. Since p14ARF has been shown to be mutated in cells from MM [53]; [52] and isolated germ cell mutations have been found in patients with MM [54]; [55], p14ARF also represents a candidate predisposition gene of MM. Recent studies show that mutations in the BRAF gene may be of major importance in the development of MM [56]; [57]; [60]; [44]; [58]; [59].

In models of melanoma progression, benign nevi (moles) are thought to be a possible precursor stage of MM [63]; [61]; [62]. It is suggested that p16INK4A controls the growth of nevi and that they have arisen by clonal proliferation from melanocytes, which probably cease proliferation due to cellular senescence [65]; [64]; [67]. This growth inhibition can be abolished, for example, by ras mutations detected in some forms of nevi [69]; [68]; [71]; [70] . Mutations in the BRAF gene may also contribute to this [75]; [73]; [72]; [74]; [76]. This can lead to the formation of dysplastic nevi and subsequently to the radial growth phase of MM [77]. Deficiencies in p16INK4A and in the retinoblastoma gene (RB) are thought to be necessary in these cells for this to occur. In a next step, nodular melanomas develop in a vertical growth phase, penetrating deep into the dermis and already capable of metastasis [78]. Recent studies using, e.g. NGS, could show that, depending on the mutation status, three molecular subtypes of malignant melanoma can be distinguished: BRAF (mut), RAS (mut), and non BRAF (mut)/non RAS (mut) [79].

The number of UV-induced benign nevi acquired in early childhood (0-6 years) is a significant (if not the primary) risk factor for the formation of MM [37]. MM not only arise from nevi, but a large number arise de novo, i.e. nevus-independently [80], so

that the risk marker “number of benign nevi" must initially be regarded as no more than a significant indication of pigmentation disorders, which is then associated, in a way that has not yet been clarified, with an increase in risk for the development of MM. This suggests that different reaction pathways may be responsible for the formation of MM, even if UV radiation is causative for its initiation. For example, Maldonado et al. [81] demonstrated through an analysis of 115 patients with invasive MM that BRAF mutations occur far more frequently in melanomas arising on intermittently sun-exposed skin sites. They occurred very rarely in MM on chronically exposed skin sites. This suggests that different genetic alterations may be responsible for the formation of MM.

However, it is now accepted that 50–60% of all MM have BRAF mutations, 90% of which lead to valine glutamate mutations in codon 600 (BRAFV600). These BRAF mutations lead to kinase activation in the constitutive MAPK response pathway [82]. Thereby, phosphorylations of the tumour suppressor LKB1 (a serine/threonine protein kinase) lead to its negative regulation, thereby contributing to melanoma cell proliferation and attenuation of the apoptotic response to metabolic stress [83]; [84]; [85].

In contrast to SCC and BCC, UV-induced mutations in the p53 gene appear to be of secondary importance. Only about 20% of malignant melanomas have p53 mutations [86]. Evidence suggests that the involvement of p53 in the etiology of MM is complex [87] and needs further elucidation. It is possible that other mechanisms, such as the induction of genetic instability, play a more important role.

The etiology of MM is characterized by a high degree of UV-induced genomic instability, which increases as MM progresses to metastasis. Genomic instability manifests itself in the gain or loss of chromosomes (or chromosomal segments), the occurrence of chromosomal aberrations and LOH. Depending on the localization (eye or skin), two genetically distinct subtypes can be distinguished. Loss of chromosome 3 and 1p and gain of 8q are often observed in melanomas of the eye, while gain of 6p and loss of 6q appear to be specific to melanomas of the skin [88]. Studies using “Spectral Karyotyping" (SKY) on cell lines from melanoma metastases show that genomic instability at the chromosomal level in late stage melanoma metastasis can be so pronounced that almost every chromosome is involved in numerical or partially complex structural aberrations [89].

The gain of 7q associated with overexpression of c-MET (localized to 7q33-qter) appears to be a late event in melanoma progression. The tyrosine kinase receptor c-MET for hepatocyte growth factor (HGF) is found in both keratinocytes and melanocytes. Stimulation of the HGF-MET cascade not only supports cell proliferation and motility, but particularly disrupts the important adhesion between keratinocytes and melanocytes by down-regulating E-cadherin and desmoglein [90], thereby supporting melanoma progression.

LOH have been found in MM for a number of chromosomal loci: 1p, 3p, 3q, 6q, 9p, 9q, 11q, 17p, 17q, and 22q [91]. At these loci often map the localizations of tumour suppressor genes that play a particular role in the etiology of MM (e.g., 9p21 as the localization of CDKN2A). Moreover, LOH in chromosome 10q23 were found in 30% of metastatic melanomas [92] and in melanoma cell lines [93]. This LOH involves the PTEN phosphatase gene, another tumour suppressor gene that acts as a negative regulator of the phosphatidylinositol 3-kinase response pathway, which supports proliferation and cell survival [94].

A link between UV exposure and induction MM of the skin is always doubted, since malignant melanomas also occur on body sites that are usually not exposed to UV. However, if one takes a closer look at the literature on this subject, it turns out that in both men and women, only about 6% of all diagnosed melanomas occur in body regions (lower abdomen, buttocks, genito-anal, mucous membrane, occult) that typically have little UV exposure. In contrast, the vast majority of malignant melanomas (94%) localize to body regions that may be frequently or intermittently exposed to UV radiation, such as the face, head, neck, chest, back, upper arms, forearms, hands, thighs, lower legs, and feet [95].

However, the association between UV exposure and development of MM is strongly supported by recent studies. In 2010, Pleasance and co-workers catalogued for the first time the entire spectrum of somatic mutations in the whole genome of a melanoma metastasis [111]. They found that the majority (approximately 70%) of the single base substitutions detected were of the C-T type and approximately 70% of the dinucleotide substitutions were of the CC-TT type. Since it is known that these are “signature-mutations" for exposure to UV radiation, this finding represents important evidence for the connection between the development of MM and UV exposure.

4.1.2. The Clinical Course of BCC, SCC, and MM Considering the Histopathological Classification and TNM Classification (WHO Classification of Tumours)

E.W. Breitbart

4.1.2.1. The Basal Cell Carcinoma

BCC arises on clinically inconspicuous skin without a precursor. It is a slowly growing tumour, which is so discrete in its initial growth that it is hardly noticed. At this stage it is characterized by a grey-white induration of a few millimetres in size with a few telangiectasias. In most cases it is skin-coloured and grows slowly locally. The greatest danger with this tumour lies precisely in this slow unstoppable growth, which can grasp and destroy all local tissue structures. Metastasis is rarely described [180].

The BCC can occur on the whole integument, but it prefers in the frequency of its occurrence the areas exposed to UV radiation, such as the head, neck, forearms, and back of the hands. At a lower frequency, BCC can also be found on the upper body, arms and legs.

As it progresses, BCC develops a wide clinical range of variation.

Therefore, different appearance types are distinguished according to their growth and pigmentation development:

1. Nodular Basal Cell Carcinoma

Nodular BCC is the most common form of BCC. It usually develops in the UV-exposed areas of the head, neck, and nape of the neck and first appears as a small, sharply defined, dome-like, coarse consistency with a pearly cord-like border interspersed with telangiectasias. After a prolonged period of growth, a central depression develops, which is intermittently prone to hemorrhage, crusting, and oozing, and finally changes to a permanent slowly increasing ulceration.

In the absence of therapy and with progressive tumour growth, deep infiltrating tumours develop, destroying all tissue structures, historically known as ulcus rodens/ulcus terebrans.

2. Pigmented Basal Cell Carcinoma

Pigmented basal cell carcinoma is considered a variant of nodular basal cell carcinoma. The increased melanin deposition can lead to the fact that the classical criteria of the BCC, such as glassy surface with telangiectasia, as well as the pearl cord-like rim, can no longer be recognized. This may cause problems in the differential diagnosis between malignant melanoma and other pigmented changes, such as nevi, seborrheic warts, etc.

3. Superficial Basal Cell Carcinoma

Superficial basal cell carcinoma is also called trunk skin basal cell carcinoma because of its preferred location on the trunk. Because it clinically appears to occur multiply at one site, it is also often referred to as multicentric BCC.

Due to the fact that superficial BCCs differ from the other subtypes in both clinical and biologic behaviour, they are often misdiagnosed and confused with inflammatory dermatoses.

Clinically, they are sharply but irregularly circumscribed, reddish-brown, very flat changes that may resemble eczema on the skin. They may cause fine scaling, even itching, but may also crust over and show the typical pearly cord-like nodules in the marginal areas. They can become very large, but even very large tumours do not ulcerate.

4. Sclerodermiform Basal Cell Carcinoma

Sclerodermiform BCC is often overlooked because of its clinically discrete findings. This tumour is often recognizable only as a scar-like change that is slightly riddled with telangiectasias and feels gross on palpation. With further growth, it occasionally resembles a slightly raised scar. The particular problem of sclerodermiform BCC is that the often very delicate but extremely richly branched tumour cell clusters extend well beyond the border of the clinically recognizable central plaque, which is often somewhat raised and scarred with a yellowish appearance. This growth pattern is of particular importance in later therapy, as sclerodermiform BMCs tend to infiltrate even deeper anatomical structures very rapidly.

Histopathological Classification of Basal Cell Carcinomas

(according to WHO 2006 histological classification of keratinocytic skin tumours [181])

- Superficial BCC,
- Nodular BCC (solid, adenoid, and cystic),
- Micronodular BCC,
- Infiltrative BCC (non-sclerosing, sclerosing),
- Fibroepithelial BCC,
- BCC with adnexal differentiation (follicular, apocrine, eccrine),
- Basosquamous carcinoma,
- Keratotic BCC.

Mixed forms of these types are frequently found [182]. Collision tumors with squamous cell carcinoma are also possible.

4.1.2.2. The Squamous Cell Carcinoma

More than 90% of SCC develops on chronically UV-exposed skin such as the face, ears, lower lip, and back of the hand. It has a precursor, actinic keratosis (see Chapter 4.1.1).

The AK appears in most cases as a sharply limited, faint redness with a very fine, firmly adherent scaling (sandpaper phenomenon). Over the course of time, brownish yellow cornifications form which can be scraped off without any problems. These hyperkeratoses continue to form until they become firmly adherent, inducing a fine light pain when an attempt is made to scrape them off, and then change into a clinically clearly visible, firmly adherent, brownish yellow keratosis, the cornu cutaneum. At the base of this cornification, the SCC often forms as a nodule that rapidly increases in size as it progresses, may rupture in the center, and may then develop weeping tumours of varying sizes.

This invasive growth leads to metastasis after prolonged persistence, initially to regional lymph nodes and later to other organs.

Squamous cell carcinomas arise primarily on chronically UV-damaged skin, but may also develop on X-ray-damaged skin. The chemical carcinogens arsenic and tar lead to squamous cell carcinoma, as do human papillomaviruses (HPV) 16 and 18.

Histopathological Classification of Squamous Cell Carcinoma

(according to WHO 2006 histological classification of keratinocytic skin tumours [181])

- Acantholytic SCC,
- Spindle cell SCC,
- Verrucous SCC,
- Pseudovascular SCC,
- Adenosquamous SCC,
- M. Bowen.

TNM classification of carcinomas of the skin (PEK and BZK) according to UICC (2017) (excluding eyelid, head and neck, penis, vulva, and perianal region) ([183]).

Classification applies only to carcinomas, excluding Merkel cell carcinomas. Histologic diagnostic confirmation and subdivision of cases by histologic type are required.

Procedures for determining T, N, and M categories are:

- T categories: Clinical examination
- N categories: Clinical examination and imaging techniques
- M categories: Clinical examination and imaging procedures

Table 4: T category of skin cancer

T category of skin cancer (primary tumor)	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour 2cm or less in greatest extension
T2	Tumour > 2cm, but ≤ 4cm, in largest extension
T3	Tumour > 4cm in greatest extension *or* superficial bone invasion *or* perineural invasion *or* deep invasion*
T4a	Tumour with macroscopic bone invasion/ bone marrow invasion
T4b	Tumour with invasion of the axial skeleton including foramina and/or involvement of the vertebral foramen up to the epidural space
* A "deep invasion" is defined as invasion beyond the subcutaneous fat or >6mm (measured from the stratum granulosum of the adjacent epidermis to the base of the tumor). Perineural invasion as a criterion for T3 is defined as clinical or radiological involvement of named nerves without involvement of the foramina or skull base. In the case of multiple simultaneous tumors, the tumor with the highest T category is classified and the number of delineable tumors is indicated in parentheses, e.g. T2 (5).	

Table 5: N Category of skin cancer

N category of skin cancer (regional lymph nodes)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastases
N1	Metastasis(s) in a regional lymph node, 3cm or less in greatest extent
N2	Metastasis(s) in one lymph node, >3cm but not >6cm at greatest extent *or* in multiple lymph nodes, none >6cm at greatest extent
N3	Metastasis(s) in a lymph node, >6cm in greatest extent
Note: The regional lymph nodes correspond to the respective localization of the primary tumor.	

Table 6: M Category of skin cancer

M category of skin cancer (distant metastases)	
M0	No distant metastases present
M1	Distant metastases present
Note: Bilateral or contralateral lymph node metastases in non-melanoma carcinomas and not located in the head and neck skin are classified as distant metastases.	

Table 7: Clinical stages of skin cancer

Clinical stages	T category	N category	M category
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3 T1, T2, T3	N0 N1	M0 M0
Stage IV	T1, T2, T3 T4 Any T	N2, N3 Any N Any N	M0 M0 M1

4.1.2.3. Malignant Melanoma (MM)

Malignant melanomas often appear as brownish to reddish-bluish, blackish, greyish-white, often asymmetrical skin changes. However, they can also be completely pigment-free. MM occurs in a wide variety of clinical manifestations and can occur in all areas of the human skin, the hairy scalp, the mucous membranes of the eye, mouth, genitals, and also under the toenails and fingernails. In addition, in all organs of ectodermal origin, such as the meninges, bile, etc.

The different forms, the frequent asymmetry (which, however, does not necessarily have to be present), the discolourations, and the secondary changes such as oozing and crusting underline the extraordinary variety of this tumour in the clinical picture. Malignant melanoma has no defined precursor. The clinical diagnosis also requires many years of experience because of the extraordinarily high number of possible differential diagnoses.

According to their growth pattern, four main clinical types are distinguished:

- Lentigo Maligna Melanoma (LMM), which requires chronically UV-damaged skin as a prerequisite and for this reason also occurs in UV-damaged areas,
- Superficial Spreading Melanoma (SSM),

- Nodular Melanoma (NM), and
- Acrolentiginous Melanoma (ALM).

Depending on its vertical tumor growth, MM leads very rapidly to metastasis and is responsible for the highest mortality rate in skin cancer.

Histopathological Classification of Malignant Melanoma

(according to WHO 2006 histological classification of melanocytic tumours [181])

- Superficial spreading melanoma,
- Nodular melanoma,
- Lentigo-maligna melanoma,
- Acrolentiginous melanoma,
- Desmoplastic melanoma,
- Malignant blue nevus,
- Melanoma on large congenital nevus,
- Nevoid melanoma,
- Spitzoid melanoma,
- Persistent melanoma.

For malignant melanoma, a TNM classification and staging was proposed by the AJCC in 2018 (see the four tables below), which now underlies the classification of malignant melanoma.

Table 8: T category of primary tumor in malignant melanoma (2018).

T-stage	Tumor thickness	
T1	≤ 1.00 mm	a: ≤ 0.80 mm + Ø ulceration b: > 0.80 mm or ulceration
T2	1,01-2,00	a: without ulceration b: with ulceration
T3	2,01-4,00	a: without ulceration b: with ulceration
T4	> 4.00 mm	a: without ulceration b: with ulceration

Table 9: N category of regional lymph nodes in malignant melanoma (2018).

N category	Number of metastatically affected lymph nodes (LK)	Extent of lymph node metastasis
N1 or	1 LK intralymphatic without LK	a: only microscopic metastasis(s) (clinically occult) + b: only macroscopic metastasis(s) (clinically detectable) c: satellite/intransit without LK
N2 or	2-3 LK intralymphatic with LK	a: only microscopic nodal metastasis(es) + b: only macroscopic nodal metastasis(s) c: satellite(s) or in-transit metastasis(s) without regional lymph node metastases
N3 or or	> 3 LK LK packages ("matted") Intransit with > 1 lymph node	

Table 10: M category of distant metastases in malignant melanoma (2018).

M category	Type of distant metastasis	LDH
M1a	Metastases in skin, subcutis or lymph nodes beyond regional lymph nodes	Normal
M1b	Lung metastasis(s)	Normal
M1c	distant metastasis(s) of other localization or distant metastasis(s) of any site with elevated serum levels of lactate dehydrogenase (LDH)	Normal Elevated

The M1a category also includes the iliac lymph nodes. Source: WHO Classifications of Tumours, Pathology & Genetics, Skin Tumours

Table 11: Staging of malignant melanoma (2018).

Stage	Primary tumor(pT)	Regional lymph node metastases (N)	Distant metastases (M)
0	In situ tumours	None	None
IA	< 0.8 mm, no ulceration	None	None
IB	T1b: > 0.8 mm to 1.0 mm or all ≤ 1.0 mm + ulceration	None	None
	T2b: 1.01–2.0 mm, no ulceration	None	None
IIA	1.01–2.0 mm with ulceration	None	None
	2.01–4.0 mm, no ulceration	None	None
IIB	2.01–4.0 mm with ulceration	None	None
	> 4.0 mm, no ulceration	None	None
IIC	> 4.0 mm with ulceration	None	None

4.2. Incidence, Prevalence, and Mortality of Skin Cancer

Revision: A. Waldmann, A. Korthals, I.-M. Hübner

In principle, population-related statements on the frequency and burden of disease can be made on the basis of data from epidemiological cancer registries. A nationwide registration of all new cancer cases has been realized in Germany with a reporting obligation of the treating physicians and the pathological institutions, whereby there are federal states with a long tradition of registration (such as Hamburg, new federal states, Saarland) and those in which the cancer registries have only recently started to collect data nationwide (e.g. Baden-Württemberg (since 2011), Hesse (since 2007)). International experience shows that it takes several years before cancer registration is established and full data can be expected. It follows that regional differences exist in the informative value of cancer registry data. This applies to both national and internationally available data. The differences are due, among other things, to the different reporting regulations (compulsory reporting, right to report, nationwide coverage, coverage of model regions, coverage of primary tumours with/without coverage of metastases and recurrences), the different completeness of the reports, and, not least, the quality of the reports (e.g. proportion of missing values for information on tumour size).

For the epidemiological cancer registries in Germany, and also for most international cancer registries, it can be stated that the recording of MM can currently be classified as good (systematic, high completeness), while the recording of non-melanocytic skin tumours (BCC, SCC) is not systematic in all federal states. Since the epidemiological cancer registries are incidence registries, only newly occurring cases are registered. With the introduction of nationwide clinical cancer registries according to § 65c SGB V, progression events such as metastases and recurrences are now also registered, although exceptions apply to non-melanocytic skin cancers (for example, they are excluded from the flat rate payment and are therefore not registered). If the burden of disease is to be estimated via cancer registries, the problem arises in the case of the non-melanocytic skin cancers in which multiple metachromic tumours of the same histology or recurrences frequently occur (multiple BCC occur in about 15% of the patients, multiple SCC in about 10%; [184]), but are not registered. However, these represent a high burden for the affected patients and the health care system.

4.2	**Consensus-based Recommendation**	**new 2020**
EC	In the clinical cancer registries, basal cell carcinomas (including multiple basal cell carcinomas occurring in one person) and squamous cell carcinomas should be included in the registration.	
	Strong Consensus (100%)	

If this is not done, the goal of clinical cancer registration, i.e. to improve the care of people with cancer in Germany and (as far as possible) to record and evaluate all tumour diseases in Germany, cannot be fulfilled. It is also possible to initially limit this to model regions.

4.2.1. Malignant Melanoma

In Germany, population-based cancer registration is carried out at the level of the federal states. Based on these data, estimates of the incidence in Germany are published by the Society for Epidemiological Cancer Registries (GEKID) and the Centre for Cancer Registry Data (ZfKD) at the Robert Koch Institute (RKI). Currently, it is estimated that approximately 21,200 persons, of whom 51.4% are male, develop invasive MM in Germany each year (Table Table 9). MM is the fifth most common new cancer in men and women. The incidence of disease increases with age. Young women are more likely to develop MM than young men. This ratio and the rather high incidence at a young age compared to other tumour diseases are unusual. However, from the age of 60 years, the ratio reverses and the incidence in men increases to twice the incidence in women. The time course shows an almost continuous increase since the 1970s, a fivefold increase in incidence from about 5 to about 25 cases per 100,000 population. With the introduction of SCS in 2008, the incidence continues to rise, and more markedly than before [185].

Survival after MM has improved markedly over the past 20 years and is high compared with other cancers [186]; [188]; [187]. Currently, the five-year relative survival of all melanoma patients is estimated to be greater than 90% (Table 9 table) [186]; [185]; [187]. In contrast to the rising incidence, the age-standardized mortality rate has remained at a constantly low level over the last 30 years. Currently, about 3,070 people die of melanoma in Germany each year, of which 58.8% are men (table Table 9) [189]. One of the main reasons for the constantly low mortality despite increasing incidence is probably the improved early detection of prognostically favorable melanomas.

In 2013, it is estimated that there were approximately 96,600 individuals living in Germany who had developed MM in the previous five years. The 10-year prevalence is 162,700 persons, which is 1.7 times higher [188]; [187]. Due to the increasing incidence and comparatively constant mortality, it can be assumed that the 5-year and 10-year prevalence will increase in the future.

In an international comparison, Germany, together with the other European countries, the USA, and Australia, is one of the countries with the highest incidence of melanoma ([190]). Within Europe, Germany is in the top third of melanoma incidence and prevalence (see figure Figure 5) [191]; International Agency for Research on Cancer). The mortality rate in Germany, on the other hand, is lower than in most other European countries (see figure Figure 6) and lower than in the USA and Australia/New Zealand (International Agency for Research on Cancer).

Table 12: Current key figures for malignant melanoma in Germany

Key figures	Men	Women
Incidence 2014*		
New cases	10.910	10.310
Age-standardised rate (European standard) per 100,000	19,5	18,6
Mortality 2014**		

Key figures	Men	Women
Deaths	1.804	1.270
Age-standardized rate (European standard) per 100,000	2,9	1,7
Relative 5-year survival*		
Total	91 %	94 %
Relative 5-year survival stage-specific (2007-2013)***		
pT1	103,2 %	102,5 %
pT2	92,8 %	96,0 %
pT3	77,3 %	82,4 %
pT4	49,6 %	58,7 %
Prevalence*		
5 years	47.600	49.000
10 years	78.200	84.500
Data sources: * [185] [187] ** [189] *** [192]		

While an increase in incidence has been observed in Germany over the last 30 years, various studies have been published in journals over the last 15 years describing either a slight decrease or stabilization in incidence. In a global analysis of melanoma incidence, Erdmann et al. 2012 showed that incidence continues to rise in most European countries, while in Australia, New Zealand, the USA, and Canada, as well as Israel and Norway, there are signs of stabilisation. This can be explained primarily by falling or stable incidence in the 25-44 age group [193].

The gender-specific differences and the incidence and mortality trends over time in Germany largely reflect differences and trends found in other industrialised countries. A special feature is evident for Australia/New Zealand, where MM is the fourth most common new cancer and the ninth most common cause of cancer-related death [194]. Incidence has been increasing in recent years (males: increase by a factor of 2.3 from 28 cases (1982) to 63 cases per 100,000 population (2014; age standardised to Australian population); females: increase by a factor of 1.6 from 26 to 42 cases per 100,000) [194] with a levelling off of the increase in the last decade). For melanoma mortality, a comparatively small upward trend has been observed over the last 30 years [194]. Age differentiated shows a slight decrease in mortality for

persons < 60 years, stable rates for persons in the age group 55-79 years and an increase in melanoma mortality for persons 80 years and older until 2002 [196]; [195].

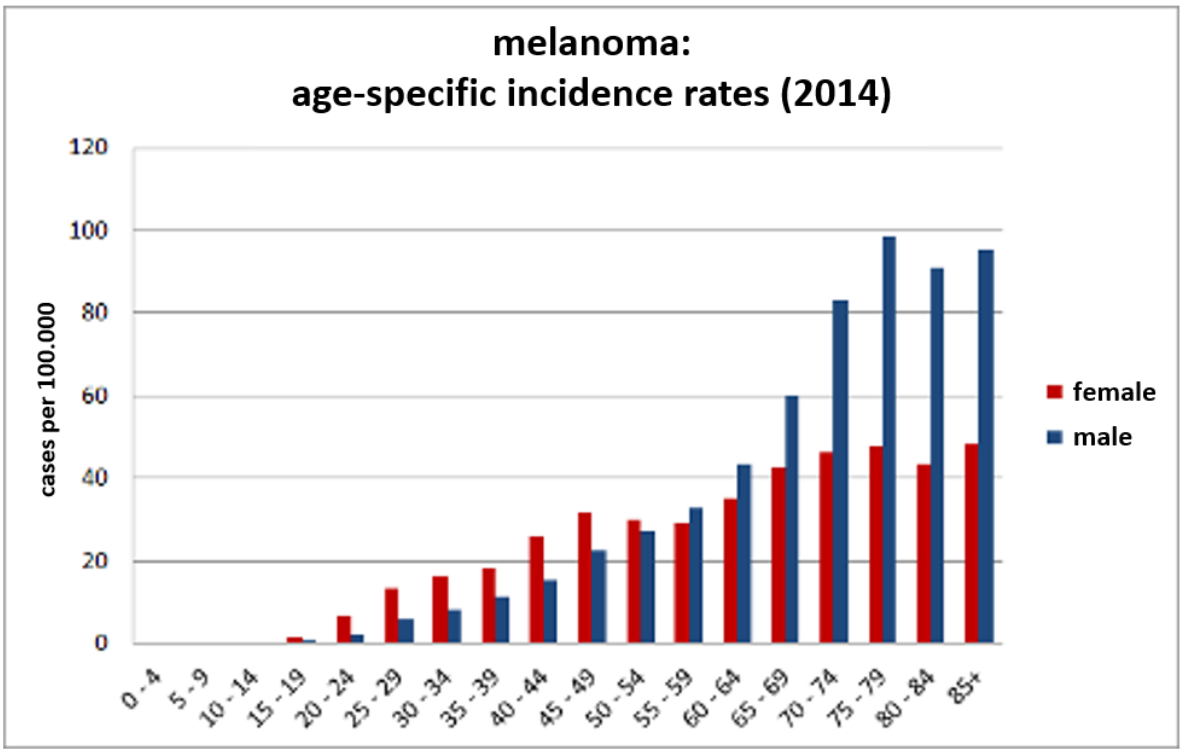

Figure 3: Age-specific melanoma incidence rates in 2014 differentiated by sex (Center for Cancer Registry Data at the Robert Koch Institute, 2019).

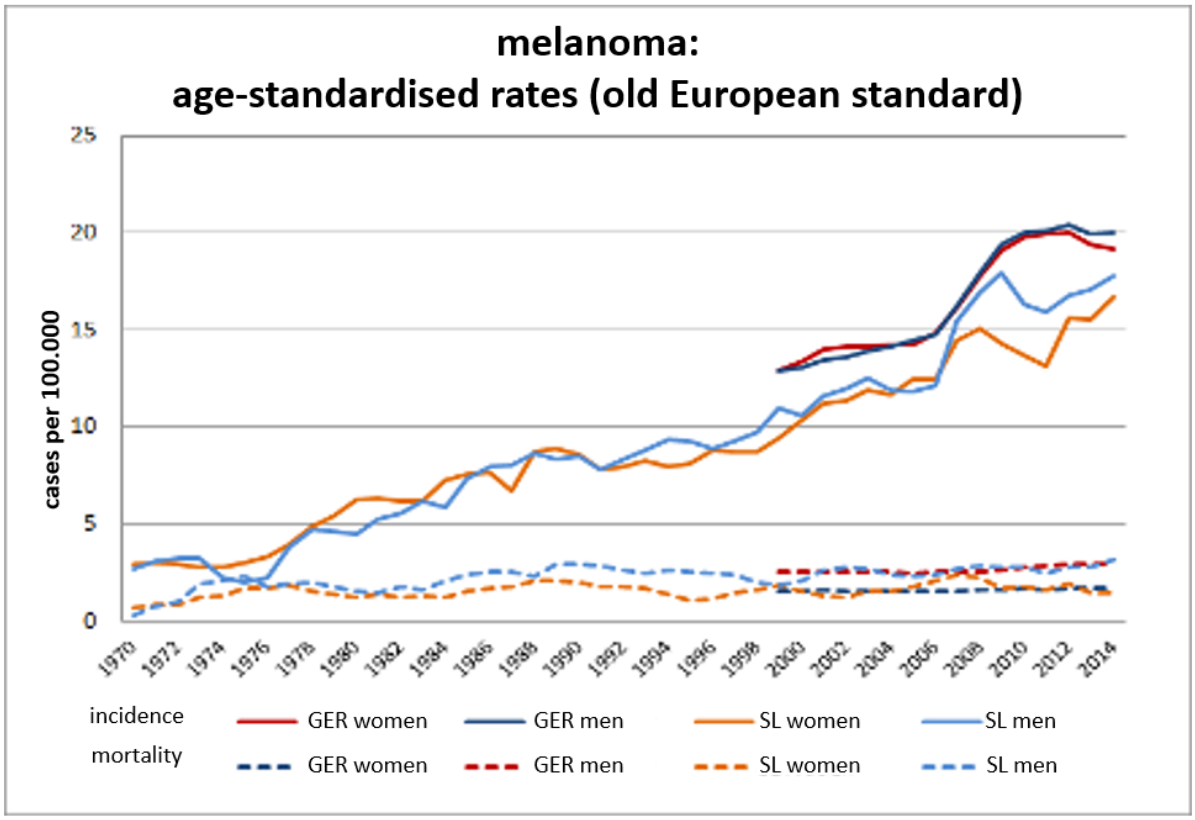

Figure 4: Time course of incidence rates in Saarland and Germany (smoothed; 3-years-floating means; old European standard; SL=Saarland, GER=Germany) (Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V., 2019; Saarland; Zentrum für Krebsregisterda

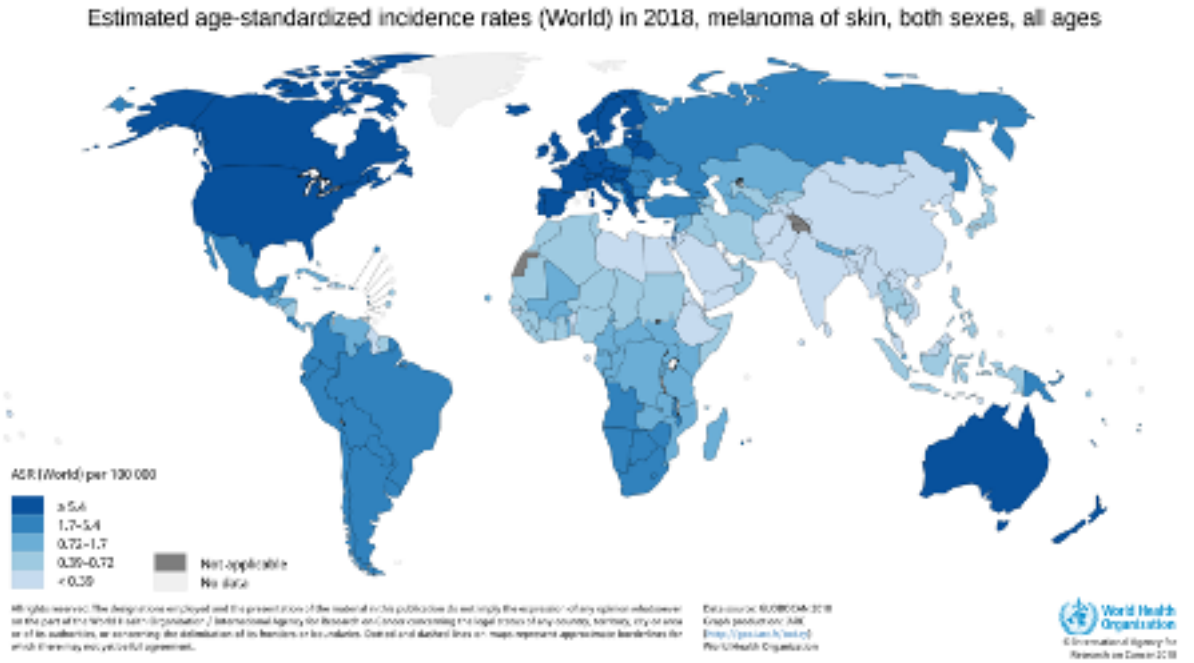

Figure 5: Age-standardized melanoma incidence in Europe in 2018 (world standard).

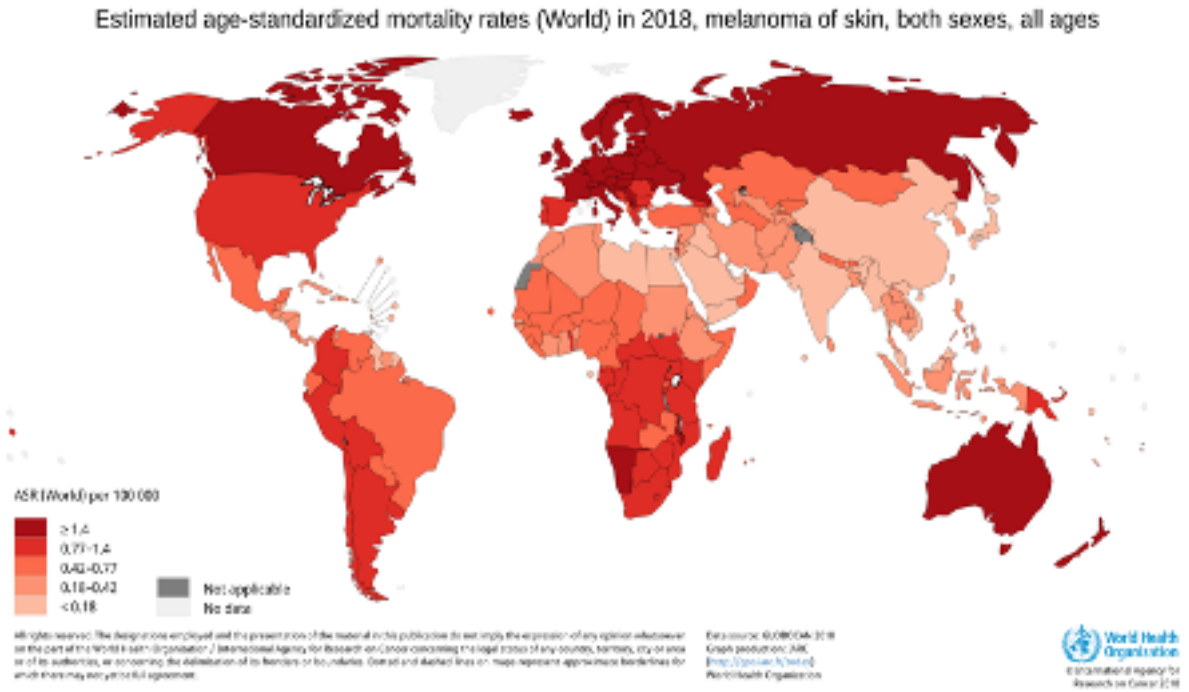

Figure 6: Age-standardized melanoma mortality in Europe in 2018 (world standard) (International Agency for Research on Cancer, 2010b).

Need for Research

A monitoring of the stage-specific incidences as well as the MM-mortality in Germany (and worldwide) could provide information on whether the early detection measure of the SCS by means of whole-body inspection in Germany leads to an increase of early stages and a decrease of late stages of melanoma and subsequently to a decrease of MM-mortality. To achieve this, it is necessary to reduce the currently high proportion of missing tumour stages among the cancer registry reports and, if possible, to register information on the tumour stage for all melanomas. Monitoring of melanoma mortality five to ten years after the introduction of the SCS could provide information on whether early detection will lead to a decrease in mortality. In a first analysis, Katalinic et al. were able to show that there was no decrease in mortality for Germany until 2013 (five years after the start of skin cancer screening), whereas such a decrease had been shown in the pilot region for skin cancer screening [198]; [197]. This difference is attributed to the different intensity or complexity of the screening program implemented [198].

The evaluation report on the SCS according to the cancer screening guideline of the G-BA from 2015 contains results on the number of participating physicians, the utilization by those entitled to benefits, as well as the incidence. However, it also impressively shows that questions regarding the benefit assessment of screening cannot be answered with the routine data [199].

It remains to be stated that the monitoring of mortality, incidence, and also of participation rates should be carried out regularly and that accompanying research seems to be absolutely necessary in order to be able to reliably assess the effectiveness of the screening and, if necessary, to make suggestions for optimising the screening programme.

Accompanying research has only been carried out in isolated cases so far. One example of this is the project to evaluate the nationwide SCS, which will be launched in 2019 and will use routine data from 2008 to 2016 to investigate, among other things, which group of people benefits most from the screening examinations [200].

4.2.2. Non-Melanocytic Skin Cancer (NMSC)

With about 137,700 registered new cases per year, non-melanocytic skin cancer occurs 6.5 times more frequently in Germany than malignant melanoma [185]; [187]. However, the actual number is probably significantly higher due to registration deficits [201]. Approximately 53.1% of all patients are men (table Table 10). In men, the level of estimated new cases is slightly higher than the incidence of prostate cancer (93/100,000 European Age Standardised Rate (EASR); 2014) [187], which is the most common tumour in men. The estimated incidence of NMSC in women is between that of the most common tumour (breast cancer; 114.6/100,000; EASR, 2014) and that of the tumour commonly cited as the second most common (colorectal cancer; 35.7/100,000; EASR; 2009) [187]. The incidence of the disease increases with age. In men aged 60 years or older, the incidence increases much more than in women. In the age group 85 years or older, the incidence in men is almost twice as high as in women (Figure Figure 7) [185]. Over time, the incidence has quadrupled (men) to quintupled (women) over the past 30 years. In contrast, mortality has remained at a constantly very low level over the last 30 years (Saarland; [187]). Currently, about 780 people die of NMSC in Germany each year; of these, 55.3% are men (Table Table 10) [189].

Table 13: Current key figures for non-melanocytic skin tumours in Germany

Key figures	Men	Women
Incidence 2014		
New cases	73.163	64.357
Age-standardized rate (European standard) per 100,000	113,2	85,1*
Mortality 2014**		
Deaths	435	351
Age-standardized rate (European standard) per 100,000	0,7	0,3
Data sources: * (Society of Epidemiological Cancer Registries in Germany e.V., 2014.) ** (Federal Statistical Office, 2012)		

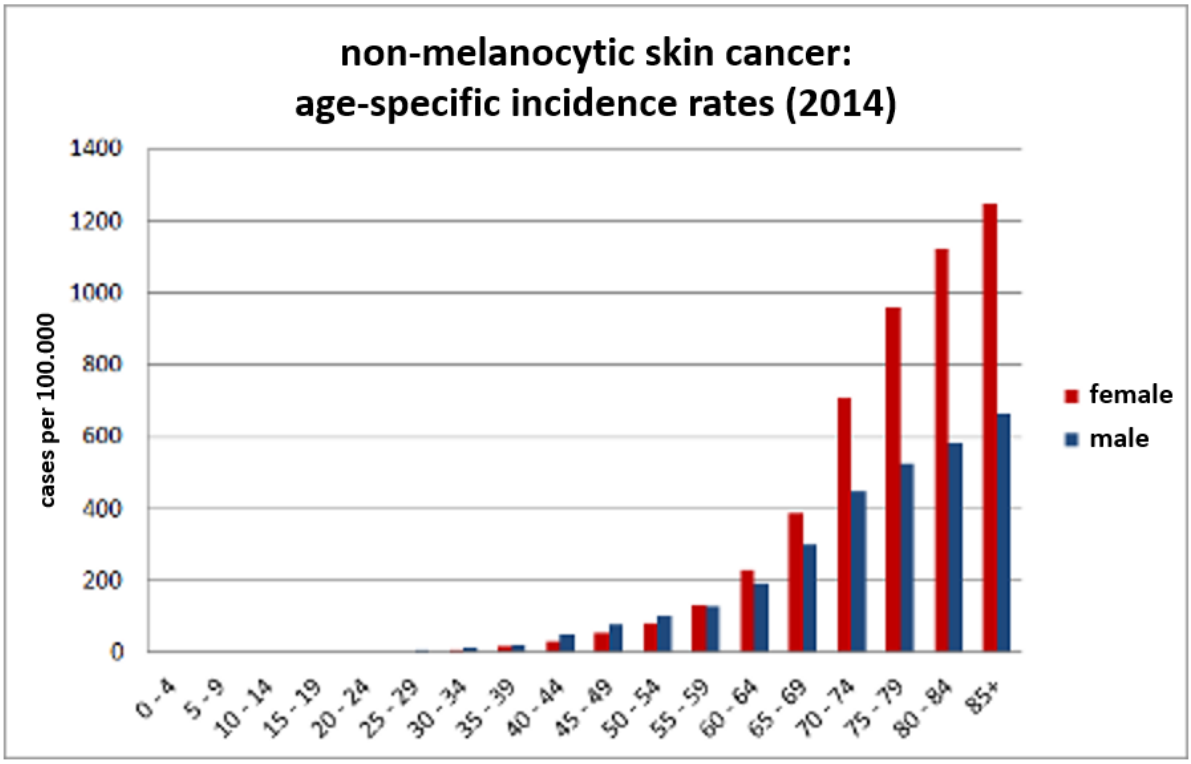

Figure 7: Age-specific incidence rates of non-melanocytic skin cancer in 2014 differentiated by sex (Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V., 2019).

In contrast to MM, the data situation for the non-melanocytic skin cancers is still to be regarded as incomplete. International comparative data on incidence and mortality are often available from studies or model regions and only rarely from epidemiological cancer registries. For New Hampshire, USA, an increase in the incidence of BCC from 1979/1980 to 1993/1994 of 235% in men and 350% in women and an increase in the incidence of SCC of 82% could be observed [184], also for younger Americans [Christenson, L. J. et al. 2005]. Canadian cancer registry data [202] as well as comparative data from Scotland [203] and Great Britain [204] also confirm the gender-specific differences and temporal incidence trends reported for Germany.

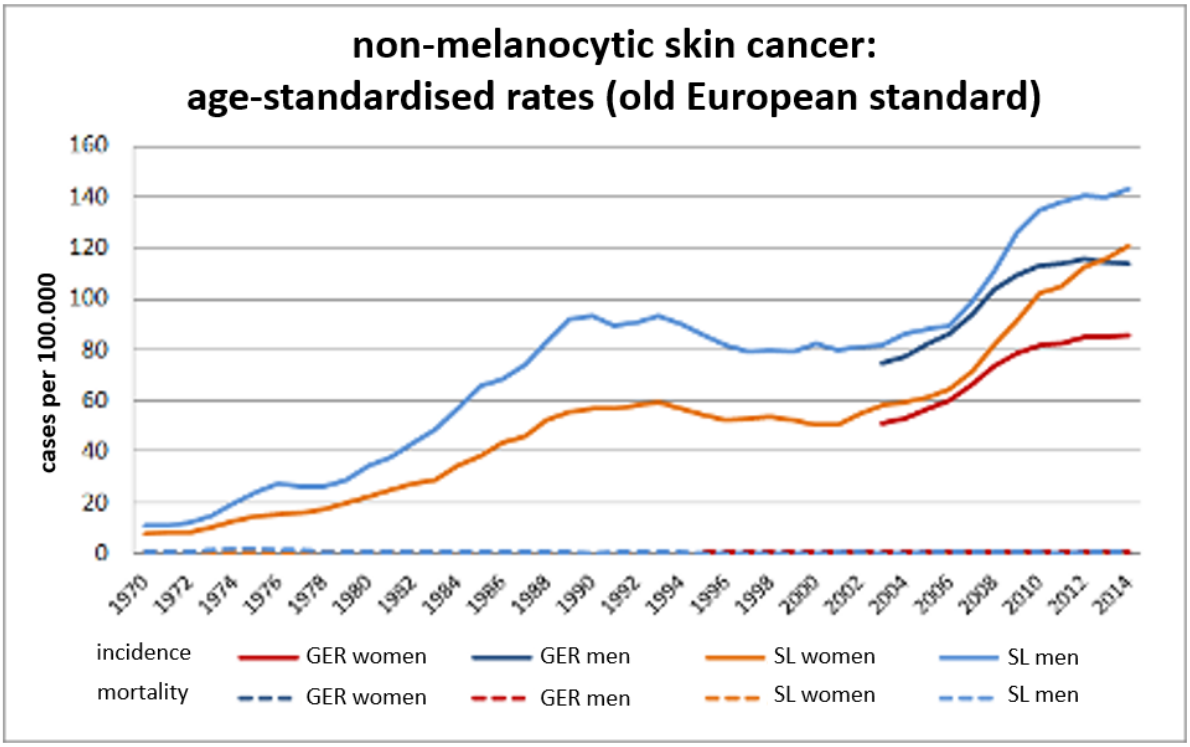

Figure 8: Time course of incidence rates in Saarland and Germany (smoothed; 3-years-floating means; old European standard; SL=Saarland, GER=Germany) (Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V., 2019; Saarland).

Need for Research

Compared to the data situation for melanoma, the data situation for the non-melanocytic skin cancers can be described as poor. In order to be able to reliably describe epidemiological trends in the future, a more stringent reporting of all incident non-melanocytic skin cancer types to the population-based cancer registries is required.

4.2.3. Effects of Skin Cancer Screening on Incidence and Mortality

Based on the data from the epidemiological cancer registries, temporal trends of new cancer cases can be described at the population level. A valid description of cancer incidence requires a high completeness of the registry, i.e. (as far as possible) all new cases of cancer are reported to the registry, as well as (as far as possible) complete information on tumour description such as histology, morphology and tumour spread. In the context of national health reporting, mostly only invasive new cases are described, whereas in the area-wide cancer registries according to § 65c SGB V, information on in situ tumours is also available. Thus, these cancer registries are able to describe not only the incidence of invasive but also that of in situ tumours.

In the period from 7/2003 to 6/2004, the SCREEN project was carried out in Schleswig-Holstein [205], hich was a model project for the skin cancer screening introduced throughout Germany in 2008. The effects of a SCS on the population-based incidence were investigated on the basis of data from the epidemiological cancer register of Schleswig-Holstein and Saarland (comparative region). Saarland served as the comparator region because no population-based SCS was conducted in this state during the SCREEN period.

The table Table 11" shows that in Schleswig-Holstein both the incidence of in situ and the incidence of invasive melanoma were significantly higher during the SCREEN period than in the period before the model project (1998-2000), whereas the incidence in Saarland increased only slightly over time. After the end of the model project (2005-2007), Schleswig-Holstein showed a slight decrease in the incidence of in situ melanoma and a significant decrease in the incidence of invasive melanoma, with only minor changes in Saarland during the same period [206].

Table 14: Age-standardized incidence rates of malignant melanoma

	Schleswig-Holstein (SH)		Saarland (SL)		p-value (comparison SH and SL)	
	Women	Men	Women	Men	Women	Men
	Incidence rate, age standardized (European standard)					
Before SCREEN Project (01/1998-12/2000)						
MM (in situ) (ICD-10 D03)	5.7 (5.0; 6.4)	3.7 (3.2; 4.3)	2.4 (1.8; 3.2)	1.0 (0.6; 1.6)	<0.001	<0.001
MM (invasive) (ICD-10 C43)	16.8 (15.7; 18.0)	15.2 (14.1; 16.4)	9.2 (7.8; 10.6)	10.7 (9.3; 12.4)	<0.001	<0.001
SCREEN Project (07/2003-06/2004)						
MM (in situ) (ICD-10 D03)	13.3 (11.5; 15.2)	7.7 (6.4; 9.2)	3.5 (2.1; 5.3)	3.1 (1.8; 4.8)	<0.001	<0.001
MM (invasive) (ICD-10 C43)	25.7 (23.2; 28.3)	19.2 (17.2; 21.5)	10.9 (8.4; 13.8)	11.8 (9.2; 14.9)	<0.001	0.003
After SCREEN Project before HKFP2 (01/2005-12/2007)						
MM (in situ) (ICD-10 D03)	10.4 (9.5; 11.4)	6.6 (5.9; 7.3)	4.0 (3.1; 5.0)	3.6 (2.8; 4.6)	<0.001	<0.001
MM (invasive) (ICD-10 C43)	15.1 (14.0; 16.2)	15.1 (14.1; 16.3)	12.2 (10.6; 13.9)	11.5 (10.0; 13.1)	0.044	0.002
	Absolute differences in incidence rates, age-standardised (European standard) [observed incidence – preceding incidence as described above].					
SCREEN Project						
MM (in situ) (ICD-10 D03)	7.6 (5.6; 9.6)	4.0 (2.5; 5.5)	1.1 (-0.5; 2.7)	2.1 (0.6; 3.6)	<0.001	0.164

	Schleswig-Holstein (SH)		Saarland (SL)		p-value (comparison SH and SL)	
MM (invasive) (ICD-10 C43)	8.9 (6.1; 11.7)	4.0 (1.6; 6.4)	1.7 (-1.3; 4.7)	1.1 (-2.0; 4.2)	0.005	0.373
After SCREEN/Before HKFP						
MM (in situ) (ICD-10 D03)	-2.9 (-5.0; -0.8)	-1.1 (-2.7; 0.5)	0.5 (-1.2; 2.2)	0.5 (-1.2; 2.2)	0.019	0.264
MM (invasive) (ICD-10 C43)	-10.6 (-13.3; -7.9)	-4.1 (-6.5; -1.7)	1.3 (-1.8; 4.4)	-0.3 (-3.4; 2.8)	<0.001	0.252

[1] Poisson based 95% confidence interval.

[2] Skin cancer screening program

In the figure {LINK_c092c7eac29b4bcc93b34a5476a556f3}" and the figure Figure 10" the data from Schleswig-Holstein are compared with the estimates for Germany. Here it becomes clear that especially for women in Schleswig-Holstein, changes in melanoma incidence can be described with the implemented screening measures (starting with the field phase of SCREEN 1999/2000, implementation of SCREEN 2003/2004 and implementation of population-based screening from 2008).

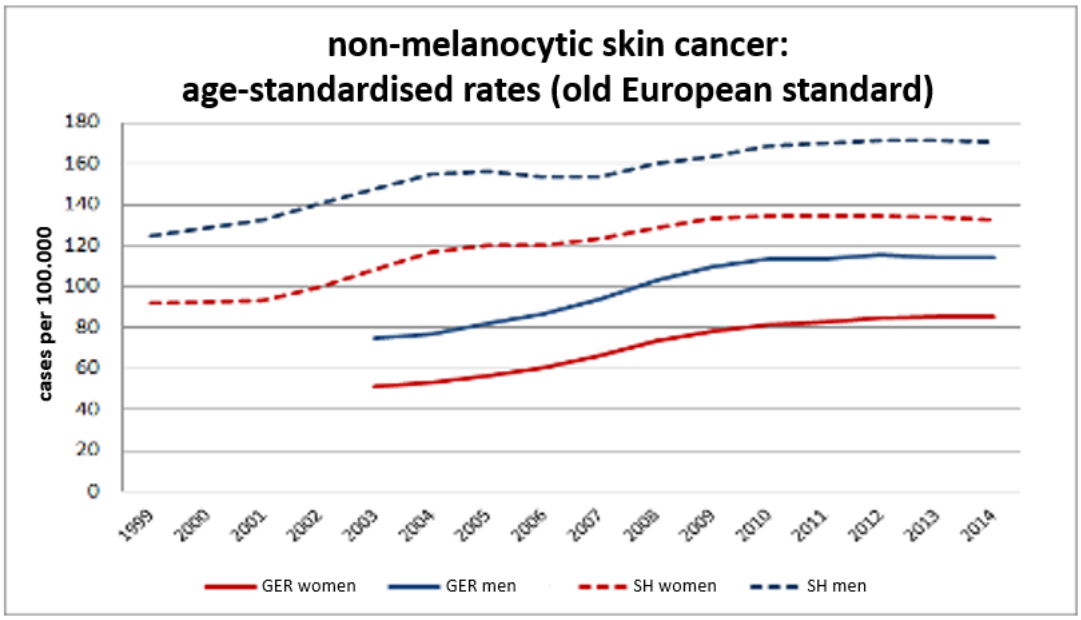

Figure 9: Time course of incidence (EASR; age standardized according to European standard) for non-melanotic skin tumors in Schleswig-Holstein (dashed line) and Germany (solid line; each floating means) (Gesellschaft der epidemiologischen Krebsregister in Deutsch

Brunssen et al. [192] summarized in a systematic review the influence of screening measures on skin cancer-related incidence and mortality. A total of 15 international articles (from the USA, Australia, Belgium, France, and Germany) could be included by the systematic searches. The included studies vary considerably in their population

due to different study designs (cohort studies, ecological studies, survey, case-control studies). As a result, the studies show an increase in incidence (in situ and invasive) after the start of screening (for melanoma: melanoma (in situ) from +1.6 per 100,000 (WASR) to +24.0 per 100,000 person-years (crude rate); for non-melanocytic skin cancer: from +16.5 per 100,000 (EASR) to +50.2 per 100,000 (EASR) and a decrease in melanoma incidence (invasive) as soon as screening is suspended again, to a level below the original level. There is also a stage shift with an increase in diagnoses to earlier stages and thinner melanomas (+0.3 per 100,000 (EARS) to +9.0 per 100,00 person-years (crude rate) and a decrease in thicker melanomas (e.g. melanoma >1.5mm = -9.8 per 100,00 person-years (crude rate)). Mortality analyses provide SCREEN (see above) with recorded melanoma mortality varying from -0.4 per 100,000 (crude rate) in persons up to 50 years of age to -3.7 per 100,000 (crude rate) in women over 70 years of age. Two other studies also reported fewer deaths than expected. However, the evidence of these results is limited due to the study design (mostly ecological studies).

Hübner et al. [207] also conducted an analysis of mortality rates in Germany for the years 1998 to 2017. As can be seen in Figure Figure 11, skin cancer-related mortality can be attributed primarily to melanoma and is significantly higher in men than in women.

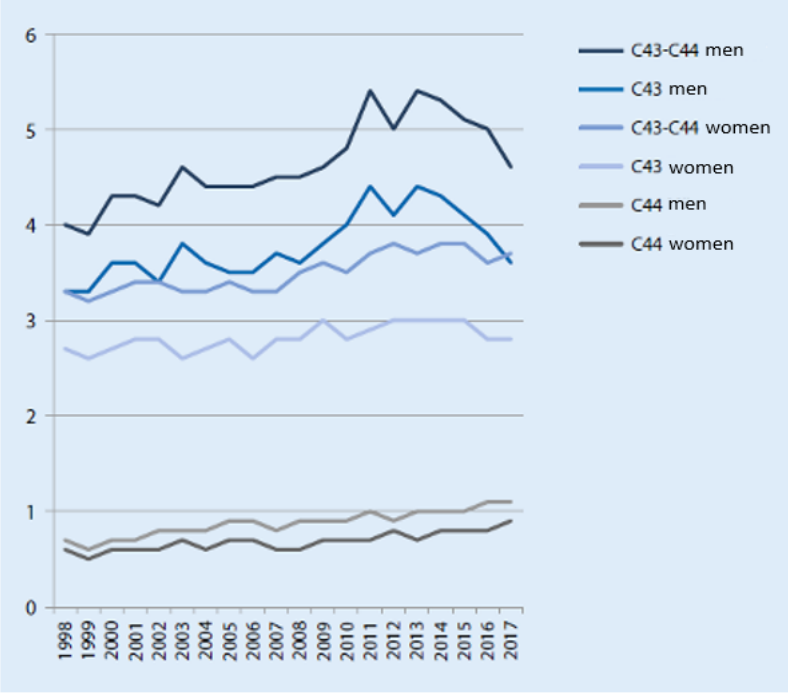

Figure 10: Age-standardized mortality (per 100,000 women or men) of melanocytic (ICD-10 C43) and nonmelanocytic (ICD-10 C44) skin cancer by sex (Hübner et al., 2019, p. 989)

However, with regard to the question of the screening-induced reduction in mortality, the reduction in mortality observed since 2013 (annual change in age-standardized mortality rate –2.1% (95% CI: –4.0 to –0.2%) vs. +3.4% (95% CI: 1.3 to 5.4%) before 2013) and the discussion of possible causes of this reduction should be noted in particular. Thus, it is suspected by the authors and plausibilized with the help of trend analyses that both new therapies and skin cancer screening may have influenced this change (see figure below).

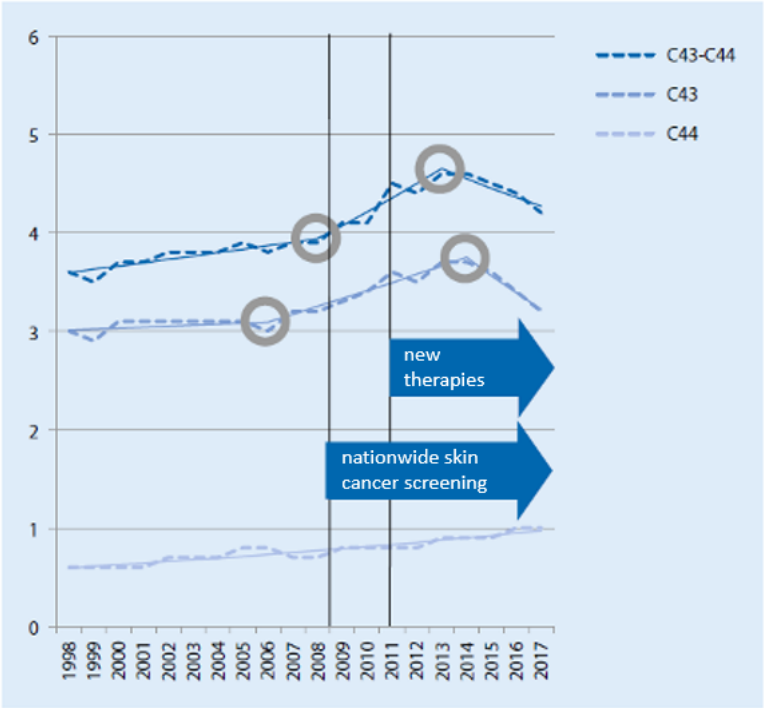

Figure 11: Age-standardized mortality (per 100,000 population) of melanocytic (ICD-10 C43) and non-melanocytic (ICD-10 C44) skin cancer for both sexes. Solid lines represent modeled trends in each case. Circles denote annual values in which these change. Vertical

4.3. Risk Factors of Skin Cancer

Revision: B. Volkmer, R. Greinert

4.3.1. The Constitutional Risk Factors (Phenotypic or Genotypic) of Skin Cancer

With regard to the risk factors for NMSC and for MM, a distinction must be made between constitutional, acquired, and exposure risk factors. Purely constitutional risk factors include skin type in the case of non-melanocytic skin cancers (BCC, SCC). In MM, it is the skin type and large congenital nevi.

4.3	Consensus-based Statement	modified 2020
EC	Constitutional risk factors: **Non-melanocytic skin cancer (NMSC).** An important constitutional risk factor for non-melanocytic skin cancer (basal cell carcinoma and squamous cell carcinoma) is: • **skin type.** Other risk factors (see 4.3.2, 4.3.4) can be acquired during the course of life.	
	Strong Consensus (100%)	

4.4	Consensus-based Statement	checked 2020
EC	Constitutional risk factors:**Malignant melanoma (MM)**The class of constitutional risk factors for MM includes**a) skin type andb) large congenital naevus.**Other risk factors (see sections 4.3.2, 4.3.4, and 5.1) can be acquired during the course of life.	
	Strong Consensus (100%)	

Non-Melanocytic Skin Cancer (NMSC)

From a large number of epidemiological, medical, and experimental studies, the most important constitutional risk factor for NMSCs can be identified as skin type. The risk of developing NMSC is higher for fair skin types (I, II) than for skin types III and IV (for skin types, see table Table 12 Types). Gallagher and coworkers report crude odds ratios (OR) of 5.1 (95% CI: 1.4-11.3) and 5.3 (95% CI: 1.7-10.6) for the occurrence of NMSC and ORs of 1.4 (95% CI: 0.5-3.0) and 2.2 (95% CI: 0.7-3.8) for the occurrence of PEC in two large studies [208]; [218] comparing skin types I and II with skin type IV.

Malignant Melanoma (MM)

a.) *Skin Type*

Skin type is an important constitutional risk factor for malignant melanoma. It has been shown that individuals with skin type I, II, or III are at significantly higher risk for MM than those who experience sunburn extremely rarely and already have very dark skin (skin type IV). Relative risks (RR) for skin type I, II and III (vs. skin type IV) have been reported in a meta-analysis with a RR of 2.09 (95% CI: 1.67-2.58), of 1.87 (95% CI: 1.43-2.36) and of 1.77 (95% CI: 1.23-2.56) [209].

b.) *Congenital Nevi*

According to the current international classification [212]

based on an expert consensus (EC), congenital, i.e. melanocytic nevi (CMN), already present at birth with a diameter of more than 20 cm up to 40 cm are designated as “large congenital nevi,” nevi above 40 cm as “giant nevi.” This classification is based on the maximum diameter of the nevus expected for adulthood.

Large congenital melanocytic nevi undoubtedly have a risk of malignant degeneration, which is particularly important in very large congenital nevi. Especially so-called “giant nevi" (> 40 cm in diameter) have an increased risk for the development of MM [210]; [211]; [213]. However, such nevi are extremely rare [214].

The risk of degeneration of congenital nevi correlates with size. On BMN up to 20 cm in diameter the development of melanoma has been described [215]

; however, the risk of degeneration is epidemiologically not demonstrably increased compared to “acquired,” non-congenital nevi. Especially until puberty, melanoma development on such BMN seems to be extremely rare. “Small" (up to 1.5 cm in diameter) and “medium-sized" CMN (1.5 to 20 cm) should therefore (like all nevi) be examined as part of the SCS and any changes recorded.

In contrast, “giant CMN,” which often show numerous so-called “satellite nevi" and in some cases a central nervous pigment cell proliferation, are a pathogenetically distinct entity based on NRAS mutations of the embryonic neural crest [216]. These BMN are associated with a significantly higher risk of developing cutaneous or even central nervous melanoma, starting in early childhood [210]. Typically, cutaneous melanomas arising on these nevi are a deep-seated, dermal, or subcutaneous nodule that can be palpated. These melanomas should be differentiated molecularly from so-called benign proliferative nodules [217].

Table 15: Skin types (Law on Protection against Non-Ionizing Radiation) ("Ordinance on Protection against Harmful Effects of Artificial Ultraviolet Radiation (UV Protection Ordinance - UVSV)," 2011).

Skin type	I	II	III	IV	V	VI
Description						
Natural skin colour:	very fair	light	light to light brown	light brown, olive	dark brown	dark brown to black
Freckles/sunburn spots (lentigines):	very frequent	frequently	rarely	none	none	none
Natural hair colour:	reddish to reddish-blond	blond to brown	dark-blond to brown	dark-brown	dark-brown to black	black
Eye color:	blue, grey	blue, green, grey, brown	grey, brown	brown to dark brown	dark-brown	dark-brown
Reaction to the sun						
Sunburn:	always and painful	almost always, painful	rarely to moderately	rarely	very rarely	extremely rare
Browning:	none	hardly to moderately	progressive	fast and deep	none	none
Erythema effective threshold irradiation:	200 Jm-2	250 Jm-2	350 Jm-2	450 Jm-2	800 Jm-2	> 1 000 Jm-2

4.3.2. The Acquired Risk Factors of Skin Cancer

4.5	Consensus-based Statement	checked 2020
EC	Acquired risk factors: **Non-melanocytic skin cancer (NMSC).**The main acquired risk factors for non-melanocytic skin cancer (basal cell carcinoma and squamous cell carcinoma) are:**a) actinic keratosis,b) previous history of NMSC,c) immunosuppression,d) chronic radiation keratoses.**	
	Strong Consensus (100%)	

4.6	Consensus-based Statement	checked 2020
EC	Acquired risk factors: **Malignant melanoma (MM)**The main acquired risk factors for malignant melanoma are:**a) previous history of melanoma,b) family history of melanoma,c) number of acquired naevi,d) clinically atypical naevi.**	
	Strong Consensus (100%)	

- **The probability of developing squamous cell carcinoma correlates with the UV dose to which a person has been exposed during his lifetime (cumulative dose).**
- **For basal cell carcinoma, both cumulative UV exposure and intermittent UV exposure and sunburns seem to be of importance.**
- **For malignant melanoma, intermittent UV exposures and sunburns (at any age) are of major importance.**

Age-stratified analysis of epidemiological data for skin cancer (BCC, SCC and MM) (see Section 4.2) show that incidence increases with age. In the broadest sense, therefore, ageing can also be regarded as an acquired risk factor.

Non-Melanocytic Skin Cancer (NMSC)

For BCC and SCC, risk factors that may be acquired through UV exposure or other exposures during life include:

a.) actinic keratosis,

b.) self-history non-melanocytic skin cancer,

c.) immunosuppression,

d.) x-ray combination damage.

a.) Actinic Keratosis (AK)

AK represents a precursor of SCC [153]. In the literature, conversion probabilities of AKs into invasive SCC are found in a range from < 1% up to 16% [155]; [156]; [157]. In individual cases, even up to 70% have been reported [159]. The presence of multiple AKs over a 10-year period has been reported to have a lifetime risk of developing SCC

in the range of 6-10% [144]. AK thus represents an important risk factor for NMSC, particularly SCC.

b.) Non-Melanocytic Skin Cancer (NMSC) in Self-History

Epidemiological studies show that individuals with NMSC or SCC in their own history have a significantly higher risk of developing non-melanocytic skin cancer again in later life [220]. The risk of developing a second SCC within five years of treatment of the first SCC is 30% [221]. TThe corresponding three-year risk is 18%, which is a 10-fold increased likelihood compared with the occurrence of a primary SCC in the general population. The three-year risk of developing a secondary BCC if the primary tumour was also a BCC is as high as 44%, which also corresponds to a 10-fold increased probability compared to the occurrence of primary BCC in the population [220]. The risk of developing a BCC in patients with a past SCC is approximately the same as that in individuals with a past BCC (approximately 40%). The risk of developing a SCC [222] as a second tumour if the initial tumour was a BCC is comparatively low (6%) [220]. Given these statistics, follow-up strategies (e.g. continuous risk group screening) are necessary for patients with SCC and BCC, since the presence of non-melanocytic tumours in the history represents a significant risk factor for the development of further non-melanocytic tumours.

c.) Immunosuppression

Organ transplant patients carry a significantly increased risk for the occurrence of non-melanocytic skin cancers, which is due to the use of immunosuppressive drugs [223]; [224]; [225]; [226]; [227]; [228]. SCC develops up to 65 times more frequently in transplant patients compared to controls [229]. Patients after heart transplantation seem to have the highest risk of developing SCC, followed by patients after kidney and liver transplantation [230]; [231]; [232]; [226]; [233]; [234]. The ratio of SCC to BCC after previous heart transplantation is approximately 3:1 to 4:1 in an Australian study, representing an inverse ratio to the incidence of SCC and BCC in the general population [235]. Compared to the normal population, SCC occurring in organ transplant recipients are more aggressive, metastasize more frequently, and result in approximately a tenfold increase in mortality (0.4-0.5/100,00 vs. 4.9/100,000) [Madeleine, M.M. et al. 2017].

Individuals with non-drug induced immunosuppression may also be at higher risk for non-melanocytic skin tumours. In general, HIV-infected individuals show a slightly increased incidence for SCC at younger ages compared to non-immunosuppressed individuals [236]. HIV-infected individuals with fair skin type and high UV exposure during leisure or gainful employment performed outdoors show an increased risk for SCC and BCC [237]; [238]; [239]. In addition, HIV patients appear to develop aggressive, fast-growing SCC associated with high risk of local recurrence and metastasis [236].

d.) X-Ray Combination Damage

Patients who have undergone radiation therapy with ionizing radiation (e.g. X-rays) are at risk of developing chronic radiation keratosis. This is a keratotic skin lesion that has been detected in radiotherapy patients or clinical staff who have been exposed to ionising radiation or worked with radioactive material for many years [240]. The X-ray combination damage is of importance given that BCC or SCC is more likely to develop. However, further findings show that exposure to therapeutic (ionizing) radiation is more likely to contribute to the formation of BCC and probably

not to that of SCC [241]. The risk of SCC on the grounds of X-ray combination damage increases with UV exposure of individuals who easily suffer sunburn (skin type I, II) [242].

Malignant Melanoma (MM)

Many of the risk factors for malignant melanoma mentioned in this chapter were examined in studies used for three systematic reviews including meta-analyses [243]; [244]; [209]. These included studies published between 1966 and 2002 on risk factors for MM. After analysis of approximately 600 original papers using various inclusion criteria (only case-control, cohort, or cross-sectional studies were included; ecological studies, case studies, reviews, and editorials were excluded), pooled relative risks could be calculated for the number of acquired and atypical nevi, family history, skin type, freckles, skin colour, eye colour, and hair colour (Table Relative Table 13).

For MM, risk factors that may be acquired through UV exposure or other exposures during life include:

(a) history of MM

(b) family history of MM

(c) number of acquired nevi

(d) clinically atypical pigmented moles.

- History of MM

The relative risk for a second melanoma after a MM in one's own history is high and is given as 8.5 [245]. This is approximately a factor of 4 higher than the relative risk of developing MM in the presence of MM in a 1st degree relative (RR = 2.2) [246]; [247]. Further studies show that approximately 3% of patients with MM are at high risk of developing MM again as a second primary tumor [248]; [250]. Standardized incidence ratios (compared to individuals who did not have a primary tumor) of 2-10 are reported [251]; [252]. Hübner et al. [278] give the risk of second melanoma in MM in the history based on data collected in the SCREEN project in Schleswig-Holstein with an odds ratio of 5.3 (95% CI: 3.6-7.6).

- MM in Family History

There is strong evidence that MM is autosomal dominant heritable, as 5-12% of affected patients have one or more first degree relatives who also have MM. In these individuals with familial predisposition, the cancer appears early. It is often accompanied by multiple other (skin) tumours [41]; [42]; [253]; [45]. These individuals are at particularly high risk of developing melanoma. The relative risk of melanoma development may be increased up to 500-fold if two first degree relatives are affected by MM and dysplastic nevus syndrome is also present. The lifetime risk of melanoma development is then higher than 50% [254]; [95]; [253]. Strong evidence for the importance of familial melanoma in the development of melanoma in individuals of the subsequent generation is also provided by studies on the aetiology of melanoma (see Section Chapter 4.1.1).

- Number of Acquired Nevi

A large number of studies demonstrate that the number of benign acquired nevi (nevus cell nevi, NCN) should be considered the quantitatively significant risk factor for

melanoma development [255]; [259]; [256]; [260], [261]; [262]; [249]; [263]; [257]; [258]; [264]; [265].

Risk estimates reported in these studies range from 1.3-30. Twin studies show that nevus number is genetically controlled [266]; [267] and that it depends on constitutive factors such as skin type, hair color, and tendency to freckle [268]; [270]. A clear association has been demonstrated between severe sunburns (intermittent UV exposure) in childhood and the number of acquired benign nevi [37]; [269]; [260], [261]; [271]; [272]; [273]. Recent studies show that the predisposition to UV-induced formation of melanocytic nevi is particularly important in early childhood (0-6 years) [219] and, in the case of certain genetic predisposition, can already be caused by suberythemal UV exposure [274].

The listed studies prove the close connection between UV exposure and the development of melanocytic nevi, which are regarded as a decisive risk factor for the development of MM.

- Clinically Atypical Pigmented Moles (Nevi)

Clinically atypical (dysplastic) pigmentary moles (nevus cell nevi) can occur all over the body. They are defined by their fuzzy and irregular borders and often variable colour components. The association between the presence of atypical nevi as risk markers for the development of MM has been widely documented.

In German-speaking countries, a multicenter study in 1994 described atypical melanocytic nevi as the second most important risk indicator for melanoma development next to the number of common melanocytic nevi. According to this study, the presence of few (1-4) atypical nevi is associated with a 1.6-fold increase in risk (compared to individuals without atypical nevi). When five or more atypical melanocytic nevi are detected, there is a significant 6-fold increase in risk for melanoma development. This finding has been interpreted to mean that at least five of these pigmentary moles must be present to identify at-risk individuals [260], [261]. However, Grob and coworkers [275] found that the presence of even one atypical pigmentary mole increased the relative risk for melanoma development three-fold. A relative risk of 3.8 was calculated for 1-5 atypical nevi, a value of 6.3 in the presence of six or more atypical nevi [276].

Approximately 40% of patients with sporadic MM (especially of the superficial spreading type) have atypical nevi, in contrast to 10-15% prevalence in the rest of the population [277].

Table 16: Relative risks for malignant melanoma (MM)

Risk factor	Reference	Relative risk (95 % CI)
Number of acquired nevi	101-120 vs. < 15	6,89 (4,63-10,25)
Number of atypical nevi	5 vs. 0	6,36 (3,80-10,33)
Melanoma in family history	yes vs. no	1,74 (1,41-2,14)
Skin type I	I vs. IV	2,09 (1,67-2,58)

Risk factor	Reference	Relative risk (95 % CI)
Many freckles	high density vs. low density	2,10 (1,80-2,45)
Skin colour	light vs. dark	2,06 (1,68-2,52)
Eye colour	blue vs. dark	1,47 (2,80-2,55)
Hair colour	red vs. dark	2,02 (1,24-3,29)
Precancerous lesions and skin cancer lesions*		4,28 (2,8-6,55)
Actinic damage**		2,02 (1,24-3,29)
* actinic keratosis, PEK, BZK ** solar lentigines, elastosis		
Source: [243]; [244]; [209]		

4.3.3. UV Exposure as a Risk Factor

Data on the incidence of skin cancer as a function of latitude in Germany are not available. However, it will be difficult to prove clear causalities in the occurrence of any correlations between latitude-dependent UV exposure and the incidence of skin cancer, since the induction of cellular UV damage that can lead to skin cancer can also occur independently of geographical point of residence (e.g. during holidays, behaviour).

Furthermore, the form of the dose-response relationship for UV-induced skin cancers has not been sufficiently clarified. Only future research can reveal whether a threshold value or a linear dose-response relationship without a threshold value exists for the occurrence of certain skin diseases. This also applies to the possibility of quantitative information on the risk increase per dose (risk coefficients).

Non-Melanocytic Skin Cancers (NMSC)

In NMSC, UV exposure from natural or artificial radiation is the most important factor in disease development [112]; [174]; [280]. The fact that SCC and BCC usually develop on chronically UV-damaged skin or on body parts that are constantly exposed to light makes this connection clear. While the likelihood of developing SCC correlates with increasing lifetime acquired UV dose (cumulative dose) and occupational exposure [112]; [279]; [281], the UV dose-response relationship for BCC has not been fully elucidated. In addition to intermittent exposure [112]; [279], recent studies show that cumulative UV exposure, especially occupational, also plays a significant role [282]; [284]. Sunburns may also be responsible for BCC and possibly SCC [112].

Malignant Melanoma (MM)

Although the form of the dose-response relationship is largely unknown, as early as 1991 the "Consensus Development Conference on Sunlight, Ultraviolet Radiation, and the Skin" stated that the only established reason for the occurrence of melanoma--in the white population--was UV exposure from the sun [283]. The International Agency for Research on Cancer (IARC) also considered sun exposure to be the main cause of MM in humans as far back as 1992 (and again in 2012) [98].

However, other issues have arisen since then, mainly concerning the role of UV exposure patterns in the development of MM. In this regard, the literature distinguishes intermittent, chronic, and total UV sun exposure as well as sunburn. However, it is often difficult, especially retrospectively, to distinguish between these exposure patterns when reconstructing the "UV history" of individuals. Thus, it is difficult to separate interactions between sunburns, general sun exposure behaviour, individual tanning ability, and other phenotypic factors (eye colour, hair colour, skin type, etc.). UV radiation can act as an initiator, for example, through sunburn or intermittent exposure, but also as a promoter through subsequent chronic exposure [285]; [98]; [257]; [286]. Recent meta-analyses have shown that the number of acquired, UV-induced nevi is closely associated with melanoma risk and that their number is greater in individuals with high UV exposure [37]; [243]. Acquired UV-induced nevi thus occupy a central role in the causal chain between UV exposure and the development of MM

Gandini et al. [244] give in a meta-analysis (pooled) relative risks (RR) for different UV exposure patterns and their association with MM (Table Table 14).

Table 17: Influence of the UV exposure pattern on the relative risk for melanoma development

UV exposure pattern	RR for association with MM (95% CI)
Total (intermittent + chronic + sunburn)	1,34 (1,02-1,77)
Intermittent	1,61 (1,31-1,99)
Chronic	0,95 (0,87-1,04)
Sunburn	2,03 (1,73-2,37)
Source: [244]	

Because the control groups in the individual studies were different, the control group with the lowest possible exposure was used to calculate the pooled RR in the meta-analysis.

Differences in the determination of risk estimators (e.g. odds ratio, rate ratio, risk ratio) between the analysed studies were ignored and each risk estimator for an association was transformed into logRR and associated variance according to a procedure from Greenland [287]. Four hundred thirty-eight studies (up to 2002) were found in the literature search, 87 of which appeared potentially suitable for meta-analysis and 57 eventually met the authors' inclusion criteria ([244]). The meta-analysis included 38,671 cases distributed among 32 studies in Europe, 19 in North America, two in Australia, and one each in New Zealand, Argentina, Brazil, and Israel. Fifty case-control studies, five cohort studies, and two embedded ("nested") case-control studies were included.

Despite the lack of well-designed cohort studies as well as systematically recorded UV exposures in case-control studies, and given the difficulties in retrospective surveys of UV exposure (recall bias) and in recruiting representative control groups, Gandini et al. [244] conclude in their meta-analysis that the vast majority of data support the importance of intermittent sun (UV) exposures for melanoma development. Particularly irregular and intense exposures (such as sunburns) significantly increase the risk of melanoma (Table Table 14).

However, the table "Influence Table 14 also shows that a more regular (chronic) exposure may even be inversely associated with the occurrence of melanoma [244]. In particular, this is also shown in studies by Elwood and Jopson (1997) and Nelemans et al. (1995) [288]; [289]. Looking at the topographical distribution of cutaneous melanomas, studies in Lithuania, Finland, and Germany [290]; [291] find the highest incidence rates for MM on the trunk of the body in males, while females have the highest incidence for MM on the legs. This distributional property is also used as an argument that MM results from intermittent rather than chronic UV exposure.

However, the topographical comparison of incidence ignores the fact that the body areas being compared have very different body surface areas or melanocyte counts. The estimated body surface area of the trunk, for example, is 32% of the total body surface area, while the face, including lips and eyelids, accounts for about only 2.7%. If the topography-specific incidence rates are adjusted to the affected body surface (body surface adjusted rates, RSA), another interpretation possibility arises with regard to the predisposition of the skin areas to MM. The highest RSA is then found in women and men in the face, which is more likely to be classified as chronically UV-exposed.

Further studies are needed to clarify whether chronic UV exposure, possibly in conjunction with intermittent periods, is important for certain types of melanoma.

Other behavioural risk factors (e.g. tanning bed use) are addressed in Section Chapter 5.1 this guideline.

4.3.3.1. UV Exposure as a Possible Exogenous Source of Damage to the Eyes

V. Kakkassery, L.Heindl

The mechanisms and data on skin carcinogenesis described above also apply to the eyelid skin. Due to the increased sun exposure, the eyelid is classified in most skin cancer guidelines as a high-risk zone for skin tumour development. In addition, further damage can occur directly to the eye following UV radiation exposure. Here, a distinction is made between acute damage to the eye and chronic damage to the eye from UV radiation.

Acute Ocular Surface Damage

Photokeratitis and photoconjunctivitis are acute UV radiation-induced damages (especially by UV-B and UV-C) of the conjunctival and corneal epithelium. In addition to artificial, non-sun-induced UV exposure (welding work, solar equipment, etc.), sun-induced UV exposure from about six hours onwards can also lead to swelling and exfoliation of the corneal and conjunctival epithelium [292]; [294]; [293]. This is associated with symptoms such as a temporary reduction in vision, very severe pain, tearing, and conjunctival swelling. Damages as well as complaints of this kind are self-limiting and have a recovalence time of approx. 8-12 hours [292]; [294]; [293]. Healing processes can be supported with caring and antibiotic eye ointments/drops.

Acute UV-Induced Retinopathy

Acute UV radiation-induced retinopathy, whether with natural or artificial UV radiation, can lead to thermal damage to the fovea. This damage is reversible or partially irreversible, depending on the temperature in the fovea centralis (visual fossa) [296]; [295]. The reversible damage can then also vary in visual recovery over time (period of up to six months after the damage). Visual impairment can then vary between 0.1 and 0.5 [296]; [295]. The damage can occur during sunbathing as well as when looking into the sun (in this case, of course, more frequently). Damages of the fovea show up by a typical yellowish-white spot at the fundus as well as in the optical coherence tomography defects in the area of the inner and outer segments of the photoreceptors [296]; [295]. Rare late consequences of sun-induced retinal damage can be the formation of choroidal neovascularization, which then significantly reduces the vision in the eye and which can be treated with intravitreal injections into the eye [296]; [295]. Protective factor for UV radiation-induced retinopathy may be an aging lens, so clear juvenile lenses are less protective accordingly [296]; [295].

Pterygium

Pterygium represents hyperplasia of the bulbar conjunctiva that grows over the cornea. It can cause astigmatism, dry eye, and vision loss by growing into the area of the imaging light path of the eye (depending on pupil width). It is generally accepted that UV radiation is a strong trigger of pterygium here and significantly favors progressive growth on the cornea, as studies in Australia as well as in the USA (Chesapeake Bay study), among others, have shown [297]; [298]; [299]; [300].

Pinguecula

Pinguecula is a hyaline-elastotic degeneration of the bulbar conjunctiva. In contrast to a pteryium, a pinguecula has hardly any disease value. Cosmetic aspects are more important. Studies in the Red Sea region as well as in the USA (Chesapeake Bay study) could also prove a connection between UV radiation and the frequent development of pinguecula [301]; [300].

Climatic Drop Keratopathy

Climatic droplet keratopathy is a formation of ball-like degenerations in the upper part of the corneal stroma directly below the Bowman's membrane (epithelial border) [302]. Massive UV-radiation leads to band-like opacities especially in the palpebral fissure area due to the remodelling of plasma proteins. Regional studies could prove the connection between climatic drop keratopathy and UV radiation [304]; [303]; [300].

Squamous Cell Carcinoma (Squamous Neoplasia) of the Ocular Surface

Squamous cell carcinomas (also called squamous neoplasms) of the conjunctiva develop via the precursors/progenitors of dysplasia and carcinoma in situ. [305]. Alternatively, conjunctival intraepithelial neoplasia, with the grading of mild/moderate/severe (CIN I, II and III) is designated [305], where CIN III is the carcinoma in situ. Studies in Uganda and Sudan as well as comparisons of incidences of squamous cell carcinoma of the ocular surface between Europe and North America compared to sub-Saharan countries in Africa demonstrate the association of UV radiation as well as the sun in the formation of neoplasms [310]; [307]; [311]; [309]; [308]; [306].

Conjunctival Melanomas/Pigmented Neoplasms of the Ocular Surface

Genetic patterns and alterations in conjunctival melanoma tissue suggest UV-induced damage to DNA [312]. However, these theoretical considerations have not yet been confirmed with data from cohort studies or similar, so it is unclear whether (and if so, at what dose) UV radiation exposure leads to pigmented neoplasia of the ocular surface.

Cataract

Evidence of the association between acceleration of age-related cataract development and UV radiation exposure has been widely demonstrated. Studies in the USA, in Australia, in India, in Nepal, and in Hong Kong could clearly prove this connection ([316]; [315]; [314]; [311]; [313]; [317]. The Chesapeake Bay Study and the Beaver Dam Eye Study from the USA reached the same conclusions [318]; [319]. Many other studies have demonstrated the connection between cataract development and UV radiation exposure.

Age-Related Macular Degeneration

The connection between age-related macular degeneration and UV radiation exposure is not clear. Several studies have failed to find an association, while other studies have found promotion of age-related macular degeneration by at least UV radiation from the sun.

In 1983 Hyman and colleagues found no association between macular degeneration and UV radiation exposure [320]. Similar findings were obtained by the Eye Disease Case-Control Study Group ([321]). Another Australian case-control study of 409 cases and 286 controls also saw no correlation between age-related macular degeneration and cumulative UV radiation exposure [322]. The Chesapeake Bay Watermann Study also failed to find a correlation between age-related macular degeneration and UV radiation exposure [323]. However, follow-up analyses of these data showed a long-term effect of blue light (but not UV radiation) on age-related macular degeneration [324]. TThe cohort study "Beaver Dam Eye Study" was able to demonstrate an association between age-related macular degeneration and sunlight exposure time [319]. However, this effect could not be seen with UV radiation exposure. A meta-analysis by Sui and colleagues suggests that there is an increased risk of age-related macular degeneration with increased UV radiation time [325].

Due to UV filtering by the natural lens, UV radiation-induced age-related macular degeneration is not currently thought to occur, but rather blue light-induced sun damage is suspected. This assumption is based on data from the Chesapeake Bay Waterman Study [324]. Especially in cataract-operated eyes with an artificial lens or without a lens, conclusions about possible damage to the macula by blue light could be suspected by pools of the Beaver Dam Eye Study and the Blue Mountains Eye Study in the comparison between the first operated eye and the subsequently operated eye [326]. Initial assumptions that blue light filter in artificial eye lenses has a protective effect could neither be proven nor disproven in a systemic review [327]. Currently, no recommendation for artificial blue light filter lenses in cataract surgery is given by professional societies.

4.3.4. Other Risk Factors for Skin Cancer

4.7	Consensus-based Statement	checked 2020
EC	Other risk factors that are described for non-melanocytic skin cancer are exposure to arsenic or tar, particularly in the work environment. HPV infections are discussed both as a sole risk factor for skin cancer and as a cofactor in combination with ultraviolet (UV) radiation.	
	Strong Consensus (100%)	

Arsenic

Arsenic (in drinking water) is considered a risk factor for skin cancer (especially SCC and BCC). According to the IARC classification, arsenic belongs to class I carcinogens ("carcinogenic in humans"). It has been reported that arsenic may contribute to, among other things, numerical chromosomal aberrations and alteration of epigenetic regulation of tumour suppressor genes.

Limits for arsenic in drinking water are set at ≤ 10 µg/L. However, these are exceeded for nearly 100 million people mainly in Bangladesh, Taiwan, Mongolia, India, China, Argentina, Mexico, Canada, and the USA.

However, robust epidemiological studies on the contribution of arsenic-induced skin cancers to the overall incidence of skin cancer are not available.

Tar

Chronic exposure to tar and tar derivatives, particularly in occupational settings, is a risk factor for non-melanocytic skin cancer [328]; [329]. An increased risk due to the therapeutic use of tar has not yet been demonstrated [330].

HPV infection

HPV infections are discussed both as a sole risk factor for skin cancer (squamous cell carcinoma) and as a co-factor in combination with UV radiation. Extensive UV exposure at the site of skin biopsies has been described as a strong risk factor for the occurrence of HPV infections, and local immunosuppression may play an amplifying role [331]; [332].

However, since both the extent of UV exposure and the expression of HPV infection are difficult to quantify, large epidemiological studies are first needed to substantiate possible causal relationships between UV exposure and HPV infection and to quantify the number of HPV-associated squamous cell carcinomas in the total number of all occurring squamous cell carcinomas [331].

Hydrochlorotiazide

- **The use of the diuretic hydrochlorothiazide, which is found in many blood pressure lowering agents, also promotes the development of non-melanocytic skin cancer.**

The diuretic hydrochlorothiazide (HCT), which is found in many blood pressure-lowering drugs, promotes the development of non-melanocytic skin cancers. In a Danish

case-control study it was shown that the intake of HCT increases the risk of developing BCC by a factor of 1.29 (1.23-1.35), for PECC a factor of 3.98 (95% CI, 3.68-4.31) was determined [333]. Another study showed a factor of 3.9 (3.0-4.9) for SCC at the lip [334]. Both studies describe a dose effect.

4.3.5. Absolute and Relative Risks

For the listed constitutional risk factors, values for relative risks (RR) or lifetime risks are given in the literature in different studies. In the following table, some of these values are listed as examples for **non-melanocytic** skin cancer (table Skin Type as Risk Factor of Non-Melanocytic Skin Cancer) and for malignant melanoma (table Exemplary Constitutional Risk Factors of Malignant Melanoma):

Table 18: Skin type as a risk factor of non-melanocytic skin cancer

Risk factor	Relative risk (95% CI)
Skin type I vs. IV (BCC)	5.1 (1.4-11.3)
Skin type II vs. IV (BCC)	5.3 (1.7-10.6)
Skin type I vs. IV (SCC)	1.4 (0.5-3.0)
Skin type II vs. IV (SCC)	2.2 (0.7-3.8)
Sources: [208]; [218]	

The presence of multiple **actinic keratoses** over a 10-year period is associated with a lifetime risk of developing squamous cell carcinoma (SCC) in the range of 6-10%.

The risk of developing another **SCC** within five years if there is a SCC in the patient's **own history** is 30%, and of developing a BCC is about 40%.

The risk of developing another **BCC** within three years in the case of a BCC in the patient's **own history** is 44%, and of developing a PECC is approximately 6%.

SCC develops up to 65 times more frequently in **immunosuppressed** transplant patients compared to controls. Immunosuppressed transplant patients develop more SCC than BCC (4:1).

For the listed constitutional risk factors, values for relative risks (RR) or lifetime risks are given in the literature in different studies. In the following, some of these values for **malignant melanoma** are listed as examples:

Risk factor	Relative risk (95% CI)
Number of acquired nevi (100-120 vs. < 15)	6.89 (4.63-10.25)
Skin type (I vs. IV)	2.09 (1.67-2.85)
Family history of melanoma (yes vs. no)	1.74 (1.41-2.14)
Number of atypical nevi (5 vs. 0)	6.36 (3.80-10.33)
Melanoma in own history (yes vs. no)	8.5 (5.8-12.2)
Sources: [243]; [209]; [245]	

Table 19: Exemplary constitutional risk factors of malignant melanoma

The relative risks (RR) for the development of different skin cancer entities (BCC, SCC, and MM) depend on the UV exposure pattern. BCC does not depend on the cumulative UV dose (RR = 0.98, 95% CI 0.68-1.41), whereas SCC depends more strongly on the cumulative dose (RR = 1.53, 95% CI 1.02-2.23). MM occupies an intermediate position with respect to cumulative dose (RR = 1.2 95% CI 1.00-1.44). However, for MM, there is an increased risk with intermittent UV exposure (RR = 1.71, 95% CI 1.54-1.90) or sunburns at any age (RR = 1.91, 95% CI 1.69–2.17) [112].

4.4. Importance of Biomarkers for Primary and Secondary Prevention of Skin Cancer

R. Greinert, B. Volkmer

As an outlook into future developments in the field of primary and secondary prevention of skin cancer the increasing importance of biomarkers should be pointed out. Biomarkers are defined, according to WHO, as follows:

"...any substance, structure or process that can be measured in the body or its products and that can influence or predict the incidence or outcome of disease." (WHO. International Program on Chemical Safety Biomarkers in Risk Assessment: Validity and Validation 2001. http://www.inchem.org/documents/ehc/ehc222.htm)

A distinction is now made between different categories of biomarkers, whereby there can be smooth transitions [336]; [335]; [338]; [337]:

- Risk biomarkers
- Diagnostic biomarkers
- Prognostic biomarkers
- Predictive biomarkers

Risk biomarkers indicate the potential risk for a disease, diagnostic biomarkers indicate the presence of a particular disease, prognostic biomarkers provide information about the course of a disease, and predictive biomarkers provide information about how a particular disease will respond to possible forms of therapy (e.g. "therapy-responder vs non-responder") [339]; [341]; [340].

Biomarkers are becoming increasingly important, especially in the context of their detection in liquid biopsies ("liquid biopsies") [344]; [343]; [342]. By this is meant that biomarkers in body fluids (such as blood, urine, cerebrospinal fluid, saliva, etc.) can be detected non-invasively after collection of the body fluids using a variety of methods [345]. New molecular-biological findings and isolation methods already make it possible to examine a large number of different biomarkers in liquid biopsies. These include, for example [345]:

- Cell-free tumour DNA/RNA
- Circulating tumor cells
- Antibodies
- Metabolites
- Extracellular vesicles
- Exosomes
- Tumour-associated exosomes (TEX)
- microRNAs (miRNAs)

Recently, the detection of exosomes and TEX as biomarkers has proven to be particularly promising, especially considering the miRNAs that are included as cargo in exosomes and TEX. The miRNAs are approximately 18-24 nucleotide long non-coding RNA segments that post-transcriptionally influence protein synthesis at all levels of cellular development and disease development [346]. They are particularly stable as cargo of exosomes and TEX in liquid biopsies and thus represent a suitable biomarker candidate for a variety of questions. Exosomes and TEX are small vesicles (50-120 nm in diameter) that are actively secreted by (tumour) cells to influence the micro- and macro-environment of disease- (tumour-) specific cells through the interaction of surface molecules they carry and through their (specific) cargo (e.g. miRNAs) that can be transferred into other cells [347]. They thus control, among other factors, the disease development, its course, and possibly also the therapy.

The importance of miRNAs, exosomes, and TEX as biomarkers in diagnostics, prognostics, and prediction of skin cancer has already been pointed out in a number of publications (e.g. [348]; [350]; [351]; [347]; [349]).

It must be noted, however, that until any form of biomarker can be used, which is already indicated in a large number of studies, a phase of consensual and large-scale validation must take place before a possible biomarker can enter clinical use or be used in any form in primary and secondary prevention.

5. Primary Prevention

5.1. Individual Behaviours

Revision: M. Asmuß, I.-M. Hübner, G. Egidi, B. Koletzko, F. Stölzel, N., Seidel, D. Großkopf-Kroiher, H. Radinger

UV radiation is a natural part of solar radiation and necessary for the stimulation of endogenous vitamin D formation. At the same time, however, the effect of UV radiation on the skin is the main cause of skin cancer. Therefore, a conscious handling of natural as well as artificial UV radiation is indispensable. The aim of primary prevention is to prevent excessive UV exposure of the skin. This applies first and foremost to UV exposure from the sun when spending time outdoors. Various measures are suitable for this purpose. The individual sensitivity of the skin to UV radiation has to be taken into account.

Risk groups that should pay particular attention to good sun protection include:

- Children (especially babies) and adolescents,
- People who are more likely to develop sunburn than a tan,
- People with lighter skin, fair or red hair, or many sunburn spots (lentigines),
- People with many noticeable and/or congenital nevi,
- People with immunosuppression,
- People with a personal or family history of skin cancer,
- Groups who spend a lot of time in the sun and are therefore at increased risk of skin cancer, such as:
- People who work outdoors
- People who spend a lot of time outdoors in their free time (e.g. sailors, golfers)

5.1.1. Risk Reduction Behaviours

5.1	Consensus-based Recommendation	modified 2020
EC	Protective measures against solar ultraviolet radiation is particularly important for persons at increased risk and must be applied in the following order: • avoidance of exposure to strong solar radiation, • wearing suitable clothing, • using sunscreens.	
	Strong Consensus (100%)	

5.1.1.1. Avoidance of Strong Solar Radiation Exposures

5.2	Consensus-based Recommendation	modified 2020
EC	The following measures must be taken to avoid exposure to strong solar radiation (taking into account the type of skin): • At medium and high UV irradiance (UVI 3-7), seek shade during midday, • In the case of very high UV irradiance (UV index 8 and higher), avoid going outdoors during the midday period if possible. If this is not possible, seek shade, • If necessary, postpone outdoor activities to the morning and evening hours, • **Avoid sunburn.**	
	Strong Consensus (100%)	

The following is a reference to the recommendation of the Radiation Protection Commission "Protection of Humans from the Hazards of Solar UV Radiation and UV Radiation in Solaria" [Strahlenschutzkommission et al. 2016].

Avoidance of excessive sun exposure is the most important sun protection measure and has the highest priority.

The level of potential UV radiation exposure depends on, among other things:

- Season
- Time of day
- Weather conditions (cloud thickness and cloud cover)
- Altitude (sea level, mountains)
- Reflection from the ground (earth, sand, snow, water)
- Shade

The strength of the solar radiation can usually be estimated well by looking at the sky. However, when the sky is cloudy, it is possible to underestimate the UV exposure, because even when there is a closed thin cloud cover, UV radiation penetrates through the clouds and is scattered by the clouds. In this case, the so-called UV index helps to assess the possible UV radiation exposure. It is determined by measurements and calculations and published by the weather service and other institutions in the media (internet, newspaper, television). Depending on the level of the UV index, various sun protection measures are recommended by the WHO.

If the UV index is not known, the so-called "shade rule" can be used to determine whether dangerous sun exposure is to be expected. The sun is higher than 45° above the horizon when the shadow is shorter than the object casting the shadow. In this case, strong UV radiation is to be expected. However, solar radiation can already contain high UV components at a lower position of the sun (about 35° - 40°).

The strongest solar radiation occurs at the highest sun position at midday when there is little cloud cover. About 50% of the total UV dose of a day occurs in the time window of two hours both before and after the sun's highest position. Therefore, it is recommended to avoid longer stays outdoors between 11:00 and 16:00 o'clock if possible, especially in the case of very strong solar radiation. Even before and after

this time, strong UV exposure can occur under clear skies, so that even then suitable sun protection measures are recommended for longer stays in the sun. If possible, sports and leisure activities should be moved to the morning and evening hours if the weather is suitable.

It should be noted that the highest point of the sun within a time zone depends on the geographical longitude. In the east of Germany, the sun is highest in summer at 13:00 (Central European Summer Time), while in the west of Germany it is only around 13:40. In relation to the entire area of Central European Summer Time, for example, this results in a time window of the sun's highest point between 12:30 p.m. (Poland) and 2:30 p.m. (Spain). Therefore, the recommendation to avoid the midday sun (+/- two hours around the peak of the sun) should be adapted to local conditions, especially when travelling abroad.

The skin's own protection time depends on the respective skin type. In order to avoid overloading the skin with UV radiation and sunburns, the duration of stay in the sun should not exceed this self-protection time of the skin. Self-protection time is understood to be the maximum period of time during the course of a day for which the untanned skin can be exposed to the sun without getting a sunburn (however slight).

If a longer stay outdoors takes place in strong sunlight, the duration of the unprotected stay in the sun should be kept as short as possible in order to minimise the UV radiation dose. With regard to the protective measure "Seek Shade," it should be noted that not every type of shade reduces the UV radiation intensity to the same extent. UV radiation comes not only directly from the direction of the sun, but also indirectly from the environment, since solar UV radiation is scattered by water and air molecules (diffuse radiation). Therefore, the shading of direct solar radiation (e.g. by a sunshade) alone does not mean that UV radiation no longer reaches the skin and eyes, as the diffusely scattered UV radiation still reaches the body. The reduction of UV radiation varies depending on the type and extent of shading. The nature and orientation of the shading elements play a role. In this case, additional sun protection measures are necessary. If, in addition to direct solar radiation, the sky is also shaded over a large area (e.g. in deep urban canyons or in a dense forest), then the scattered proportion of solar UV radiation is lower and the shade is sufficient.

Avoiding Sunburns

As already described in Chapter Chapter 4.3.3 and the table "Influence of UV Exposure Pattern on the Relative Risk for Melanoma Development," a correlation between the occurrence of BCC (and presumably also of SCC), as well as melanoma, with sunburns can be established [97]; [352][353]. In addition, the prospective Nambour Skin Cancer study (1992-1996, follow-up to 2004) showed a strong association between BCC on the upper body and the number of reported sunburns. Study participants who had experienced more than 10 sunburns, compared with those without sunburns, had a more than doubled risk of upper body BCC (OR 2.49, 95% CI 1.04-5.99). The incidence of BCC on the head also increased with the number of sunburns (OR 1.79, 95 % CI 0.93-3.45 at > 10 sunburns) [354].

Slow Habituation to the Sun

In principle, it is always important to accustom the skin slowly to the sun. This is particularly important with increasing sun exposure in spring or during holidays with increased UV exposure. Accustoming can be done by repeated short stays in the sun, which are so short that no reddening of the skin occurs.

5.1.1.2. Wearing Appropriate Clothing

5.3	Consensus-based Recommendation	checked 2020
EC	When staying outside in the sun, suitable clothing, headwear and sunglasses should be worn for protection.	
	Consensus (90%)	

If it is not possible to avoid spending time outdoors in strong sunlight, the UV exposure of the skin should be reduced as far as possible by individual shielding from the sun's rays. This is done, for example, by suitable clothing which covers the skin as much as possible.

Suitable clothing is preferable to the use of sunscreen products as individual sun protection. Clothing absorbs UV radiation. The unit of measurement of absorption is the UV protection factor (UPF), which is comparable to the sun protection factor (SPF) of sunscreens. Simple T-shirts can have a UPF of 20 or more, which is usually sufficient for individual sun protection. More solid clothing and special UV-protective clothing may also have a UPF of 50, 80, or more. Unlike the SPF of sunscreens (see below), the UPF is immediate and actual for as long as the garment is worn. For very thin fabrics (e.g. shirts, blouses, mesh shirts, some swimwear), the UPF is less than 20 and may not be sufficient.

5.1.1.3. Protection of the Eyes from UV Radiation

5.4	Consensus-based Recommendation	checked 2020
EC	Suitable sunglasses should be worn when exposed to strong sunlight. Never look directly at the sun in the sky. This also applies when wearing sunglasses.	
	Strong Consensus (100%)	

In addition to protecting the skin, protecting the eyes from solar radiation is of great importance, since UV radiation can also cause acute and chronic damage to and in the eye (see Chapter Chapter 4.3.3.1).

Melanoma, basal cell carcinoma, and squamous cell carcinoma can also develop in the eye. Therefore, this has been included in the recommendations for the primary prevention of skin cancer. Suitable sunglasses are used to protect the eyes when exposed to strong sunlight. The suitability is given, if the sunglasses show the sign "UV400," offer sufficient protection against lateral UV radiation, and correspond to the standard DIN EN ISO 12312 for sunglasses. This standard defines five different glare categories (degree of darkening). Sunglasses in glare category 2 or 3 are sufficient for everyday wear. Sunglasses in glare category 4 are used for extreme conditions, e.g. on glaciers, but are not suitable for road traffic. Overall, care should be taken to ensure that sunglasses have adequate side protection.

Looking directly into the sun high in the sky can cause irreversible damage or even blindness in a very short time. This also applies to the use of sunglasses. Sunglasses

are not suitable for observing the sun. Only with special sun filters with very high radiation absorption can solar eclipses, for example, be observed without danger. Only at sunrise and at sunset is the use of eye protection filters not necessary.

Regarding the protection of sunglasses, refers to the recommendation of the WHO [355]. In this, the use of sunglasses is recommended from a UV index value of UVI 3 or more. Furthermore, it is recommended that sunglasses be worn especially near water as well as in snow and high mountains. Background is besides the UV protection to avoid formation of skin tumours at the eyelids, the proven connection of acute damage by UV radiation, the acute keratitis, acute retinopathy, as well as the chronic damage such as pterygia, pinguecula, climatic drop keratopathy, cataract formation as well as ocular surface carcinoma (see section Chapter 4.3.3.1). A correlation between macular degeneration and UV radiation cannot be shown at present. However, the blue component of sunlight may possibly play a role here, which is more penetrating in young people with clear lenses. A weak data situation exists concerning the UV intensity from which the mentioned damages occur, so that the WHO recommendation must be reconsidered given new data.

5.1.1.4. Use of Sunscreen Products

5.5	Evidence-based Recommendation	modified 2020
GoR **A**	Appropriate sunscreen products should be used for skin areas that cannot be protected in any other way. The use of sunscreens must not result in a prolonged stay in the sun.	
LoE **1+** **2++**	[356]; [357]; [358]; [359]; [360]; [361]	
	Consensus (87%)	

5.6	Consensus-based Recommendation	modified 2020
EC	Sunscreens should be applied carefully to free areas of skin that are not covered by clothing (head, face, hands, arms, legs) and the following should be observed: • use an adequate sun protection factor, • apply a sufficiently thick layer (2 mg/cm²), • apply evenly to all uncovered areas of skin, • apply before exposure to the sun, • repeat the application after 2 hours and after bathing (the protective time is not prolonged as a result).	
	Consensus (95%)	

5.7	Evidence-based Statement	modified 2020
LoE 1++ 2+	There is contradictory data on whether the risk of melanoma is reduced by sunscreen use.	
	[359]; [360]; [361]; [362]; [363]; [364]; [365]	
	Strong Consensus (97%)	

The correct application of sunscreen products is of great importance. Incorrect application can greatly reduce the effect of sunscreens.

Sunscreens should be applied in a sufficiently thick layer. When determining the sun protection factors of sunscreens, an application layer of 2 mg/cm² is taken as a basis (see e.g. [367]).

To achieve the SPF indicated for a sunscreen product, an adult (approx. 1.5 - 2 m² skin) must use about 30 to 40 ml for the entire body. This is equivalent to about 1/5 of a standard 200ml bottle.

Sunscreen should be applied evenly and to all exposed areas of the skin. It is estimated that in practice often only one third to one fifth of the stated SPF is actually achieved, which leads to an overestimation of the protective effect. The application should be done before the beginning of the sun exposure and not only during the stay in the sun. Sweating and bathing will cause the sunscreen to come off the skin after some time. Therefore, waterproof sunscreen is preferable and application should be repeated at least every two hours. After bathing, the sunscreen must be reapplied. The lips should also be protected with a suitable product.

As the informative value of the sun protection factor for practical use is limited, the effectiveness of sunscreen products is now no longer described with numerical values but, in accordance with Recommendation 2006/647/EC of the EU Commission, verbally in four categories for different protection levels (low, medium, high, very high).

Sunscreens were originally developed to protect the skin during unavoidable stays in the sun to prevent major damage/sunburns. They absorb, scatter, and reflect UV radiation to a large extent, but not completely. They still allow some UV radiation to pass through to the skin, so the UV dose can accumulate there and contribute to long-term effects, such as the development of skin cancer.

Systematic reviews and meta-analyses of observational studies showed that no significant change in the incidence of malignant melanoma can be observed in users of sunscreens [363]; [368]. Other studies find evidence that sunscreen use may even be associated with an increased risk of melanoma [358]. This is thought to be due to a false sense of security due to sunscreen use and resulting prolonged exposure to the sun [356]. People who used creams with a higher SPF took longer sunbaths [366].

The use of so-called "self-tanning sunscreens," which contain psoralens (bergamot oil), appears to be associated with an even higher risk of melanoma development [358].

Gorham et al. [359] describe that in fair-skinned individuals the use of sunscreen may increase the risk for melanoma development. Overall, the authors do not find a significant increase in melanoma risk associated with sunscreens in their systematic review. However, when studies conducted in the northern hemisphere above 40 degrees latitude are pooled, the odds ratio is 1.6 (95% CI 1.3-1.9). The authors conclude that the use of sunscreens, which almost completely filter UVB radiation but transmit much of the UVA radiation, may contribute to melanoma risk in populations living above 40 degrees latitude [359].

Lin et al. [361] reported in a systematic review that regular use of sunscreen reduced the risk of SCC but did not reduce the risk of developing BCC [361]. After a follow-up of 10 years, a reduced risk of melanoma was found in the intervention group [360]. In subtropical areas, the development of solar keratoses can be reduced by the use of sunscreen [362].

A prospective cohort study within the Norwegian Women and Cancer Study (NOWAC) analysed participants' use of sunscreen at latitudes <45 degrees (i.e. closer to the north/south pole than the arithmetic mean between the equator and the north/south pole. In Europe, the northern 45th parallel is generally considered the northern boundary of southern France) [365].

The study included women aged 40-79 years who testified to having spent at least one week of vacation sunbathing in their lifetime in said regions (n=42,479). Endpoints represented sunscreen use, skin reactions, and cancer incidence. According to the results, users of sunscreens who had a history of sunburns have a higher risk of melanoma compared to non-users, while users of sunscreens without such a history have a lower risk. Non-users have a lower risk of melanoma compared to users of sunscreens with SPF < 15. However, use of sunscreens with SPF ≥ 15 results in an 18% reduction in melanoma incidence over a 10-year period compared with users of sunscreens with SPF < 15.

A case-control study [364] concluded that melanoma patients used sunscreens less frequently or not at all compared with a control group (use of sunscreens never/ infrequently: OR 12.28 (95% CI: 5.56-27.14, p<0.001); use of sunscreens always and repeatedly: OR 2.19 (95% CI: 1.23-3.91, p=0.01)); however, this does not allow the reverse conclusion that sunscreens reduce the risk of melanoma. According to this study, melanoma patients and controls mainly differ in the number of sunburns in childhood (six to ten sunburns in childhood/adolescence: OR 4.95 (95% CI: 2.29-10.71, p<0.001; >11 sunburns in childhood/adolescence: OR 25.52 (95 CI%: 12.16-53.54, p<0.001).

Need for Research

With regard to the use of sunscreens with exclusively mineral sun protection factors (such as zinc oxide or titanium dioxide) or chemical sun protection factors, no recommendation can be made due to the lack of a systematic literature review. The advantages and disadvantages of the respective sunscreens, especially with regard to the absorption of chemical agents (see e.g. [369]) as well as the question of a sufficient sun protection factor (and this especially for the application in children) must be reviewed and evaluated on the basis of evidence before a statement on this is

possible. Additionally, it is essential to further investigate the relationship between melanoma risk and the use of sunscreens in order to clarify the question of a protective effect. Furthermore, application aids for the implementation of the dosage recommendations should be developed.

5.1.1.5. Avoidance of UV Exposure from Artificial Sources

Exposures from artificial UV sources, such as tanning beds, increase the risk of damaging the skin and eyes. Artificial UV exposure is just as dangerous as natural sun exposure with regard to the development of skin cancer (Chapter Chapter 4.1.1, Etiology).

5.8	Evidence-based Statement	new 2020
LoE 1+ 1-	The risk of malignant melanoma (MM) is increased in sunbed users compared to non-sunbed users and increases with the frequency of sunbed visits. The younger the tanning bed user was at the first visit, the higher the risk.	
	[370]; [371]; [372]; [373]	
	Strong Consensus (100%)	

All publications report data or pooled data from cohort or case-control studies, meaning that the rate ratios reported here are measures of association. Evidence for a possible causal association includes: correct temporal association, dose-response association, consistency, and specificity of association.

A total of three systematic reviews and one cohort study not yet included in the systematic reviews were included.

The three systematic reviews included mostly the same studies. Almost exclusively case-control studies with a total of more than 11,000 melanoma cases were included.

Regarding the occurrence of malignant melanoma in "tanning bed users" compared to "non tanning bed users," the most recent review by Burgard (2018) reported an adjusted OR of 1.21 (95% CI: 1.08 – 1.36; 31 studies), representing an increased risk of MM occurrence in comparison. Colantonio (2014) reported an adjusted OR of 1.16 (95% CI: 1.05-1.28, 31 studies) and Boniol (2012) reported a relative risk of 1.20 (95% CI: 1.08-1.34; 27 studies; 25 and 24 studies already included in Burgard and Boniol, respectively). The weakness of Boniol's (2012) study is that the study quality of the included studies was not assessed and the included studies were only observational studies (case-control studies and cohort studies). A subgroup analysis of studies assessed as having low risk of bias (risk of bias according to the Newcastle Ottawa Scale (NOS): 67.7% of the 31 included studies scored less than four stars) was conducted by Burgard (2018), which found no association (OR 1.15 95% CI: 0.94 – 1.41). The subgroup analysis received a SIGN score of 2++. The weaknesses were the lack of interventional studies and serious limitations in the form of unobserved and unrecorded confounders. Subsequently, further studies with higher quality and adjustment for important confounders are needed. Colantonio (2014) classified six of the studies

included here as having unclear bias risk and three as having high bias risk. Boniol (2012) had not conducted a quality/bias assessment.

Analyses were also conducted in all three systematic reviews on the influence of frequency of tanning bed use and age at first tanning bed visit (see Table Table 17").

Boniol (2012) included a total of 27 studies in the systematic review as mentioned above, Colantanio (2014) included 31 studies and Burgard (2018) also included 31 studies. The results are congruent – a statistically significant association was described regarding the occurrence of MM and an increased frequency of tanning bed visits. A non-statistically significant association was found for infrequent visits (e.g. < 10). A statistically significant association was reported between the incidence of MM and the proportion of those who visited the tanning bed for the first time at a young age (25 or 35 years cut-off). This was not the case in the older subgroup.

In another prospective cohort study, Ghiasvand (2017) examined melanoma incidence in tanning bed users and reported a relative risk of 1.24 (adj 95% CI: 1.05-1.46) versus the comparison group. This result, as well as the result for the group of young tanning bed users, is in line with the results of the reviews. Due to the study design and the unclear potential for bias, the significance of the results is limited.

The following table summarizes the study results in total and by subgroup per review:

Table 20: Study results on the relationship between sunbed use and skin cancer risk

	Total	By region	Recruitment time spans in the studies	By number of solarium visits	First solarium visit	Bias risk
Boniol 2012 (RR, 95% CI)	"Summary relative risk": 1.20 (1.08-1.34) Only adj. studies (sun exposure and sun sensitivity) = 1.29 (1.13-1.48) 11, 428 Melanoma cases.	-	-	Frequent use of sunbeds 1.42 (1.15-1.74)	< 35 years old = 1.87 (1.41-2.48)	(not performed)
Colantonio 2014 (Crude and and adjusted	Crude OR/when available adjusted OR) =.	North America = 1.23	<2000 =	1-10 times tanning bed use= 1.07	< 25 years old= 1.35	high bias risk=

	Total	By region	Recruitment time spans in the studies	By number of solarium visits	First solarium visit	Bias risk
OR combined, 95% CI)	1.16 (1.05-1.28) 14,956 Melanoma cases and 233,106 Controls	(1.03 - 1.47) Europe = 1.10 (0.98 - 1.24) Oceania= 1.33 (0.99 - 1.78),	1.12 (1.00-1.26) ≥2000 = 1.22 (1.03-1.45)	(0.90-1.26) >10 times tanning bed use= 1.34 (1.05-1.71)	(0.99-1.84) ≥ ≥25 years old= 1.11 (0.86-1.42)	19 studies unclear bias risk= 18 studies
Burgard 2018(crude and adjusted OR combined, 95% CI)	Crude OR/when available adjusted OR) = 1.21 (1.08-1.36) Crude OR only: 1.19(1.04-1.35) 11,706 Melanoma cases and 93,236 controls	America (North)= 1.35 (1.10-1.67) Europe= 1.11 (0.98-1.25) Australia= 1.31 (0.98-1.74)	≤1990=1,21 (1.01-1.45) ≥1991=1.19 (1.02-1.38) 1991-1999=1.11 (0.94-1.31) ≥2000=1.34 (1.03-1.74);	≤10 solarium visits=1.13 (0.92-1.39 >10 solarium visits =1.39 (1.08-1.80)	< 25 years old= 1.52 (1.23-1.89) ≥ 25 years old= 1.11 (0.86-1.42)	low bias risk= 11 studies 1.19 (0.98-1.43) high bias risk= 19 studies 1.22 (1.06-1.41)

5.9	Evidence-based Statement	new 2020
LoE 1- 2-	Tanning bed users have an increased risk of basal cell carcinoma compared to non-tanning bed users. The risk is even higher for people who use a tanning bed for the first time at the age of less than 20 years.	
	[374]; [375]	
	Strong Consensus (100%)	

Wehner (2012) reported in their meta-analysis with 12 studies (cohort studies and case-control studies, n=80,661) an increased risk of developing epithelial tumours comparing "tanning bed users" vs. "never tanning bed users" (odds ratio [OR] SCC: 1.67 (95% CI: 1.29-2.17) and OR BCC: 1.29 (95% CI: 1.08-1.53), respectively).

A subgroup analysis for "intensive tanning bed use" revealed an OR of 1.5 (95% CI: 0.81-2.77) for the development of BCC, i.e., the risk of having developed BCC under "intensive tanning bed use" is not significantly increased.

For SCC, not enough data were available for a meta-analysis. A subgroup analysis for "onset of tanning bed use at a young age" showed an OR of 1.40 (95% CI: 1.29 - 1.52) for developing BCC. However, this was not significant when analysing SCC (OR 2.02; 95% CI: 0.70 - 5.86).

Karagas et al. (2014) identified 657 cases of BCC occurring between the ages of 25 and 50 years through the New Hampshire Skin Cancer Study database. Age- and sex-matched controls (n=452) were identified through the New Hampshire Department of Transportation. The authors reported an adjusted OR of 1.6 (95% CI: 1.3-2.1) comparing tanning bed users to the control group. A subgroup analysis clarified that the chance of "first tanning bed use at a young age (<20)" was two times greater (OR 95% CI: 1.4 – 3.0) among sufferers than the chance among controls.

Conducting more targeted studies for BCC and SCC is necessary.

5.10	Evidence-based Recommendation	new 2020
GoR A	The use of sunbeds must be avoided in order to reduce the risk of developing skin cancer (especially melanoma).	
LoE 1+ 2-	[370]; [371]; [372]; [373]; [374]; [375]	
	Strong Consensus (100%)	

Similar recommendations are made internationally: in general, WHO, ICNIRP, EUROSKIN, SSK, DKH, and ADP do not recommend the use of sunbeds. The WHO comes to the following conclusions in this respect: sunbed use is associated with an increased risk of skin cancer. This risk increases with the number of solarium visits and first-time use of a solarium at a young age. First-time use of tanning beds before the age of 35 increases the risk of melanoma by 60% (based on 13 studies, RR 1.87 (95% CI: 1.41-2.48) [372]. Each additional visit to a tanning bed in a year increases skin cancer risk by 1.8% (based on four studies, RR 1.018 (95% CI: 0.998-1.038)) [372]. First-time tanning bed use before the age of 25 increases the risk of squamous cell carcinoma by 102% (RR 2.02; 95% CI: 0.70-5.86) and the risk of basal cell carcinoma by 40% (RR: 1.40; 95% CI: 1.29-1.52) [375].

In Germany, a law for the protection of humans against non-ionizing radiation (NiSG) and a corresponding UV protection regulation (UVSV) have been in place since July 2009, regulating the operation and use of sunbeds. In particular, it was stipulated that young people under the age of 18 may not use sunbeds (§ 4, NiSG). The regulation stipulates, among other things, that people with skin type I and II should be advised not to use tanning beds and that qualified personnel must be available to check UV irradiation equipment and to contact users in order to fulfil the consultation and information obligations under the UVSV. According to the UVSV, since August 2012, old devices that do not comply with the EU requirement in force since 2007 of a limit on the total erythema-effective UV irradiance of 0.3 W/m² may no longer be operated – a value that corresponds to the erythema-effective UV irradiance at the equator at noon under a cloudless sky.

5.1.1.6. Food Supplements, Nicotine, and Caffeine Consumption

5.11	Evidence-based Recommendation	checked 2020
GoR **A**	Food supplementation with selenium, vitamin A and beta-carotene must not be recommended as a measure for skin cancer prevention.	
LoE **1++** **1+**	[362]; [376]; [377]	
	Strong Consensus (100%)	

A meta-analysis of randomized clinical trials showed that the incidence of BCC and SCC of the skin was not reduced by taking antioxidant supplements (selenium, beta-carotene, vitamin A) [377]. Similarly, the development of AKs was also not reduced by beta-carotene intake [362].

No firm results are available from cohort or intervention studies suggesting a particular dietary pattern as a prevention strategy.

There is increased promotion in the lay press of taking antioxidant substances such as selenium, beta-carotene, and vitamin A as an additional means of UV protection. Beta-carotenes have no UV-protective effect [376]. A meta-analysis also showed no

clinical evidence for the preventive effect of antioxidant supplements on skin cancer [377].

Caffeine-Containing Substances

There is evidence for protective effects of caffeine-containing foods on the development of skin cancer (primary studies: [379]; [378], meta-analysis: [380]). However, a recommendation for or against certain behaviours cannot be derived on the basis of the available data.

A meta-analysis [380] concludes that consumption of caffeinated coffee is associated with a reduced risk of melanoma, at least for individuals in the group with the highest coffee consumption (RR = 0.81, 95% CI: 0.68-0.97). The effect of caffeinated coffee was significant for women (RR = 0.76, 95% CI = 0.61-0.95) but not for men (RR = 1.11, 95% CI: 0.91-1.36). On a dose basis, the authors calculated a 4.5% reduced risk of MM (pooled RR = 0.955, 95% CI: 0.912-0.99) for one cup of coffee per day compared with non-users. However, the authors point out that possible chemopreventive effects of caffeinated coffee need further investigation. Also, the issue of confounders has not been adequately addressed.

From the Norwegian Women and Cancer (NOWAC) study, compared with low consumption of caffeinated coffee, there was a statistically significant negative association between low to moderate consumption of caffeinated coffee (> 1-3 cups/day, HR=0.80; 95% CI: 0.66-0.98) and moderate to high consumption (> 3 cups/day, HR=0.77; 95% CI: 0.61-0.97) and risk of malignant melanoma [379].

A prospective cohort study (1997-2007) [378] included participants (n=1,325) from a skin cancer study conducted in 1986 and resurveyed in 1992 and 1996. Participants were sent a questionnaire on caffeine consumption frequencies every six months (inclusion criterion: at least one completed questionnaire). Reported skin cancers were confirmed by histopathological findings. Whole-body skin examinations of all active participants were performed in 2007. The study describes a negative association between daily caffeine consumption (coffee and other caffeinated foods such as black tea, cola, chocolate) and BCC (RR=0.96 (95% CI: 0.87-1.05, p trend=0.20)), but only in individuals with previous skin cancer and mainly for individuals with high caffeine consumption (corresponding to an average of four cups of regular coffee) (RR=0.17 (95% CI: 0.57-0.97, p trend=0.025)). The results suggest that caffeine consumption may be an effective preventive measure in individuals diagnosed with skin cancer. This is especially true for individuals with high caffeine consumption (e.g., an average of four cups of regular coffee daily). However, the guideline group is unable to assess the risks potentially associated with heavy coffee consumption and therefore abstains from recommending.

Alcohol and Nicotine

No firm conclusions can be made about alcohol and nicotine in the context of skin cancer prevention.

A case-control study [381] investigated possible associations between cigarette consumption and the risk for BCC and SCC. An association was found in particular between cigarette consumption and SCC (OR=1.97; 95% CI: 1.19-3.26). In particular, among women the risk increased with the number of pack-years (OR at ≥ 20 pack-years = 3.00, 95% CI: 1.02-8.80). The study concludes that cigarette use is more strongly associated with SCC than with BCC, especially in women.

In the Woman's Health Initiative Observational Study (WHI OS) [382] it is postulated that higher alcohol consumption in post-menopausal white women is associated with increased risk of NMSC and MM. However, confounders were only collected at baseline. Recall bias and confounding are possible. High-risk behaviour alcohol consumption could influence other behaviours, e.g. lack of sun protection behaviour or tanning bed use.

A systematic review found ten studies on the association between cigarette consumption, melanoma risk, and mortality. Seven studies showed a negative association between cigarette use, melanoma risk, and mortality. Two studies showed a positive association, particularly in older individuals, and two studies found no association. The weaknesses of the review are, for example, that the association between socioeconomic status and lifestyle factors are not considered, although these are significant for explaining variance in behaviour [383].

Nicotinamide

The S3 guideline "Actinic Keratosis and Squamous Cell Carcinoma of the Skin" [384] cconsiders that nicotinamide can be used to prevent NMSC in patients with a history of NMSC or in organ transplant patients. The S2k guideline "Basal Cell Carcinoma" [385] recommends nicotinamide in patients predisposed to BCC for secondary prevention. Retinoids, on the other hand, should not be used for the prevention of BCC according to the BCC guideline, and further large-scale studies are considered desirable for COX2 inhibitors.

The guideline group does not see the use of nicotinamide as a means of primary prevention for the general population on the basis of the guidelines on SCC and BCC. No studies are available that allow conclusions to be drawn about the consequences of continuous administration of nicotinamide in the general population (including children and adolescents). The focus of primary prevention in the general population is on the risk reduction measures mentioned in the guideline.

5.1.2. Behaviour for Specific Groups of People

Intensive sun/UV irradiation poses a skin cancer risk for all groups of people and should be avoided. However, protection against intensive UV irradiation is particularly important for groups at increased risk. Although many studies deal with the behaviour, especially of children and adolescents, with regard to sun protection and focus on the sustainability of changes (e.g. [386]; [387]; [388]; [389]), there are very few studies that recommend scientifically justifiable differences for the sun protection measures of certain groups.

Throughout all papers, the damage to health that can occur in all observed groups due to increased or intense sun exposure is emphasized.

In assessing the need for and type of sun protection measures, the individual sensitivity of the skin to solar radiation is essential. The extent and type of sun protection required depends on the skin type. Children, persons with skin types I and II, and persons with a genetic or disease-related increase in UV radiation sensitivity are particularly sensitive.

5.1.2.1. Children

5.12	Consensus-based Recommendation	checked 2020
EC	Children must not get sunburned.	
	Consensus (92%)	

5.13	Consensus-based Recommendation	checked 2020
EC	Babies must not be exposed to direct sunlight.	
	Strong Consensus (100%)	

5.14	Consensus-based Recommendation	checked 2020
EC	Children must be required to wear skin-covering clothing in strong sunlight.	
	Strong Consensus (100%)	

5.15	Consensus-based Recommendation	modified 2020
EC	In the development of nevi, textile sunscreen is protective. The role of sunscreens is open.	
	Strong Consensus (100%)	

5.16	Consensus-based Recommendation	modified 2020
EC	Children's eyes must be protected by suitable sunglasses.	
	Strong Consensus (100%)	

Children's skin is very sensitive to the effects of solar radiation. This is especially true if they have a fair complexion. Sunburns in childhood increase the risk of developing skin cancer later. Therefore, very careful sun protection is necessary for children. As with adults, this includes first avoiding prolonged UV exposure, then wearing appropriate clothing that covers the body as completely as possible, suitable headgear and eye protection/sunglasses, and finally, as an additional measure, applying sunscreen to exposed areas of skin.

Gallagher et al. [390] showed in a randomized controlled trial that the number of nevi in children with fair skin (statistically significant in children with freckles), can be decreased by extensive use of sunscreen.

The systematic review by de Maleissye et al. [391] indicated that there is no evidence to date to support a protective effect of sunscreen on melanocytic nevi development in children. The included epidemiological studies were not homogeneous with respect to the age of the children and, moreover, different methods of counting melanocytic nevi were used. Thus, the study concludes that the assessment of the effect of sunscreens under real conditions is difficult and further studies with a uniform, standardized protocol have to be performed in order to be able to draw a conclusion.

5.1.2.2. Immunocompromised/Transplanted Patients

5.17	Evidence-based Recommendation	checked 2020
GoR **A**	Immunosuppressed transplant recipients must use sunscreens to protect themselves from skin cancer as part of a consistent, comprehensive ultraviolet (UV) radiation protection strategy.	
LoE **2+**	[392]	
	Strong Consensus (100%)	

5.18	Consensus-based Recommendation	checked 2020
EC	Immunosuppressed people must ensure they have a consistent, comprehensive untraviolet (UV) radiation protection strategy.	
	Strong Consensus (100%)	

Ulrich et al. [392]

onducted a prospective study over two years with 120 organ transplanted patients. The study group received sunscreen in addition to information on sun protection; the control group received information material only. It was shown that in immunosuppressed recipients after organ transplantation, the regular application of sunscreen – as part of a consistent protection against UV radiation – protects against the development of further actinic keratoses, invasive SCC, and, to a lesser degree, also against BCC.

The above recommendation is in line with the international KDIGO guidelines for the care of renal transplant recipients, which recommend consistent, intensive UV protection, regular self-examinations, and annual whole-body examinations by a dermatologist for all transplant recipients [393].

For the risk of low vitamin D levels due to consistent UV protection in immunosuppressed individuals, see the following chapter, Chapter Chapter 5.1.3.

5.1.3. Potential Side Effects

UV radiation has been shown to cause skin cancer. UV exposure increases the risk of disease for malignant melanoma as well as for SCC and BCC. Since this association is well known, the most important primary preventive measure is to avoid increased UV exposure. This can be achieved by various individual behaviours and measures (e.g. avoiding midday sun, textile sun protection, sunscreen).

UV radiation is necessary for vitamin D synthesis in the skin; a potential adverse side effect of consistent sun protection measures may be associated with decreased vitamin D levels. In addition, avoiding increased UV exposure when outdoors could result in a lack of exercise as an undesirable side effect. Some studies have investigated the issue of adverse side effects.

5.1.3.1. Role of Vitamin D

5.19	Consensus-based Recommendation	checked 2020
EC	In people at high risk for skin cancer (e.g.: transplant recipients, immunosuppressed patients) who practice consistent, extensive sun protection, vitamin D levels should be checked and vitamin D supplements given where necessary.	
	Strong Consensus (100%)	

Vitamin D plays an important role in calcium balance and bone metabolism.

Sun protection measures reduce cutaneous vitamin D synthesis. Consistent sun protection may promote vitamin D deficiency in certain groups of individuals [394].

Srikanth et al. [395] found an inverse association between skin cancer and fractures: older individuals with a fracture were less likely to have NMSC, which was interpreted as lower cumulative lifetime sun exposure. Avoiding sun exposure may have adverse long-term consequences for future bone health. A review reported inconsistent studies on the reduction of fractures by administration of calcium and vitamin D [394]. However, the analysis showed a reduction in falls in the elderly with the administration of vitamin D.

Ulrich et al. [392] found no differences in vitamin D levels after 24 months in organ transplant recipients who practiced maximal sun protection compared with the control group.

Nevertheless, they recommend that especially in risk groups (immunosuppressed, transplanted, etc.) who practice intensive sun protection, the vitamin D level should be checked and vitamin D should be substituted if necessary.

In a prospective cohort study, the 25(OH)D level was found to be higher in children with fair phenotype (fair skin, sunburn spots, often sunburned), compared to children with darker phenotype, although the former were more likely to use sunscreen and wear protective clothing according to their parents. The authors conclude that vitamin D synthesis in low-pigmented skin at northern latitudes is not completely suppressed by use of sunscreen or clothing. The study's validity is limited by the fact that children were studied in the 1990s, i.e., at times when awareness about adequate sun protection (e.g., in terms of sufficient amount of sunscreen) may have been less

pronounced. In addition, some variables, e.g. 25(OH)D level, were determined only once per child [396].

Lindquist et al. [397]; [398]

examine associations between sun exposure behaviours and all-cause mortality in a cohort study. They conclude that avoidance of sun exposure (never sunbathing, either on holiday or in summer, and never visiting solariums) is a risk factor for all-cause mortality in countries with low UV intensity. They speculate that the effect is due to vitamin D deficiency. However, vitamin D levels were not studied, nor were individual sun protection behaviours interrogated. Conclusions on a causal relationship between sun exposure behaviour and total mortality are not possible on the basis of the analyses.

Within the framework of an interdisciplinary scientific discourse initiated by the BfS and the UV Protection Alliance to harmonize hitherto contradictory recommendations regarding UV exposure for the formation of the body's own vitamin D, a consensual recommendation on UV radiation and vitamin D was developed [399]. In particular, the following recommendations were made:

- According to current findings, for sufficient vitamin D synthesis it is sufficient to expose the face, hands, and arms uncovered and without sunscreen two to three times per week to half of the minimum sunburn-effective UV dose (0.5 MED), i.e., half of the time in which one would otherwise get a sunburn without protection. For people with skin type II, for example, this means an exposure time of about 12 minutes at high sunburn-effective UV radiation intensities (UV index 7).
- Sunburn should always be avoided.
- UV protection measures should be taken for longer stays in the sun.
- The UV index (UVI) is recommended as a guide to the UV irradiance that causes sunburn and when UV protection measures should be taken. The UV index is a globally uniform measure of the highest possible sunburn-effective UV irradiance on a given day. The individual UVI values are assigned recommendations for the fair-skinned population regarding the UV protection measures to be taken.
- In the case of infants, children, and adolescents, particular care should be taken to avoid high levels of UV exposure and sunburns, because especially in childhood and adolescence, high levels of UV exposure and sunburns increase the risk of developing skin cancer later on.
- Infants should not be exposed to direct sunlight.
- Strong, non-medically controlled UV irradiation (sun or solarium) for the purpose of vitamin D formation, self-therapy of a vitamin D deficiency, or tanning is strongly discouraged.
- A vitamin D deficiency can only be diagnosed and treated by a doctor. Supplementation or medication with vitamin D preparations should be carried out under medical supervision. Infants and small children up to the second experienced early summer should receive vitamin D preparations.

5.1.3.2. Effect of Vitamin D on the Development of Various Types of Cancer

5.20	Consensus-based Statement	modified 2020
EC	For sufficient vitamin D synthesis, it is sufficient to expose the face, hands, and arms uncovered and without sunscreen two to three times a week to half of the minimum sunburn-effective UV dose (0.5 MED), i.e., half of the time in which one would otherwise get a sunburn without protection.	
	Strong Consensus (97%)	

Moderate exposure to UV radiation and high vitamin D levels may have a protective effect on the initiation and development of various cancers, including malignant melanoma. However, the available evidence regarding an association between overall cancer risk and vitamin D supply is insufficient.

One review addressed the question of whether sun exposure has a protective effect on the development of other cancers. It is possible that there were protective effects of sun exposure on the development of breast and prostate cancer. However, the studies were inconclusive; no association was found for the other cancers

[400].

Tuohimaa et al. [401] showed in a historical cohort study that individuals with skin cancer (all types) had an increased risk of another primary cancer. Individuals who lived in sunnier latitudes had a slightly lower risk of a second tumour, which was attributed to a possible protective effect of vitamin D.

A review paper by Krause [402] compiled studies indicating a protective effect of sun exposure on colon and breast cancer. The authors also conclude that high levels of vitamin D appear to be a protective factor for cancer. The optimal UV exposure, the target level of circulating vitamin D, and whether vitamin D is the only way is not conclusively understood. Due to study deficiencies, the results have limited validity.

Schwalfenberg [394] cited studies in a review indicating a protective effect of vitamin D on heart disease and certain cancers. However, the review was methodologically flawed.

Using various ecological studies, WHO [International Agency for Research on Cancer (IARC). et al. 2008] examined whether there is a causal relationship between vitamin D levels and cancer risk. The results indicate an increased risk of colorectal cancer and colorectal adenoma with low vitamin D levels. Other studies again found no effect on the incidence of colorectal and breast cancer. This apparent contradiction between observational studies can be attributed to several factors, such as the use of low doses or an additional interaction with hormone therapy within the study. Epidemiological data suggest that vitamin D levels influence cancer progression and thus cancer mortality, and rather influence cancer incidence less.

Even the DGE [Linseisen, J. et al. 2011] could not find consistent and clear results based on various meta-analyses on the relationship between vitamin D intake and the risk of different types of cancer. A conclusion cannot be drawn due to the inconsistency of the available results. The evidence regarding the association between individual cancer types or overall cancer risk and vitamin D intake is insufficient.

Lucas et al. [Lucas, Robyn M et al. 2007] found an association between vitamin D deficiency and increased risk of disease. Observational studies indicate an increased risk of colorectal cancer attributable to low vitamin D intake. No further conclusions could be drawn regarding other cancers, as either no results were available or the results already available were inconsistent.

Due to this inconsistent data situation, this S3 guideline follows the consensus recommendation on "UV Exposure for the Formation of Endogenous Vitamin D" of the scientific authorities, professional societies, and professional associations of radiation protection, health, risk assessment, medicine, and nutritional sciences (https://www.bfs.de/DE/themen/opt/uv/wirkung/akut/empfehlung-vitamin-d.html).

5.2. Status Quo: Sun Protection and Exposure Behaviour

I.-M. Hübner, A. Dost, E. Grossmann

The following chapter provides an overview of the sun protection behaviour of different population groups. Differences are highlighted, and in particular, vulnerable population groups are identified and factors influencing sun protection behaviour are shown.

5.2.1. Sun Protection and Exposure Behaviour of Different Population Groups

Differences can be observed in the sun protection and exposure behaviour of different population groups. These are described below. It is important to note that the data is often based on self-reporting by respondents and rarely on observation, and representative data for Germany could not be identified during the research.

General Population

The main sun protection measures taken by the general population are the use of sunscreen products, wearing suitable clothing, and seeking shade. Nevertheless, a large proportion of the general population reports having suffered a sunburn at least once in their lifetime.

- **Younger people in particular are more likely to intentionally expose themselves to the sun**

The cross-sectional study by Haluza, Simic, and Moshammer [405] examined the sun exposure behaviour of the population of Austria. Data from 1,500 participants aged 18 to 74 years were analysed. Responses to questions on sunscreen use, repeated sunscreen application, avoidance of midday sun, seeking shade, wearing protective clothing, hats, and sunglasses were combined into a sun protection score. The population has a mean score of 2.6 on a scale of 1 (always) to 5 (never). In addition, sun exposure was recorded, dichotomized by 0-5 days of sun exposure in the past year as no exposure, and more than five days in the past year as exposure. Sun exposure behaviour decreases significantly with increasing age of the study participants. The highest proportion of sun exposure is found in the age groups 18-49 years with 60.3 to 51.2% (proportion of respondents who reported more than five days of sun exposure during the past year), as well as participants with a child (51.7-50.3%) and divorced or widowed study participants (58%). In addition, increased sun exposure behaviour was observed among individuals with a higher level of education as well as a higher

socioeconomic status (50.1%, p=0.039; 51.0%, p=0.001). Sports activity, intention to tan, darker skin type, use of tanning beds, and sunburns are significantly associated with increased sun exposure behaviour.

In an interview survey conducted in Germany, 865 people were asked about their sun exposure and sun protection behaviour. A sunburn had already occurred in the lifetime of 97% of the participants. Thirteen percent had never used sunscreen. Using hats and clothing for sun protection was reported by 56% of participants. In addition, 94% of participants reported never having used a tanning bed. The group with regular use of sunscreen was found to spend significantly fewer days in the sun compared to the group with no use of sunscreen at all (60 days vs. 90 days, p=0.035). Furthermore, a positive association was found between sunburns experienced and sunscreen use (p<0.001) [403].

The study by Gavin et al. [404] examined the sun protection behaviour of participants at three survey time points in 2000, 2004 and 2008. Sun avoidance is proportional to age in the Northern Ireland sample. In 2008, 16% of ≥65 year olds and 2% aged 16-24 years reported never going out in the sun (p < 0.001). Avoidance of midday sun was reported by 27% of the ≥45 year age group compared to 13% of the 16-24 year age group (p=0.002). Younger participants aged 16-24 years were significantly less likely to report never going out in the sun (p=0.015), avoiding midday sun (p= 0.004), staying in the shade (p<0.001), or wearing a hat (p<0.001). The 2008 survey shows that women are more likely to stay out of the sun than men. Six percent of men and eleven percent of women reported never going out in the sun (p=0.002). Of women, 30% reported avoiding the midday sun, as did 19% of men (p<0.001). Staying in the shade was reported by 29% of women compared to 18% of men (p<0.001). Twenty-three percent of both men and women reported using clothing that protects from the sun. In addition, men were significantly more likely to use headgear (37% vs. 28%, p=0.001).

5.2.1.1. Gender-Specific

A gender-specific difference in sun exposure is shown in several studies. Women are more likely to seek shade for protection compared to men. In addition, sunscreen is used more by women, with a Norwegian study indicating a decrease in sunscreen use by women.

- **Men and women differ in their sun protection behaviors, with women more likely to protect themselves from severe UV exposure. The extent of the gender differences differs for different sun protection-related behaviours.**

Ghiasvand et al. [406] used data from the population-based Norwegian Woman and Cancer Study (NOWAC) to investigate changes in the sun protection behaviour of Norwegian women aged 41 to 75 years over the period 1997 to 2007. It was found that the use of sun protection products among Norwegian women increases over the years, but this is not accompanied by a reduction in the number of sunburns.

The cross-sectional study by Haluza et al. [405], which is representative for the population of Austria, showed that women protect themselves more from the sun overall compared to men. They used sunscreen more often, avoided the midday sun, sought out shade, and wore sunglasses (each p ≤ 0.001). Men were more likely to wear hats to protect themselves from the sun compared to women.

The study by Antonov et al. [403] showed a statistical difference in sunscreen use. Of the men, 15%, and of the women, 11%, had never used sunscreen in their lives (p=0.04).

A study conducted in Sweden on the sun protection behaviour of skin cancer patients (as intervention group) and patients with seborrheic keratosis (as control group) highlighted gender differences. Frequent sunbathing is more common for women ($p<0.05$), as is the use of sunscreen ($p<0.001$). Additionally, women were more likely than men to report seeking shade for sun protection ($p<0.001$). Use of tanning beds was more common among women [407].

The study by Blashill and Safren [408] examined the association between sun protection behaviours and sexual orientation among men aged 16 and 29 in the United States. Men belonging to a sexual minority (bisexual, homosexual) were significantly more likely to use tanning beds (27%) than heterosexual men (8.6%, p=0.002). They also tanned more often in the sun (22.3% vs. 14.5%, p=0.26). Between 70.5% and 75.9% of the men surveyed reported not using sunscreen.

5.2.1.2. Children and Teenagers

Childhood and adolescence are critical periods for reducing the risk of skin cancer. Sun protection measures are of particular importance at this stage of life. Studies for the general population have already provided evidence that younger population groups in particular are intensively exposed to the sun.

- **Although physical sun protection measures (exposure avoidance, textiles) are particularly recommended, sunscreens are the sunscreen of choice for children and adolescents, along with hats for young children.**

Ackermann et al. [409] studied the sun protection behaviours of fifth, eighth, and eleventh grade students with mean ages of nine, eleven, and 15 years. A total of 1,154 students participated in the questionnaire survey. Of the students, 60.2% reported having suffered at least one sunburn. Two sunburns were reported by 30.1% of the students, and 11.2% reported at least three sunburns. In the previous year of the survey, 43.2% of students had a sunburn. Sunburns occurred in association with aquatic activities (50.3%), other sports activities (23.8%), and non-sports activities (25.9%). Half of the children reported that they had used sunscreen. Not having used sunscreen was the cause of sunburn in 26% of the children. Five percent would have stayed in the shade. In general, 69.2% of children reported using sunscreen regularly during the summer. Of these, two-thirds applied sunscreen repeatedly during sun exposure. Explicitly after swimming, sunscreens were reapplied by 55%. In winter, 39.5% of children regularly used sunscreen for sports activities. In addition, almost 90% of older students used a sun protection factor of 20 or higher. Shade is sought out by 32.8% of students when possible. Of students in grades eight and eleven, 31.5% reported wearing long-sleeved tops for protection from the sun.

An observational study by McNoe and Reeder [410] examined the sun protection behaviours of 1,225 13- to 18-year-old students during school athletic activities. Observations took place on days with a UV index greater than seven. Tops with an arm length longer than the elbows were worn by 19% of the students. Pants longer than knee length were worn by 21.4%. Sun protective hats were worn by 3.4% and sunglasses by 1.7% of students. Sunscreen was provided at five of ten events and shade was carefully provided in four. Shade was not generally available to students.

Basch et al. [411] examined the trend pattern for sunscreen and tanning bed use among high school students in the United States from 2001 to 2011 using data from the Youth Risk Behaviour Surveillance System (YRBSS). A reduction in sunscreen use among surveyed students from 67.7% (2001) to 56.1% (2011) was observed. In 2009, 15.6% of the respondents reported using tanning beds. In 2011, the figure was 13.3%. Fair-skinned females accounted for the largest proportion (37.4% in 2009, 29.3% in 2011). The prevalence of tanning bed use increased with increasing age of the respondents.

Dobbinson et al. [412] conducted telephone interviews with 1,140 parents of children aged zero to eleven years to assess their sun protection behaviour. On the weekend prior to the interview, 73% of the children were outside during the time of highest UV radiation. Sunscreen was used as a sun protection measure by 58% and hats by 64% of the children. Fourty-two percent of the children wore a sun protection hat. A wide brimmed hat was worn by 33% of the children and/or a hat with a neck covering was worn by 20% of the children. Two sun protection measures were reported for 61% of the children. Three or more sun protection measures were used by 29% of the children.

The prospective follow-up study by Dusza et al. [413] examined the sun protection behaviours of 360 children aged ten to 14 years. At baseline, 52.5% of students reported having experienced at least one summer sunburn. Liking tanned skin was reported by 53% of the students surveyed at baseline. After three years, this percentage increased to 66% ($p<0.001$). In addition, more children spent time in the sun tanning (21.8% vs. 39.8%, $p<0.001$). At baseline, 50% of children reported using sunscreen when outdoors for at least six hours; this was 25% at follow-up ($p<0.001$). The odds ratio for girls to use sunscreen frequently or always was 0.4 and for boys, 0.3.

In Switzerland, 887 students aged eight to 17 years in grades three, six, and nine were surveyed about their sun protection behaviours. More than half of the students (56.3%) reported having experienced sunburn in the previous year of the survey. Most students experienced sunburn related to aquatic activities (52.3%), 19.6% while sunbathing, 15.2% during other outdoor activities, 4.8% during winter sports, and 1% while working outdoors. On sunny summer days, 36.3% of the students surveyed almost always used sunscreen, 19.4% often, 24.9% sometimes, and 18.2% rarely to never. Boys were less likely to use sunscreen compared to girls. This also affected sixth and ninth graders compared to third graders, dark-skinned students compared to light-skinned students, and students whose parents had an education or no vocational degree compared to students whose parents had a higher education. Nearly half (49.3%) of the sixth and ninth graders surveyed applied sunscreen once in the morning. Sunscreen was used multiple times a day by 34.9% of the students. Girls were significantly more likely than boys to repeat sunscreen application (44.2% vs. 24.3%; $p<0.0001$) and light-skinned children and adolescents were more likely than those with darker skin (50.5% vs. 23.8%, $p=0.006$). After swimming, 43.7% of students reapplied sunscreen. Students used sunscreen with an SPF greater than/equal to 20 at a rate of 56.3%. Shade was sought by 32.2% of students when possible. When temperatures were uncomfortably high, 66.1% went to the shade. A shoulder-covering top was worn by 49.9% of the respondents on sunny summer days [414].

5.2.1.3. Skin Cancer Affected

- **Skin cancer patients show better sun protection behavior than comparison groups.**

In a case-control study, Falk et al. [407] investigated sun exposure and protection behaviour of 55- to 69-year-old skin cancer patients compared to patients with seborrheic keratosis. Patients with a history of skin cancer were significantly less likely to go out in the sun to get a tan ($p<0.01$). They also protected themselves from the sun to a greater extent by seeking shade ($p<0.001$) and using sunscreen ($p<0.001$). Being more careful in the sun was reported by 77.9% of skin cancer patients. In comparison, 20.5% of patients had not changed their self-reported behaviour in the sun and 1.6% were less cautious.

5.2.1.4. Transplant Recipients

- **Knowledge about an increased risk of skin cancer and the implementation of protective behaviors are in need of improvement among organ transplant recipients.**

Recipients of donor organs are particularly at risk for developing skin cancer due to long-term use of immunosuppressants. In the study by Vural et al. [415], 70 organ transplant recipients were interviewed about their knowledge of the increased risk of skin cancer for transplant recipients and their sun exposure behaviours. Forty-eight organ recipients (68.6%) reported being informed about the importance of avoiding sun exposure. That exposure to UV radiation can have dangerous consequences was known by 38 patients (54.3%). The causal relationship between skin cancer and UV radiation was known by 28 of the respondents (40%). Of organ transplant patients, 44.3% could not recall being informed about sun protection measures by clinical staff, while 55.7% of the respondents were educated about protective measures by dermatologists and/or nurses; 42.9% of patients had their skin examined by a dermatologist at least once after organ transplantation, and 14.3% of transplant recipients saw a dermatologist regularly (once or twice a year). Before organ transplantation, three patients had used sunscreen irregularly (only when vacationing in sunny areas). After transplantation, 25 patients started using sunscreen, so 28 patients reported using sunscreen. Eighteen patients reported using sunscreen only on sunny days or holidays. Other sun protection measures, such as hats, sunglasses, or long-sleeved tops, were used by 19 patients. Eight patients used all types of sun protective clothing when outside.

5.2.1.5. Beachgoers

- **For beachgoers, sun protection measures are very much focused on the use of sunscreen. Other possible measures (clothing, seeking shade) are hardly used.**

Heerfordt, Philipsen, and Wulf [416] investigated the sun exposure behaviour of beach users in Denmark using webcam photos. During the period July 2015 to October 2015, a total of eleven days were designated as beach days. These are characterized by a daily average temperature of at least 20°C and at least ten hours of sunshine. A total of 2,259 beach users were observed on these eleven days. Of these, 26% wore clothing that covered more than 20% of the body surface area. Forty-six percent of beachgoers were present during the period from 12:00 to 15:00. The number of beachgoers peaked at 3:00 pm on weekend days and at 4:00 pm on workdays. At 1:00 pm, the minimum of 10% of people wearing clothing covering more than 20% of the body surface was observed. The average sun exposure time was 142 minutes at noon.

The interview survey by Cercato et al. [417] examined the sun protection behaviours of Spanish-speaking beachgoers. A total of 630 individuals were interviewed, who were predominantly female (62%) and had an average age of 30 years. Voluntarily exposing themselves to the sun frequently was reported by 80% of beachgoers. Seventy-six percent said they did so at the beach, 35% when playing sports, 29% in the mountains, and 22% in the pool. Sunscreen was used frequently (often/always) by 79.1% of beachgoers. Frequently using a sunscreen with a high SPF was reported by 81.2% of respondents. Using sunscreen with a high SPF throughout the day was often/always done by 62.3% of the respondents. Of beach goers, 76.4% apply sunscreen right at the beginning of sun exposure, 17.7% apply sunscreen 20 minutes before exposure, and 5.8% apply sunscreen only during exposure. Repeated application of sunscreen was frequent by 53.2% of beachgoers. With the exception of sunscreen, other sun protection measures are rarely used. Only 39.6% of respondents often or always seek shade during midday. A hat is worn often/always by 21.6% of beachgoers. T-shirts are worn frequently by 18.7% of interviewees. Sunglasses are often/always used by 49.5% of the interviewees.

5.2.2. Use of Solariums

The National Cancer Aid Monitoring (NCAM) [418] has been collecting data on sunbed use in Germany annually since 2015. Using standardized telephone interviews, 3,000 people aged 14 to 45 were surveyed. In 2018, a total of 8.8% of the participants had visited a solarium in the previous 12 months. This represents a decrease from the 11% prevalence identified in 2015 [419]. The overall frequency of tanning bed visits in the previous 12 months has also decreased from an average of 11.4 visits (2015) to six visits (2018).

- **There is no longer a gender difference in tanning bed use between men and women.**

Gender differences could be found in the first two waves of the previously mentioned study. In 2015, women used sunbeds more frequently (13.3%) than men (8.8%). However, a decrease can be seen among female respondents, while the use of tanning beds among men remained constant during the four waves of the survey. This is attributed to a higher receptivity of women to health campaigns. Due to this, the prevalences in 2017 and 2018 equalize, so that a gender difference in the use of sunbeds is no longer apparent [418].

- **Despite the ban on tanning beds for minors, there are still children and adolescents among tanning bed users. The prevalence is on the rise.**

A decline in the use of sunbeds can be observed among adult participants. This is most pronounced in the 18 to 25 year-old group and has almost halved from 16% in 2015 to 8.7% in 2018. In contrast, prevalence among 14 to 17 year-olds has increased from 1.6% to 4.6%. Since the enactment of the NiSG 2008, minors are prohibited from visiting a tanning salon. The staff of solarium businesses must prevent children and adolescents from using solariums [418].

- **Persons with a migration background continue to use sunbeds more frequently than persons without a migration background. In the trend analyses, this development continues.**

Persons with a migration background used sunbeds significantly more often in 2018 (12.1%) than participants* without a migration background (8%). While a decrease in prevalence can be observed among persons without migration background, this does

not apply to respondents with migration background [418]. However, it remains open in these analyses which differences are to be recorded within the heterogeneous group of migrants; further analyses are required here.

- **Socioeconomic variables (such as occupational status and education level) are associated with the use of sunbeds.**

In the first three waves of the survey, significantly less frequent use of sunbeds was found among unemployed persons. With regard to school education, significant differences in the use of sunbeds are evident. Persons with a medium level of school education visit sunbeds most frequently. For persons with low school education, a significant decrease in prevalence between 2015 and 2018 can be observed (Diehl et al., 2019).

5.2.3. Predictors of Sun Protection and Exposure Behaviour

The predictors of sun protection and exposure behaviour are diverse. They range from intrinsic factors (such as body self-perception, one's phenotype, smoking and alcohol consumption, education level, sexual orientation, leisure time behaviour patterns, and ancestry) to external influences (such as friends, to residence in certain geographic regions).

Predictors of sun protection and exposure behaviour include:

- **Social influences: parents, peers, friends, relationship status**
- **Origin**
- **Appearance and self-perception, intention to tan**
- **Educational level, socioeconomic status**
- **Age**
- **Gender**
- **Skin type**
- **Leisure behaviour**
- **Smoking behaviour**
- **Sexual orientation**
- **Media**
- **Weather influences**

A systematic review by Gambla et al. [419] provides an overview of factors influencing tanning behaviour among American college students. The review includes 23 cross-sectional studies from the US. Younger students were more likely to use tanning beds. In all included studies, female students had a greater intention to tan than male students. Light-skinned students were more likely to have the intention to tan than students of colour. Motivation to tan is related to attitudes about external appearance. Dissatisfaction with current skin tone represents the largest motivating factor. In addition, emotion- and health-related motives for sun exposure exist. Relaxation, mood enhancement, "energy recharge," treatment of skin diseases such as acne and psoriasis, increase in vitamin D levels, and stress reduction are given as reasons. Another reason for using tanning beds is the desire to maintain a basic level of tan, and thus supposedly counteract future sunburns. Sociocultural factors influencing tanning behaviour included parents and friends, the desire to please others, and watching reality beauty shows on television. Barriers to adequate sun protection behaviours were identified as misunderstandings about skin protection, underuse of sunscreen, lack of education about UV-related hazards, and lack of time, cost, and forgetting to use sunscreen.

In a cross-sectional study, Ackermann et al. [409] surveyed not only the sun protection behaviour of schoolchildren but also the factors influencing it. The parents of 61% of the students surveyed encouraged their children to protect themselves against UV radiation. Among eighth and eleventh grade students, 55.6% have been informed about the dangers of UV radiation by their parents. Students who were encouraged to take protective measures by their parents were more likely to report using sunscreen. Students cited forgetting (34.4%), preferring tanned skin (25.3%), having a naturally darker skin tone (18%), and feeling uncomfortable with sunscreen on their skin (11%) as reasons for not protecting themselves from the sun's rays. Sunscreen was perceived as too tiring by 6.9% of students surveyed.

The study by Petersen et al. [420] comparatively investigated the sun exposure behaviour of Danish and Spanish beach holidaymakers in Tenerife (Spain) and of Danish and Austrian skiers in Wagrain (Austria). Sun exposure was determined over six days in each case using a personal electric UV dosimeter and half-hourly diary entries. The entries showed that the proportion of Danes who spent time on the beach between 13:00 and 17:00 was more than double that of the Spanish. In the time interval from 7:00 to 18:30, 68% of the Danes and 57% of the Spaniards spent their time outside ($p < 0.0001$). For the time interval from 12:00 to 15:00, this was true for 92% of the Danes and 81% of the Spaniards ($p = 0.0001$). In both time intervals, the Danes spent significantly more time outdoors than the Spaniards ($p < 0.0001$). The evaluation of the UV dosimeters confirmed the results of the diary entries. Moreover, Danish beachgoers exposed 50% of their skin to UV radiation, while Spanish beachgoers exposed 44% of their skin ($p = 0.003$). In this survey, risky sun exposure behaviour was defined as a minimum exposure of 26.5% of the upper body skin area. Danish beachgoers exhibited risky behaviour for more than 4.5 hours per day according to this definition. For Spanish beachgoers, this amounted to 2.6 hours per day ($p < 0.0001$).

An observational study shows that students aged 13 to 18 years are more likely to wear sunscreen hats when cloud cover is less than 50% ($X^2=12.85$, $p<0.05$) and temperatures are above 20°C ($X^2=8.27$, $p<0.05$) [410].

Sunscreen use is more common among women with fair and olive skin than among dark-skinned women. Women with brown eyes and dark-haired women are least likely to use sunscreen. Women who are sensitive to acute and chronic sun exposure reported more frequent sunscreen use than less sensitive skin types. Sunscreen use is more common among women whose skin develops freckles after sun exposure. Sunscreen use increases with the number of small, symmetrical nevi located on women's arms and legs. Women who had more than four sunburns per year during childhood and adolescence were more likely to use sunscreen with an SPF ≥ 15. Sunscreen with an SPF ≥ 15 was used by 30% of the women surveyed who spend at least one week of vacation sunbathing in southern countries. For holidays in northern regions, this was true for 13% of Norwegian women [406].

Dobbinson et al. [412] investigated the influence of parents on sun protection in children aged zero to eleven years. Of the parents, 88% strongly believed that sunburn during childhood was dangerous. Forty-three percent agreed with a less sun-protective statement, such as: protecting the child is too much effort; sun tanning is attractive; the child is resistant to hats or sunscreen. If parents use certain sun protection measures, the likelihood of children being protected from the sun with appropriate measures increases. An exception is when parents wear long-sleeved clothing. Sunscreen with a sun protection factor ≥ 15 is twelve times more likely to be used.

For wearing long pants the OR is 10.3, while staying in the shade has an OR of 9.6 ($p<0.001$). The odds ratio for wearing a hat is 3.1 ($p<0.01$).

Parental influence on sun protection behaviour of students aged eight to 17 years was surveyed by Reinau et al.[414]. Of the students surveyed, 52.5% reported that sun protection measures are discussed at home and that they are regularly encouraged by their parents to protect themselves from the sun. Another 18.5% of students are informed by their parents. Sun protection is less frequently discussed in families with a lower level of education ($p<0.0001$). In addition, 41.1% of third graders have sunscreen applied by their parents. 27.2% of students are reminded to apply by their parents and do so independently. Seeking shade is reminded by parents of 18.8% of students and 33.1% are encouraged to wear a t-shirt for sun protection when swimming or playing outside.

5.2.4. Motives for solarium use

As part of the National Cancer Aid Monitoring of Tanning Bed Use (NCAM), motivations for visiting a tanning bed were surveyed. In the last survey wave in 2018, the most frequently cited motive was to increase attractiveness (60.5%). 58.3% of respondents also cited relaxation as a reason for their tanning bed visit. Pre-holiday tanning was cited as a motive by 52.3% of respondents. 45.7% justified their solarium use with the desire for light and warmth, 29.8% named the formation of vitamin D. Preventive health care was given as a reason by 22.8%, skin diseases by 14% and medical recommendation by 7.9% of the respondents. The data largely correspond to the previous waves of the survey, with only a slight decrease for relaxation, light and warmth, and a slight increase for vitamin D formation.

5.3. Status Quo: Skin Cancer-Related Knowledge, Perceptions and Attitudes

E. Baumann, I.-M. Hübner, S. Weg-Remers, E. Grossmann

5.3.1. Knowledge about Skin Cancer and Risk Factors of the Population

- **Basic knowledge about risks and hazard potentials of UV radiation, especially skin cancer, is available in the German population.**

Börner et al. [421] conducted a cross-sectional survey on the UV risk perception of the German population, representative of the total German population aged 14 and over. The data collection was carried out via standardized telephone interviews of 1,501 persons. Overall, the survey showed that knowledge of UV risks is present and realistic in the population. The assessment of the severity of health consequences due to UV exposure (skin cancer, skin aging, and sunburn) was high overall. The assessment of personal risk from UV exposure was in the middle range (higher for women and decreasing with age, no differences in education). UV risks are also present in everyday life with a medium risk assessment. Nevertheless, the benefit perception of UV exposure is high overall: more than half agreed to a large extent or completely that tanned skin is attractive and sun feels good; whether UV exposure is healthy was viewed more skeptically (see conclusions on the influence of knowledge under Chapter 5.4.1).

Eichhorn et al. [422] conducted a telephone survey on the level of knowledge of UV radiation and sun protection. For this purpose, 545 persons between 14 and 45 years of age from two Bavarian districts were asked largely open-ended questions. Women were slightly overrepresented, while young people were rather underrepresented. In general, 97% of the respondents are aware of sunburn and skin cancer as consequences of UV radiation, whereas photoaging is not well-known. Furthermore, almost all respondents had general knowledge about sun protection (98.5%). Sunscreen was mentioned most frequently (91%), followed by clothing (54%), limited outdoor exposure (46%), and avoiding the midday sun (45%).

International studies from Northern Ireland [404] and the USA [423] also show that correct knowledge about skin cancer and its risk factors is available in the population.

- **Information deficits regarding prevalence, symptomatology, early detection, and risk factors of malignant melanoma are evident in various populations. Furthermore, there is insufficient knowledge about the risk potential of sunbeds and their legal regulations (especially among young women). No knowledge is available on this subject for Germany.**

Hajdarevic et al. [424] carried out a country comparison of the awareness of risk factors of malignant melanoma. For this purpose, 8,355 adults over 50 years of age in Denmark, Norway, Sweden and Northern Ireland were interviewed by telephone. The lowest risk perception is for childhood sunburns (especially in Norway, only 63%). Comparatively high-risk perception was found for sunbed use and altered moles (91% and 97%, Norway, Sweden, and Northern Ireland lower than Denmark).

Boynton & Oxlad [425] investigated knowledge and risk perception regarding sunbed use and melanoma in young women. To do this, 27 young women (seven use sunbeds, 20 do not) aged 18 to 26 years were interviewed in six focus groups/group interviews in Australia. In general, there is awareness of the need for sun protection, but there is a lack of information regarding malignant melanoma. A need for information is evident here regarding prevalence, symptomatology, early detection, and risk factors. Furthermore, the participants have only a rough knowledge about the legal regulation of solariums. Also using qualitative methods, Gordon et al. [426] analyzed tanning bed use and its problem perception with 22 mothers and their 15 to 17-year-old daughters in the United States. Overall, problem perceptions of tanning bed use tend to be low compared to other forms of risk behaviours (e.g. smoking).

- **Adolescents/young adults and men show lower knowledge of sun protection and skin cancer prevention, as well as lower risk perception, than women and older individuals.**

In the study by Eichhorn et al. [422] already mentioned above, gender differences are shown in the analysed topics on the level of knowledge about UV risks and sun protection behaviour in Bavaria. Overall, women show significantly better knowledge and sun protection behaviour than men and adolescents.

In an international review (non-systematic), Keeney et al. [427] conclude that women overall show a higher knowledge and problem awareness than men regarding skin cancer risks. Butler et al. [428] confirm these results for Great Britain, and Hajdarevic et al. [424] demonstrated the gender differences in a country comparison, as men were found to have a lower risk perception than women in all countries.

The intervention study by Kyle et al. [429] assessed risk perception for various forms of cancer in 478 adolescents aged 11-17 years. The adolescents were asked about

this in writing at four different schools in the UK. Overall, there is a low level of awareness regarding risk factors for developing cancer. For example, only 52% of participants mentioned sun exposure as a risk factor. A gender difference was not evident among adolescents.

- **Among parents of kindergarten children, an overall good knowledge about risk factors of skin cancer, sun protection, and as well as a positive attitude towards sun protection measures are evident. However, knowledge gaps exist regarding the risk of long-term intensive sun exposure as well as the supposed protective function of clouds.**

Gefeller, Uter & Pfahlberg [430] conducted three cross-sectional surveys over a period of 19 years. A total of 8,184 parents of three- to six-year-old kindergarten children were surveyed about their knowledge and beliefs about skin cancer risks. In general, it can be seen that parents' knowledge became increasingly specific and correct in terms of distinguishing proven and non-proven risk factors for skin cancer. For example, knowledge of fair skin/blond hair and childhood sunburn as risk factors has improved by 20% each. Knowledge of having many moles as a risk factor increased by 19%. Furthermore, attitudes towards sun protection behaviour also improved significantly when comparing the first and last wave of the survey. Sun protection of children is rated as very relevant and necessary by parents overall. This applies especially to sun protection at the beach, in the midday sun, and during outdoor activities, while sun protection in the evening sun and on cloudy days is rated as less relevant. Knowledge gaps that have grown over time are that prolonged and intense sun exposure is underestimated as a risk factor for skin cancer, and that clouds do not provide adequate protection from UV radiation during midday hours.

The review by Keeney et al. [427] shows that parents are well informed and sensitized regarding the necessary sun protection of their children, which is mainly attributed to campaigns and educational programs.

- **Parents see both advantages and disadvantages in sun protection behaviour for children, with the disadvantages outweighing the advantages to some extent.**

An Australian study by Hamilton et al. [431] investigated parents' knowledge and attitudes about sun protection in children. Twenty-one parents (14 mothers and seven fathers) of two- to five-year-old children were interviewed in five focus groups. It was found that knowledge about general sun protection recommendations for children was broadly available among parents. The parents see various advantages of sun protection behaviour for themselves and the child: reduction of sunburn and the risk of cancer, greater well-being for children (cooler, being able to spend more time outside), early development of healthy behavioural routines, and their own relief from feelings of guilt. However, disadvantages are also seen as: protective measures being uncomfortable or unpleasant for the child, own inconvenience (e.g. time-consuming, overcoming children's reactance, expensive, soiling of clothing), or health-related (sun protection limits absorption of vitamin D). Overall, the perceived barriers are often dominated by those resulting from the interaction with the child.

5.3.2. Relationship of Knowledge, Perceptions, and Attitudes with Sun Protection Behaviour

- **Studies on the relationship between knowledge of the risks of UV radiation and skin cancer prevention have produced contradictory results.**

Overall, higher knowledge is associated with stronger protective behaviour in parts of the population. However, knowledge is not a reliable predictor of higher protective behaviour and lower risk behaviour. In particular, risk behaviour is practiced despite better knowledge when there is a high perception of the benefits of sunbathing and a positive attitude towards tanned skin.

The systematic review by Day et al. [432] determines the association of the population's level of knowledge about skin cancer with sun protection and -exposure behaviour. For this purpose, 34 international studies were included through the systematic literature search. Overall, the studies indicate that sun protection behaviour is associated with higher knowledge about skin cancer (22 of 33 articles). For other forms of sun exposure behaviour, the findings are not consistent: six studies examined the role of knowledge on sun exposure behaviour, finding one positive and one negative association each, alongside four non-significant results. In addition, ten studies are available, of which three identified a positive association, one identified a negative association, and six identified no association between knowledge and tanning behaviour in the general population.

Butler et al. [428] identified the sun protection and exposure behaviours of 1000 GP patients. In this study, those aged 16-39 years who were identified as having lower knowledge of skin cancer prevention reported higher sun exposure, higher likelihood of sunburn, and lower sun protection behaviour compared to the other age groups. Being affected by skin cancer (on one's own or in the family environment) is also not associated with higher sun protection behaviour or lower sunburn likelihood. Only women show, in parts, a more pronounced sun protection behaviour than men. However, in most cases where sunscreen is not applied, it is not due to lack of knowledge or the price of sunscreen; it is simply forgotten.

The review by Keeney et al. [427] found an overall high level of knowledge among the general population about UV radiation as a risk factor of skin cancer, with this being higher among women than men. However, the knowledge is often not translated into corresponding behaviour. Although women show better protective behaviour than men in accordance with their increased knowledge, higher risk behaviour is also observed here (conscious sunbathing and solariums).

In their cross-sectional study, Börner et al. [421] determined a high level of knowledge among the German population about UV risks and consequences. However, the assessment of personal risk from UV exposure and the presence of UV risks in everyday life is only in the middle range. The benefit perception of UV exposure is strong: tanned skin is attractive and sun feels good.

- **There are conflicting study results regarding the relationship between parents' knowledge of UV radiation and sun protection behaviours in their children. In part, parents' perceived disadvantages of sun protection counteract the potentially positive influence of knowledge on behaviour. Overall, however, more intense sun protection behaviour is evident among parents with high knowledge.**

The study by Hamilton et al. [431] mentioned above found that knowledge about sun protection recommendations for children is available among parents, but is not adequately implemented. Sun protection, contrary to the recommendations, is differentiated by season and focused on summer. Furthermore, the perceived

disadvantages of implementing sun protection measures seem to partly outweigh the benefits, especially with regard to interaction with the child.

The aforementioned review by Keeney et al. [427] provides a research overview regarding knowledge of skin cancer risk factors and protective behaviours. This showed a high level of knowledge among parents regarding sun protection in children. This is associated with parents practicing more intensive sun protection behaviour with their children than with themselves. Campaigns and educational programmes are primarily responsible for the higher sun protection behaviour of parents among children.

5.3.3. Sources of Information and Knowledge

- **Media represent the central source of information on skin cancer, UV radiation, and sun protection for adults.**

Butler et al. [428] identified the most relevant sources of information from 1000 GP patients regarding skin cancer. Seventy percent of respondents cited media as the most important source of information and only 7% cited the physician. For those affected by skin cancer, the physician was named as the most important source of information by 15% of the respondents.

In the Bavarian study already mentioned, Eichhorn et al. [422] conducted telephone interviews on the subject of UV radiation and sun protection and also asked the participants' sources of information. Eighty percent of the interviewees named the media as the central source of information, followed by 49% naming the doctor/pharmacist, acquaintances/family (47%), profession/school (32%), specialist literature (25%), and campaigns (9-10%).

A study in Northern Ireland [404] determined the central sources of information on sun protection for people aged 16 and over. The television was the most frequently mentioned source of information (79%), followed by magazines (52%), newspapers (49%), doctors (35%), and family and friends (31%). Overall, women show a higher information behaviour than men.

- **The information quality of YouTube videos is often low. In parts, misleading or incorrect information is provided, e.g., about vitamin D and sun protection measures.**

Ruppert et al. [433]

investigated YouTube videos as a source of information on sun protection behaviour and skin cancer. For this purpose, 281 international videos in six languages were evaluated. Overall, English-language videos are used significantly more often and have a higher rating response than videos in other languages. Across countries, videos on vitamin D were viewed most frequently, followed by videos on sunscreen, tanning beds, skin cancer prevention, and sun protection. Only 57% of videos discuss negative consequences of UV radiation. Videos on tanning beds and sunscreen contained false or misleading information (e.g. tanning beds for vitamin D) in 17 and 36% of the cases, respectively. Videos on sun protection (n=183) mentioned sunscreen most frequently (77%). Of the videos on skin cancer prevention (n=57), 51% recommend screening by a doctor and 42% recommend self-examination of the skin, 37% mention symptoms, 39% refer to increasing rates of skin cancer, and 37% refer to sunburn as a risk factor. Almost all (94%) of the videos on vitamin D recommend (usually solar) UV radiation for self-synthesis of vitamin D, while only 57% point out that this should be limited. References to risk groups (children, people with light skin, those with family

history of skin cancer) were found in one third of the videos, comparatively more often in German and Spanish. Seventy-seven percent of the videos were aimed at adults; 26% (also) at adolescents, and 9% at children as the target group. Medical experts were featured in 37% of the videos, most frequently in German (64%). Knowledge transfer seemed to be in the foreground in 72% of the videos, whereas 32% aimed for attention enhancement.

Need for Research

The overall study situation on the population's sources of information is rather weak; findings are based almost exclusively on cross-sectional studies and thus cannot be considered empirically validated. There is a need for theoretical foundation and higher methodological quality, given that very different indicators are used to measure similar constructs, making the establishment of standards and scales necessary. Findings are primarily based on low-complexity analyses (descriptive, bivariate) that produce little depth of field. There is a lack of systematic reviews and, especially for Germany, of a comprehensive data basis, as the transferability from countries with completely different framework conditions (UV intensity; skin types in the population) can be assumed to be limited.

5.4. Primary Prevention Measures for the Population

Revision: The chapter was prepared in collaboration with the WG Primary Prevention and the WG Population Information Base. The responsible WG is noted under each recommendation.

5.21	Consensus-based Statement	new 2020
EC	Measures of primary prevention of skin cancer start well before the development of a disease and aim to reduce risk factors for the occurrence of skin cancer. Therefore, the following risk factors and indicators are considered relevant as intermediate endpoints for the evaluation of primary prevention measures: • Sun protection and tanning behaviour, use of sunbeds, etc. • Knowledge, attitudes towards skin cancer, sun protection, and exposure • Number of nevi • Number of sunburns Most studies in primary prevention were only able to influence these intermediate endpoints. Because of the long time lag before skin cancer develops and multiple other influencing factors (confounders), it is extremely difficult, if not impossible, to assess the effect of preventive interventions to reduce skin cancer incidence.When evidence-based recommendations are made in the following, the corresponding evidence refers exclusively to the above-mentioned intermediate endpoints, not to the skin cancer risk itself. Because the risk markers described increase the risk of skin cancer, the guideline group assumes a benefit.*WG Primary Prevention*	
	Strong Consensus (100%)	

Another frequently considered endpoint of primary prevention interventions is the intention to change behaviour, which is used particularly in interventions that address psychosocial parameters. However, this measure is very imprecise, as a change in behavioural intention does not necessarily predict a change in behaviour (intention-behaviour gap).

The guideline focuses on the following three approaches:

- Change in knowledge
- Change of behaviour (behavioural prevention)
- Change in circumstances (relationship prevention)

5.4.1. Knowledge-Related Measures

Successful communication of knowledge about the effects of UV radiation and about adequate UV protective behaviour is a necessary but not sufficient component of behaviour-related primary prevention.

With regard to knowledge transfer on the subject of the effects of UV radiation and UV protection measures, there is evidence that a significant improvement in the level of knowledge is possible using different methods and with different target groups. Some studies also demonstrate a certain sustainability of the improvement in the level of knowledge.

5.22	Evidence-based Statement	modified 2020
LoE 1+ 2+	Educational measures on UV radiation and protective measures in kindergartens or schools can improve knowledge on UV protection. *WG Primary Prevention*	
	[434]; [387]; [435]; [436]; [437]; [438]	
	Strong Consensus (100%)	

Bränström et al. [435] showed in a randomized controlled trial that in randomly recruited adult participants from the Swedish population register, the use of brochures on sun protection resulted in a significant increase in knowledge and a decrease in positive attitudes towards sunbathing and tanning, especially among younger women [435]. No follow-up was conducted regarding the sustainability of the intervention.

Results of a randomized controlled trial by Buller et al. [434] showed significant knowledge gains in school children aged five to 13 years from computer-based instruction on sun protection, which were enhanced when combined with a one-hour presentation by teachers [434]. However, effects on sun protection behaviour were questionable and significant only in younger children and only in the combination group (computer-based instruction with additional teacher presentation).

Gritz et al. [436] found in a randomized controlled trial as part of the campaign "Sun Protection is Fun!", that the use of training sessions, a video, a newsletter, and a curriculum significantly improved sun protection knowledge among preschool staff, even two years after the end of the intervention [436]. This improvement in knowledge was associated with an improvement in sun protection behaviours (use of sunscreen, textile sunscreen, seeking shade).

Loescher et al. [387] howed in a randomized controlled trial that knowledge and understanding of sun protection can be improved in preschool children as young as four to five years old with the help of a curriculum adapted to the age group compared to

a control group. However, the study also shows that children in this age group are not able to translate this theoretical knowledge into practical behaviour on their own and without the help of adults [387].

A similarly school-based campaign in which adolescents were used as knowledge brokers for younger classmates and gave lectures on UV protection showed a significant increase in knowledge even six months after the end of the intervention (controlled before-after study, endpoint studied knowledge transfer) [437].

Bastuji-Garin et al. [438] showed significant improvement in knowledge among nine-year-old children as late as three months after a four-week school-based campaign using educational materials created with the help of dermatologists and health professionals [438] in an intervention study. This improvement in knowledge was associated with improved sun protection behaviours (use of textile sunscreen and sunscreen, and avoidance of outdoor exposure during the sunniest time of day) after the intervention compared to pre-intervention behaviours.

5.23	**Consensus-based Recommendation**	**new 2020**
EC	UV risk communication should address aspects relevant to everyday life, the subjective perception of the benefits of UV exposure, and the beauty ideal of tanned skin. An important starting point for communication should be social ideals and behavioural routines with regard to tanned skin and sunbathing. *WG Information basis population*	
	Strong Consensus (97%)	

Börner et al. [421] showed through their cross-sectional study on knowledge, perceptions and attitudes of adults with regard to UV risk perception that a high level of knowledge about UV risks and consequences in the German population does not automatically lead to increased protective behaviour. The perception of benefit, e.g., that tanned skin is attractive and sun feels good, is weighed against the assessment of personal risk. It influences behaviour regardless of knowledge level.

Boyton & Oxlad [425] surveyed young women in focus groups regarding their recommendations for campaigns aimed at achieving behaviour change. These reported that additional knowledge would only contribute to their behaviour change to a limited extent and that a change in the social ideal of beauty was necessary.

5.24	**Consensus-based Recommendation**	**new 2020**
EC	The media information on skin cancer prevention must be qualitatively and quantitatively expanded, since the media are the most important source of information for adults. *WG Information basis population*	
	Strong Consensus (100%)	

Butler et al. [428] identified the most relevant sources of information from 1,000 GP patients regarding skin cancer. For 70% of the respondents, media represent the most important source of information, while only 7% indicate the physician as such.

5.25	Consensus-based Recommendation	new 2020
EC	Digital media literacy as part of the health literacy of the population should be promoted in order to be able to find, understand, and assess the quality of targeted information on skin cancer and skin cancer prevention. *WG Information basis population*	
	Consensus (84%)	

Media, especially the internet, are important sources of information on skin cancer risks and protective behaviour, but the content quality is often low (see e.g. [433]). Sections of the population that use the Internet as their first source of information represent a high proportion in studies on health information behaviour. However, the appropriate handling and evaluation of information is difficult for other sections of the population. According to the statements of the Federal Agency for Civic Education, media competence needs to be promoted through pedagogically designed learning opportunities, especially for children and young people. The aim should be to encourage the individual to deal with media contexts in an appropriate, self-determined, creative, and socially responsible way. As a result, the individual can exercise cultural and political participation with the media competence gained [439].

5.26	Consensus-based Recommendation	new 2020
EC	Parents with children of kindergarten age as well as educators, teachers, and directors of day-care centres must be informed about UV radiation as a risk factor for skin cancer and about the insufficient protective function of clouds against UV radiation. *WG Information basis population*	
	Consensus (95%)	

Gefeller, Uter & Pfahlberg [430] conducted three cross-sectional surveys over a period of 19 years. Parents of kindergarten children were asked about their knowledge and perceptions of skin cancer risks. Gaps in knowledge were only found with regard to permanent and intensive sun exposure as a risk factor for skin cancer and an overestimated protective function of clouds against UV radiation during midday hours. In a study by Buller et al. [440] it was also shown that educators, teachers and directors of day-care centres also have a significant role to play in the transfer of knowledge and that their level of knowledge needs to be improved.

Hamilton et al. [431] showed through findings from focus groups that a weighing of advantages and disadvantages regarding sun protection for children takes place among parents. The disadvantages, which mainly concern the interaction with the child (sun protection measures are uncomfortable and unpleasant), seem to prevail in some cases.

5.4.2. Behavioural Preventive Measures

5.4.2.1. Conceptual and Communication-Related Design of Measures

Conceptual Design

5.27	Evidence-based Recommendation	modified 2020
GoR **B**	Interventions that target a sustained effect on behaviour must involve several components and must be implemented intensively and repeatedly. *WG Primary Prevention*	
LoE **1++** **2+**	[441]; [436]; [442]; [443]; [444]; [445]	
	Consensus (89%)	

Buller and Borland [441] studied 24 sun safety programs for children under 14 years of age. Short-term interventions such as individual lessons or visits to information days ("sun safety health fair") were suitable for improving knowledge about sun protection but had little influence on attitudes and behaviour. More effective were more intensive interventions lasting several days to several weeks, combining lecture series, information materials, workbooks, and others [441].

Dietrich et al. [442] reported on a two-year multicomponent program "SunSafe," which involved schools, kindergartens, doctors' offices, and recreational facilities in several communities. Children's sun protection behaviour was successfully promoted. This effect was reinforced by a second, less intensive refresher campaign [442].

Programmes that are comparatively successful in influencing behaviour, such as "Kidskin" [445] or "SunSafe" [442] and the two-year intervention "Sun Protection Is Fun" [436], are designed for the longer term. They combine different components, e.g. age-specific curricula, training sessions for teachers and beach lifeguards, information and training materials, posters, computer-based teaching modules, etc., and involve parents and other caregivers [443].

Weinstock et al. demonstrate moderate but sustained positive effects of a two-year multicomponent intervention involving informational materials, sunscreen, personal sun sensitivity testing, and written and verbal feedback among beachgoers. Reported sun protection behaviour improved in the intervention group compared with a control group, with the most pronounced effect in the 16-24 year age group [444].

Providing parents of young children with information material on a one-off basis does not appear to be sufficient to significantly influence sun protection behaviour, even when combined with provision of free sun cream [446]. An intervention limited to swimming lessons for primary school children, consisting of three to five minute lessons before swimming lessons combined with information material for home use, was also not likely to influence sun protection behaviour and tanning [447].

Therefore, special attention needs to be paid to strategies that produce the most sustainable behaviour change possible. From the available studies, "the" successful intervention strategy cannot be derived. The approaches and methods are too diverse for this. The share of individual components in the overall success of multi-component campaigns cannot be determined. There is also often a lack of evidence on the

sustainability of observed effects and on transferability to German conditions. Nevertheless, some basic recommendations can be made.

5.28	Evidence-based Recommendation	new 2020
GoR **B**	Behaviour change interventions should be based on behavioural theories and take into account the available evidence. *WG Primary Prevention*	
LoE **1+** **2++**	[441]; [448]; [449]; [450]; [451]	
	Strong Consensus (100%)	

The studies provide evidence that a theoretical foundation of programme concepts is important and useful. According to Garside et al. [449], who conducted a systematic review of qualitative studies, the elements of the health belief model in particular provide a coherent theoretical framework underlying many interventions, from which the barriers to information uptake about protective behaviour for the prevention of skin cancer can be derived. In addition, the model provides starting points for message design. For example, lack of knowledge, low risk perception, or the perception of sun tanning as healthy and attractive are important barriers to sun protection behaviour that can be addressed in campaigns [449]. Also, Glanz et al. [451] ncluded constructs such as risk perception, cost and benefit trade-offs of behaviour change, actionable knowledge and skills, and social norms as mediating variables derived from the health belief model and social cognitive theory to measure the effectiveness of personalized feedback [451].

Knowledge about the risks of UV radiation and knowledge about how to protect oneself are a necessary prerequisite for appropriate sun protection behaviour, but not sufficient for consistent translation into practical action [441]; [449]; [387].

In a web-based intervention, White et al. [448] present a one-time web- and theory-based intervention based on changes in psychosocial variables as well as information on proper UV-protective behaviour that is shown to be beneficial over a control group in which only UV-protective information was communicated.

Communication Channels

5.29	Evidence-based Recommendation	new 2020
GoR **B**	Measures to communicate primary prevention of skin cancer should be multimedia, interactive, and integrate multiple communication channels. *WG Information basis of the population*	
LoE **1++** **3**	[452]; [453]; [451]; [454]; [455]; [456]; [457]; [458]	
	Consensus (94%)	

There is evidence in the literature that multiple as well as multimedia targeting of adults leads to better effects. For example, several studies have shown that multiple delivery leads to an increase in sun protection knowledge, self-efficacy in sun protection use, and sun avoidance. These effects were significantly different from the results of the respective control group [451] ; [454]; [460]. In addition, multimedia communication (e.g. videos) appears to be superior in effectiveness to purely text-based communication [459]. However, setting up a multimedia information booth with a touch screen at central contact points (city pharmacy, library, health centre) did not achieve improvements in knowledge, attitude, and behaviour [455]. However, there is no evidence for the general superiority of pictures over text in communication [461]. Boer et al. [456]

showed that when educating people about skin cancer through slogans and through advertisements, both additional text and additional images increased knowledge about sun protection measures.

It is already true for individual means of communication such as advertisements that positive interaction effects can be demonstrated by a combined use of images and text modules with young adults in comparison to such advertisements in which only images or only text elements are used in addition to a slogan and logo. This can increase knowledge about the consequences of overexposure to the sun and improve the perception of the benefits of sun protection behaviour. At the same time, such ads with text-image combinations are perceived as more attractive and reflection on the ad is intensified [456].

However, when evaluating these findings, the limited external validity of the experiment should be considered in view of the laboratory situation and the large number of ads presented to the subjects for evaluation, as well as signs of a saturation effect ("ceiling effect") in view of the pronounced perception of the benefits of the protective behaviour even in the control group.

With regard to education and training programs, the studies considered here also indicate that, compared to the presentation of information via only one sensory channel without the possibility of selection and feedback by the recipient, communicative address via several sensory channels (text, graphics/photo, moving image/animation) as well as additional human-computer interaction in the training situation increase

the probability of a more profound examination or higher processing depth of the information and thus the mediation performance. In addition, media and interpersonal forms of address should be combined, as this increases communication performance.

Repeated multimedia health education with animations, photos, and short information in clinical settings leads to better knowledge about melanoma and improved sun protection behaviour in at-risk individuals [Glazebrook, C. et al. 2006]. For adolescents, two sessions of interactive PC training in clinical settings combined with four telephone interviews with health advisors over a 24-month period have been shown to have a positive impact on protective behaviour, with decision balance acting as a mediator variable [452]. Multimedia interactive training or intervention programs have also been implemented in other health-related settings such as a pharmacy with moderate results [455].

Multiple communications achieve better effects in changing risk behaviours than handing out a standard brochure once [451]; [454].

Multimedia interactive training materials could also be used effectively in a setting-specific manner in primary prevention with third and fourth grade children. Hornung et al. [453] were able to show that the provision of information through a CD-ROM compared to teacher-led didactic interventions with brochures can have a positive effect on knowledge and attitude levels [453]. Evidence of the superiority of multimedia forms of delivery (video) over conventional routes via brochures can also be found in Idriss et al. and Janda et al. [459]; [462].

However, on the basis of existing studies, the positive effect of such prevention programmes can only be assumed for complex training programmes that integrate various textual, visual, and audiovisual elements. In many studies [452]; [Glazebrook, C. et al. 2006]; [455]; [457], the programmes were not tested against the effect of other programme profiles (other delivery channels or other forms or combinations of information presentation and processing), so that on this basis, despite the high level of evidence in some of the studies, it is not possible to draw any conclusions about exactly which measures or which components of a training programme have an effect and which do not contribute to an improvement in knowledge, attitude, and behavioural parameters. In studies in which different forms and ways of presenting information are compared with each other, e.g. [453]; [459]; [462]; [455], other biasing factors may have been at work, which are also reflected in the lower level of evidence. In addition, these studies only provide evidence of the effect of a complex and multipart bundle of measures, so that no statement can be made about the potential preventive influence of individual components.

Design of Messages

From various studies on prevention campaigns on sun protection behaviour, indications can be derived on the selection of effective message strategies. The effect of different message designs on behaviour change has not been clearly proven. For this reason, no recommendation is made.

Gallagher et al. 2012 examined messages in relation to framing, i.e., the different formulations of a message with the same content. They were able to show in a meta-analysis on the effects of gain and loss framing that gain-framed messages are more effective in promoting preventive behaviours, particularly regarding skin cancer. In contrast, in the 2016 study by Mays et al. loss-framed messages were more successful in decreasing tanning intentions or abandoning them altogether among female

tanning bed users aged 18-30. Therefore, the framing statements are too contradictory to derive a general statement.

Dillard and Hissler (2015) were able to show that the type of message (statistical/narrative) and the type of information processing (experiential/rational) influence risk perception and concern. Participants' risk perception and concern were higher when they processed the narrative message experientially. No influence on behavioural intentions was demonstrated. Similarly, the results of Janssen et al. 2013 showed that narrative formats led to higher risk perceptions among tanning salon users. In another study by Lemal et al. 2010, individuals who read the message with narrative were two to four times more likely to take health-promoting actions than individuals in the control group.

Myrick et al. (2015) examined the extent to which different emotional YouTube videos with prevention appeals influence willingness to change behaviour in an experiment with individuals from the United States between the ages of 18 and 69. They were able to show that videos with mixed emotions (fear and humor) were best at generating empathy, which in turn increased willingness to share the information and change behaviour.

Ruppert, 2017 and Strekalova, 2017 are both analyses of the content of YouTube videos and Facebook posts, respectively. From these studies, it can be deduced that the quality of corresponding videos is poor, as they contain false or misleading information about tanning beds or sunscreen. The analysis of Facebook posts showed that images and links were the most shared content. Posts with a risk reference were shared, commented on, and liked more often than those without a risk reference.

Personalized and tailored messages

5.30	Evidence-based Statement	new 2020
LoE 1+ 1-	Personalised messages have a greater impact on sun protection behaviour than generalised messages. *WG Primary Prevention*	
	[463]; [464]; [465]; [466]; [467]	
	Strong Consensus (100%)	

The systematic review by Finch et al. [467] showed numerous promising effects of short personalized messages delivered by SMS, email, or via an app. However, in the studies considered, the influence on sun protection behaviour was mostly measured using only subjective variables. The authors complain that objective factors such as the incidence of sunburn were too rarely examined.

Glanz et al. [463]; [464]

showed in their studies an effect of personalized information (addressing families with children at moderate or increased risk of skin cancer) on some sun protection

behaviours such as wearing clothes, hats, sunglasses, using sunscreen, and staying in the shade.

A web-based interactive and individualized intervention significantly improved self-reported sun protection behaviours over control groups in the Heckman et al. [465] study.

Crane et al. [466] examined the effect of a personalized newsletter sent to parents over three years that included sun protection information. There was a small increase in sun protection behaviours compared to a control group. The authors conclude that the intervention alone is not sufficient to reduce skin cancer risk but is promising as one component in a multi-component intervention.

5.31	**Evidence-based Recommendation**	**modified 2020**
GoR **B**	Educational and training programmes on primary prevention of skin cancer should address the target persons individually (individual-level interventions) and at the same time include individualised information and feedback elements.*AG Information base of the population*	
LoE **1++** **2++**	[449]; [468]; [452]; [451]; [458]	
	Strong Consensus (97%)	

Health information that is tailored to personal characteristics, behaviour patterns, needs, and beliefs is more likely to be perceived as personally relevant and therefore has a stronger motivating character than information that contains general information and advice. This so-called tailoring should take the form of, for example, personalized feedback on risk status, tailored behavioural recommendations, and reminders.

Prevention and intervention programmes that address individuals via personal contact with a health professional or in the form of direct media have stronger evidence of their effect on the perception of cancer risk than do interventions that start at the collective level, i.e., do not specifically address individuals [468].

he systematic review of studies also provides evidence that individualised targeting or information tailored to individual risk status ("tailoring") is more effective than general information.

Evidence for the effectiveness of "tailoring" is also provided by Glanz et al. [451]. For adults at moderate to high risk of skin cancer, the authors were able to demonstrate a positive effect with individual protective measures/self-checks as well as a change in the mean value of sun protection behaviour in the context of an information package delivered by post three times at two-week intervals compared to a non-personalised intervention in the form of general educational material on skin cancer prevention and self-examination as well as a brochure on sun protection measures and behavioural tips. Feedback was personalized based on individual risk status and personal risk factors, as well as on practiced sun protection behaviours, behaviour change

readiness, and perceived barriers to behaviour change. The constructs "risk perception," "cost and benefit trade-offs of behaviour change," "action-relevant knowledge and skills," and "social norms" were included as mediating variables [451].

Adams et al. [452] were also able to demonstrate positive influences on sun protection behaviour for adolescents using an interactive PC training programme with personalised feedback and telephone interviews with health advisors. Personalised feedback with tips on different types of sun protection behaviour and a bottle of sunscreen were sent by post following the interviews [452].

Similarly, Glazebrook et al. [Glazebrook, C. et al. 2006] worked with individualised feedback on risk status as part of their interactive PC training for at-risk individuals, which was a fear appeal aimed at increasing perceived threat and, in terms of practising protective behaviour, simultaneously provided information to lower barriers and increase perceived benefits. It contributed to an increase in knowledge, particularly among individuals with higher risk status [Glazebrook, C. et al. 2006]. Again, however, the programme was not tested against non-personalised training, so evidence on the effect of individualised information and feedback elements remains limited despite a high level of evidence from the studies in this regard.

Involvement of Peers and Multipliers

5.32	Consensus-based Recommendation	new 2020
EC	Information can be provided via parents, teachers, educators, peers, and other multipliers.*WG Information basis of the population*	
	Consensus (94%)	

Peers

Incorporating peer communication into measures of information about primary and secondary skin cancer prevention is promising, as research shows that peer communication has a moderating effect on the relationship between descriptive norms (what the majority would do or consider appropriate) and behaviour. This can be illustrated by the example of alcohol consumption among students. Alcohol consumption is influenced by more than descriptive norms. Peer communication also has a crucial influence here [470]. Therefore, peer communication is likely to support behavioural change.

Socialization Agents

Socialization, as one of the most important processes of internalization, also provides the opportunity for information. Within the socialization process, for example, parents, educators, teachers, etc. take the role of socialization agents [471]. By training and informing socialisation agents, they can act as well-informed multipliers.

In addition, the communication and role model behaviour of parents is also considered to be an important factor influencing the sun protection behaviour of young people [469].

Other Multipliers

Physicians and other medical actors such as pharmacists are considered important multipliers for the primary prevention of skin cancer. The medical setting is therefore discussed in more detail in section Chapter 5.4.2.3.

Use of New Media

5.33	Consensus-based Recommendation	new 2020
EC	Skin cancer prevention interventions can also use new media (websites, social media, SMS, apps) as a communication strategy. *WG Information base of the population*	
	Consensus (89%)	

Many interventions use new media as communication strategies. Finch et al. [467]

refer in their systematic review to five interventions (investigated in the form of RCTs) that positively change sun protection behaviour with the help of regular short messages (SMS) to the mobile phone. However, in most cases, the control group did not receive any intervention, so that conclusions about the effect of the communicative strategy are not possible.

The effects of interventions that use websites as a communication medium and aim to promote sun protection behaviour [465] or reduce the use of sunbeds [472], among other things, with the help of modularly structured and partly individually tailored topic blocks, showed positive effects on behaviour. But again, no conclusions can be drawn about the actual effect of the web-based approach compared to other approaches.

Falzone [473]

derive important factors for the design of social media campaigns from their review on psychosocial factors influencing tanning behaviour in sunbeds among adolescents and young adults. Thus, in addition to individual factors (such as internalized tanning norms, body satisfaction, and comorbidities with other mental illnesses such as eating disorders), they also name family (e.g. communication with parents and role models), peers (such as their body ideals and tanning salon use), and factors at the societal level (such as legislation, advertising, and cultural beauty ideals). Through social media, they believe that greater reach can be achieved in this age group at a lower financial cost, which can influence norms and ideals about beauty and appearance. In addition, they hope this will increase support for government action to ban tanning salon use by young people.

In terms of targeting children, adolescents, and young adults, there is evidence in the literature about which media are appropriate for reaching this audience. For example, Adams et al. found that children and adolescents aged 10 to 16 years who participated in education via computer had lower risk behaviours regarding their sun exposure than individuals in the control group [452].

This effect is presumably due to a change in decision balance (subtracting the benefits of sun exposure from those of sun protection) as a result of the intervention.

Hornung et al. report on an intervention which was directed at third and fourth grade students. The content of the intervention was knowledge about the dangers of UV radiation, attitudes toward sun tanning, and behavioural practices to protect against UV radiation. Different communication channels were used. First, one group received the content via CD-ROM (IG 1), others received teacher-led didactic instruction (IG 2), and a third group received no intervention (CG). In both groups, teachers received general information and information on the implementation of each intervention. The results show that in IG 1 knowledge increased the most, attitudes improved the most, and possible behaviours were demonstrated more often compared to IG 2 and CG. After seven months, the effects within IG 1 weaken and can no longer be statistically significantly distinguished from IG 2, but there are significant differences between these two groups and the CG in knowledge about the dangers of UV radiation. In terms of attitude, only IG 1 and CG are still significantly different from each other, while in terms of behaviour, no differences between the groups exist anymore [453].

Idriss et al. [459] provide evidence that among internet-savvy young adults (18 to 39 years), web-based communication media (online videos) are superior to purely text-based media (print media) in their effectiveness in conveying knowledge about malignant melanoma ($p<0.05$). Effectiveness was inferred based on changes in participants' melanoma knowledge at baseline compared to one month after receiving the educational intervention (questionnaire survey).

Outward Appearance Targeting

5.34	Consensus-based Statement	new 2020
EC	Skin cancer prevention interventions that also address external appearance are one strategy to change sun protection behaviour.*AG Information basis of the population*	
	Strong Consensus (97%)	

As appearance is a major motive for sun tanning/tanned skin, especially for women [474], appropriate messages/appeals can address this motive and highlight possible loss of attractiveness due to unhealthy behaviour. Thus, consequences such as skin ageing and spots on the face (due to excessive skin tanning) are used in prevention campaigns (Dodd / Forshaw 2010).

Particularly for studies on women, these appeals showed high effectiveness in preventing skin cancer. Appeals arguing for loss of attractiveness showed positive (i.e. socially desirable) effects on risk perception, self-efficacy, attitudes, behavioural intentions, and behaviour. This is illustrated not only by the many individual studies (for a review, see [475]) conducted by Mahler and colleagues in particular, but also by two research reviews on appearance-based interventions for sun protection [476]. However, the studies on attractiveness appeals were often conducted exclusively (or at least a majority) with women (Williams et al. 2013). Williams (2013) randomised a total of 70 female students from Staffordshire University in the UK to one of two intervention groups. The first intervention group used the facial ageing programme "Age Progression Software" (APRIL). An image with UV protection and an image without were then placed side by side and the women were asked about their thoughts on the two. The second intervention group received information leaflets from the National Health Service and Cancer Research UK and were then also interviewed. Each

intervention group was considered a respective control for the other. Endpoints represented attitudes towards benefits and risks of sun exposure, future sun protection intention, and perceived sun damage susceptibility.

5.35	Evidence-based Statement	new 2020
LoE 1++ 1-	The use of personalised digital methods to depict potential UV radiation-related attractiveness losses can have positive effects on sun protection and exposure behaviour in certain target groups. *WG Primary Prevention*	
	[477]; [472]; [476]; [478]; [479]; [480]; [481]	
	Consensus (92%)	

personalized variant for visualizing the possible loss of attractiveness are interventions such as UV photography or "facial morphing" (e.g. "ageing software").

Here, however, the mostly insufficient clarification of the health relevance of the visualizations, which are used as a means to influence behaviour, is viewed critically. For this reason, although positive indications of at least short-term behavioural changes have emerged from studies, no recommendation is made in the context of this guideline.

An appearance-based web-based intervention by Hillhouse et al. [472] was able to reduce intention to use tanning beds in female adolescents. The change of psychosocial variables (attitudes, perceptions, expectations, and norms) is of particular importance.

In the randomized controlled trial by Blashill et al. [480], the use of skin ageing software reduced the frequency of outdoor and tanning bed tanning in young adults compared to the use of information brochures alone or brochures combined with mindfulness exercises. This effect diminished over time. Similarly, Williams et al. [476] reported benefits of a computerized facial aging simulation intervention in young women in positively influencing intentions and attitudes toward UV exposure compared with the use of informational brochures alone.

A UV photo designed to visualize the contrast between UV-damaged and healthy skin was used in the Heckman et al. [479] study and was found to be significantly more effective in positively influencing behaviour change toward sun protection than standardized skin cancer prevention information brochures. Participants were 82% female.

Hollands et al. [481] find little evidence that the use of images visualizing individual "UV damage" or signs of skin ageing contributes to behaviour change [481]. Other research suggests that, for example, cues supported by UV photographs of negative consequences of excessive UV radiation on appearance can positively influence sun protection behaviour, at least in some target groups [482], [483]; [484]; [485].

Self-Examinations

There are no systematic studies on the question of whether and to what extent risk assessment or sun protection behaviour is influenced by regular self-examination of

the skin. This is seen as a deficit. Robinson et al. (2007) point out that in the randomized controlled trial they conducted in a high-risk group, concern about UV-induced skin damage decreased in an intervention group. In this intervention group, self-examination was performed with a partner (definition of high-risk group: melanoma patients, individuals with melanoma patients within the family, or individuals with > 50 nevi or > 2 atypical nevi). As an explanation, the authors suggest that perhaps confidence in one's own ability to control the skin had increased [486]. Whether and in what way the sun protection behaviour of the subjects was actually influenced by the intervention was not investigated.

Need for Research

When evaluating screenings and/or studies on self-examination of the skin, the effects on risk perception and sun protection behaviour should also be surveyed.

5.4.2.2. Target Groups and Settings

5.36	Consensus-based Recommendation	new 2020
EC	Measures of primary prevention of skin cancer should be designed in a target group-oriented way and take into account the target group-specific needs.*WG Primary Prevention*	
	Strong Consensus (100%)	

5.37	Consensus-based Recommendation	new 2020
EC	Measures of primary prevention of skin cancer should start in the living environment (i.e., be setting-related) in order to reach people where they live their daily lives.*WG Primary Prevention*	
	Strong Consensus (100%)	

As already described in detail in section Chapter 5.2 , sun protection and exposure behaviour as well as knowledge about skin cancer and risk factors differ in different population groups. Identified distinguishing criteria and target groups are gender [405], age (e.g. children and adolescents) [410], skin cancer sufferers and relatives [407], and organ donation recipients [415]. Following the public health action cycle, a precise problem identification including the target group-specific needs and requirements is necessary for the successful implementation of measures [487].

In addition, different access routes are suitable for reaching these different target groups. The setting approach was first mentioned in the Ottawa Charter of the WHO [488] and is considered a core strategy of health promotion and describes the need to reach people in their direct living environment and to change it (see relationship prevention) in order to bring about an improvement in health.

In the following, some selected target groups are focused on and knowledge about existing access routes and special features is listed. (Note: occupation-specific aspects and, in particular, the target group of outdoor workers are listed specifically in Chapter Chapter 7).

Children and Adolescents

5.38	Evidence-based Recommendation	modified 2020
GoR **A**	Parents of babies and young children must be informed about appropriate sun protection for their children. Regular early detection examinations must also be used for this purpose.*WG Primary Prevention*	
LoE **1++**	[489]	
	Strong Consensus (100%)	

Crane et al. (2006) provided parents of infants and toddlers with regular and comprehensive information on age-appropriate sun protection as part of the preventive medical check-ups during the first three years of life. Over the course of the three years, knowledge in the intervention group increased significantly and sun protection behaviour also improved [489].

5.39	Evidence-based Recommendation	modified 2020
GoR **B**	To improve sun protection behaviour, UV protection interventions should be implemented in schools and preschools or day care centres.*WG Primary Prevention*	
LoE **1+** **2+**	[436]; [490]; [491]; [492]	
	Strong Consensus (100%)	

Most of the available interventions were directed at the target group of children either directly or indirectly through parents, teachers, educators, or other caregivers. This makes sense for several reasons. On the one hand, childhood and adolescence represent an essential phase of life for the later risk of skin cancer, and on the other hand, several studies prove the potential for at least short- and medium-term positive influence on sun protection behaviour in 9-year-old primary school children [438], five- to six-year-old primary school children ("Kidskin," [490]; [491]), and preschool children [436]. In intervention groups, compared to control groups, use of textile sunscreen [438]; [436]; [490]; [491], use of sunscreen [436], avoidance of being outdoors during the sunniest time of day [438], or seeking shade [436]; [490]; [491] increased. In addition, the pathway "protecting children" could also influence the behaviour of the adults caring for them [436].

Already in four- to five-year-old children, an age-appropriate intervention using, for example, games, songs, and picture books improved knowledge about sun protection

compared with a control group. The effect was still significant in the intervention groups of a randomized controlled trial (sample of 12 classes with preschool children aged four to five years) seven weeks after the end of the intervention. However, adult help is needed in this age group to translate knowledge into practical action. For this reason, the authors emphasize the need to involve parents in the intervention [387].

Few studies examined effects on endpoints such as skin tanning or number of nevi. That appropriate school-based campaigns have the potential to influence these endpoints as well, at least to a moderate extent, was demonstrated by the intervention study "Kidskin," conducted over five years on five- to six-year-old elementary school children. After two years, reduced sun exposure and less tanning were described in the intervention groups compared with the control group. After five years, a slightly (although not statistically significant) lower number of nevi was observed in the intervention groups compared to the control group [492]; [491].

In contrast, the SoleSi SoleNo-GISED [493]

intervention program implemented in Italian primary schools showed no effect on the endpoint "number of sunburns" or the number of nevi one year after the intervention. As possible explanations for the negative result, the authors discuss the already high level of sun protection in the study population before the intervention, the rather general information material, and the too-short follow-up of only one year with regard to the number of nevi.

No evidence of adverse effects of interventions in schools to improve appropriate sun protection behaviour emerged from the available studies. In particular, there was no difference between children from sunscreen intervention groups and control groups in terms of body mass index or self-reported outdoor activity [361].

Users of Sunbeds

5.40	Consensus-based Recommendation	new 2020
EC	Measures of primary prevention of skin cancer must specifically address the target group of sunbed users, inform them about the risks of use, and aim to change their behaviour. The interventions must take into account the heterogeneity of the target group (e.g. migration background, level of education) and address this in their approach. Special attention must be paid to underage sunbed users. *WG Primary Prevention*	
	Strong Consensus (100%)	

As detailed in Section Chapter 5.1.1.5, the use of sunbeds correlates directly with the development of skin cancer and should therefore be avoided. As the data from the NCAM study show (see Section Chapter 5.2.2), use is age-specific, with particular emphasis on the fact that young people still use tanning salons despite §4 of the NiSG. Increased use by people from migrant backgrounds and with intermediate levels of education was also recorded.

Recipients of Organ Donations and Skin Cancer Sufferers

5.41	Consensus-based Recommendation	new 2020
EC	The knowledge about an increased risk of skin cancer and the implementation of protective behaviours among organ transplant patients and skin cancer patients should be further improved. *WG Primary Prevention*	
	Strong Consensus (100%)	

Both organ transplanted (immunosuppressed) persons and persons affected by skin cancer represent a special risk group (cf. Section Chapter 5.1.2.2). However, knowledge about and performance of protective behaviours are insufficient and require further promotion (cf. Chapter 5.2.1.3 and Chapter 5.2.1.4).

5.4.2.3. Primary Prevention and Medical Consultation Moments

5.42	Evidence-based Recommendation	modified 2020
GoR A	The medical consultation (e.g. in connection also with skin cancer screening) must be used for indications of primary prevention measures on an ad hoc basis. *WG Primary Prevention*	
LoE 1+ 2+	[389]; [482]; [494]; [495]	
	Consensus (91%)	

Particularly in the case of adolescents and adults, the importance of a personal approach (e.g. in the context of a doctor-patient consultation) has been shown to be effective in influencing behaviour. Evidence from several studies shows that individualized interventions (individual risk assessment, personal doctor-patient consultation) increase the chances of influencing behaviour. A physician consultation with individually tailored feedback reports showed significant differences in sun protection behaviour between intervention group and control group in 11- to 15-year-olds even 24 months after the intervention [389]. Falk and Magnusson [495] sshowed that face-to-face advice on sun protection behaviour during a medical consultation, combined with an examination of existing nevi, still led to improved sun protection behaviour in adults three years after the intervention but significantly improved only with regard to sunscreen use. Information by letter alone had no effect. An appearance-focused intervention strategy tailored to the target group of sunbed users showed effects on attitude and behaviour (number of sunbed visits) in young female sunbed users [482], [483].

Rat et al. [494] investigated a dichotomous risk assessment in the doctor's office and were able to show that sun exposure could be reduced through targeted counselling of high-risk patients.

5.43	Consensus-based Recommendation	modified 2020
EC	The following recommendations must be given in the doctor-patient discussion on cancer prevention:Content • Information about the risks of excessive ultraviolet (UV) radiation • Motivation to change behaviour • Avoid exposure to strong solar radiation • In the case of medium and high UV exposure (UVI 3-7), seek shade during the midday period • In the case of very high UV exposure (UV index 8 and higher), avoid being outdoors during the midday period if possible. If this is not possible, seek shade • If necessary, postpone outdoor activities to the morning and evening hours • Avoid sunburn at all costs • Wear protective clothing • Use sunscreen without prolonging exposure time • Be aware of individual skin sensitivity • Give information about the different skin types • Advice on individual protective measures according to the patient's skin type • Pay attention to possible side effects of medicines in the sun • Protect children and infants in particular • Avoid sun studios (refer to NiSG) • Wear sunglasses *AG Primary Prevention*	
	Consensus (91%)	

Need for Research

There is a need for research on the extent to which it is useful to involve other professional groups in primary prevention and secondary prevention measures. In a randomized study of 54 pharmacists, it was shown that training of pharmacy staff increased counselling activities for primary prevention of skin cancer [496]. However, further research is needed to demonstrate the effectiveness and sustainability of such activities and to derive recommendations.

5.4.3. UV Index

The UV index (UVI) was developed by the WHO in cooperation with ICNIRP (International Commission on Non-Ionizing Radiation Protection), World Meteorological Organization, UNEP (United Nations Environment Programme), and other collaboration partners as an internationally uniform measure of the erythema-effective (i.e. sunburn-effective) irradiance and as an indicator of the skin-damaging potential of the solar UV radiation striking the earth's surface. The higher the UVI, the faster sunburn can occur on unprotected skin. From a UVI of three, protective measures are recommended (seeking shade at midday, textile sun protection, use of sunscreens).

5.44	Consensus-based Recommendation	new 2020
EC	The knowledge about and the importance of the UV index for the sun protection behaviour of the population is currently low and dependent on age and socio-economic status.*AG Information basis of the population*	
	Strong Consensus (100%)	

Börner, Schütz & Wiedemann [421] conducted a cross-sectional survey representative of the total population of Germany aged 14 years and older on the understanding of the UV index and its significance for sun protection behaviour. The data collection was carried out via standardized telephone interviews of 1501 persons. Overall, the level of knowledge about the UV index is very low, with only 27% of the participants having already heard of the UVI. Of these, 61% could interpret it correctly, which means that, extrapolated to the total population of Germany, only 18% know and understand the UVI (knowledge is better among men and the more highly educated). Furthermore, Börner, Schütz & Wiedemann [421] determined that only 6% of the interviewees had actively searched for information on UV radiation in the last year and 25% had come into contact with information materials. Forty-one percent of the respondents claimed to know their own skin type, which is the prerequisite for the UV index as an effective tool to promote sun protection behaviour. Thus, together only 9% of respondents could correctly practice the sun protection behaviour recommended by the UVI (9% could correctly interpret UVI and know own skin type). The authors also note a low behavioural relevance of the UVI. Knowledge of the UVI and its meaning are hardly correlated with actual combined sun protection behaviour (sunscreen, sunglasses, clothing, seeking shade, avoiding midday sun). Only the intention to implement behavioural recommendations of the UVI is a moderately strong predictor. Just 10-17% of the participants aligned their sun (protection) behaviour with this, whereby there are clear differences between the various age and education groups: 18 to 29 year-olds and the more highly educated report the lowest influence of the UVI on sun protection behaviour.

5.45	Consensus-based Recommendation	modified 2020
EC	The ultraviolet (UV) radiation index should be more intensively publicised **as part of sun protection recommendations**, firmly anchored in the media and used as an aid in UV protection campaigns. Attention must be paid to a comprehensible explanation of the UVI so that it is correctly understood and used in the sense of UV protection.*Primary Prevention WG*	
	Strong Consensus (100%)	

In the 2015 Melbourne International Workshop "The Global Solar UV Index" it was reported that in Canada, about 20% of citizens regularly check the UV index before going out in the sun for long periods of time and that over 60% take additional UV protection measures when the UV index is high. On the other hand, it became clear that knowledge about the UV index remains low in many countries. For example, Boerner et al. showed that in Germany only just under 30% of respondents had ever heard of the UV index [421]. At the workshop, it was concluded that the UV index needs to be embedded in a broader communication strategy in order to contribute to behaviour

change (Gies et al. 1015, Review of the global solar UV Index 2015 Workshop report, Health Phys. 114(1): 84-90, The systematic review by Heckman et al (2019) comes to similar conclusions, clarifying that the UVI is much better known in countries such as Australia, the USA, and New Zealand than in Europe. Evidence of positive effects emerges from some studies. For example, UVI had a significant positive effect on shade use in a study conducted in the USA and Canada. However, the review also shows significant differences between different countries. It also becomes clear that the significance of the UVI is often not sufficiently understood, even among people who claim to know it, and, moreover, that a link between UVI and sun protection behaviour is not necessarily established (Heckman et al. 2019, Preventive Medicine 123, 71-83).

There is therefore a perceived need to more firmly establish the UV index as part of sun protection recommendations, also taking advantage of the opportunities offered by new media (internet, mobile communication tools). However, the limitations of the UV index must also be clearly communicated. The UV index is defined for a horizontal surface. The irradiation of the obliquely positioned sun on inclined skin surfaces such as the nose, forehead or shoulders can be higher than on the horizontal surface of the earth. The UVI may (e.g. in environments with strong UV reflection such as snow or water) underestimate the actual erythema-effective irradiance and it cannot take into account the individual sensitivities of a person.

The UV index is published as part of weather forecasts, especially on the internet. More detailed explanations of the UV index and the international protection recommendations for the respective UVI values can be found, for example, on the BfS website (http://www.bfs.de/DE/themen/opt/uv/uv-index/uv-index_node.html).

As part of, for example, information campaigns and interventions on sun protection or in information materials, the UVI can be used to estimate the level of erythema-effective UV irradiance from the sun. It can also assist in the assessment of necessary sun protection measures and provide guidance. Several countries, such as Australia, now present the UVI not only as the daily maximum value, as originally intended, but also over the course of the day, in order to increase the understanding of changes in sunburn-effective UV radiation over the day and over the year. The BfS also provides such daily curves for the measuring stations of the UV monitoring network (http://www.bfs.de/DE/themen/opt/uv/uv-index/aktuelle-tagesverlaeufe/aktuelle-tagesverlaeufe.html).

Further research should investigate how the effectiveness of the UV index as an information tool can be further improved in terms of both behavioural and proportional prevention. Corresponding measures should be evaluated.

5.4.4. Proportional Prevention Measures

The need for behavioural prevention measures is postulated in many studies, especially as the effectiveness of interventions aimed solely at behavioural change has often proved unsatisfactory (e.g. [497]; [447]). It is known from the field of prevention of tobacco consumption that behavioural prevention measures are significantly more efficient (i.e. cheaper, more sustainable, and more effective) than behavioural prevention measures [498].

5.46	Consensus-based Recommendation	new 2020
EC	Proportional prevention measures for skin cancer prevention must be guided by the policy paper "*Preventing Health Damage from the Sun – Proportional Prevention in Urban and Rural Areas*" (2017) of the UV Protection Alliance.*WG Primary Prevention*	
	Strong Consensus (100%)	

In April 2017, the UV Protection Alliance--a federation of multidisciplinary renowned societies, organisations, and authorities from radiation protection, medicine, science and occupational health and safety--published the policy paper "*Preventing Health Damage from the Sun – Proportional Prevention in Urban and Rural Areas*." In this paper, measures are postulated on the following levels:

- Federal/state level – Political and programmatic anchoring
- Political and programmatic anchoring
- Securing funding
- · Local level – Planning and practical implementation
- Identifying interfaces and docking points for prevention measures in relation to the situation at hand
- Ratio prevention measures in the planning of buildings
- Visualization of UV irradiance as UV index
- · Research and development
- Visualization of UV heat exposure in microscale space
- Visualization of UV irradiance as UV index
- Development of a database of concrete measures and recommendations
- · Education
- Development of a basic catalogue for curricula and training plans
- Elaboration of curricula
- · Media

Note: occupational specifics are referred to in chapter Chapter 7.

5.4.4.1. Proportional Prevention Related to the Use of Sunbeds

In Germany, the NiSG, which has been in force since July 2009, and the UVSV, which has been in force since January 2012, represent important measures of protection against artificial UV radiation and thus primary prevention.

According to § 4 NiSG, it is not permitted to allow minors to use sunbeds. Violations are punished as administrative offences. The ban is intended to influence the behaviour of minors with regard to the use of artificial UV radiation for cosmetic purposes by law. However, no studies are available on whether and to what extent attitudes or behaviour of the population in connection with UV protection are changed by this ratio preventive measure.

The UVSV regulates, among other things, requirements for the operation of UV irradiation equipment. All devices (old devices since 1 August 2012) must comply with a maximum sunburn-effective total UV irradiance of 0.3 W/m2 skin for UV-A and UV-B radiation. Since 1 November 2012, qualified specialist staff must be available to fulfil the information obligations under UVSV – regarding, among other things, the effects

of UV radiation and the risks associated with sunbed use. There is no study available on whether and to what extent risk assessment and behaviour of the population are influenced by these ratio preventive measures.

5.47	Consensus-based Recommendation	new 2020
EC	In order to ensure compliance with the NiSG and the UVSV, in particular with regard to the prohibition of the use of sunbeds by minors and the presence of qualified personnel in sunbed establishments, controls and enforcement of the law and the ordinance must be improved.*WG Primary Prevention*	
	Strong Consensus (100%)	

As stated in section Chapter 5.2.2, the NCAM data show that there are still children and adolescents among sunbed users and that the number is even increasing [418]. The §4 of the NiSG and the UVSV can thus be described as insufficiently implemented to date.

5.4.4.2. Relational Prevention for Children and Adolescents

5.48	Evidence-based Recommendation	checked 2020
GoR A	Sufficient shaded areas must be established in day-care centres, kindergartens and schools.*Primary Prevention WG*	
LoE 1++	[499]	
	Strong Consensus (100%)	

Several studies address the need for the installation of shaded areas in day care centres, kindergartens, schools, or on sports fields [500]; [436]; [443]; [501]. Evidence for the basic acceptance of offered shade places in the otherwise difficult to reach target group of adolescents is provided by the randomized and controlled study of Dobbinson et al. 2009, conducted at 51 Australian secondary schools [499]. Although it is unclear to what extent the results are transferable to Germany, the findings of this study suggest that provided shade spaces have the potential to reduce students' UV exposure during school hours. The provision of shaded areas is considered to be an essential building block of relationship prevention. The recommendation by the World Health Organization and other national and international organisations to seek shade during midday hours above a UV index of 3 (e.g. [502]) falls flat if no shaded areas are provided. This applies in particular to facilities such as day-care centres, kindergartens and schools, in whose care children and adolescents generally spend the hours of the day that are associated with the strongest UV intensity.

5.49	Evidence-based Recommendation	modified 2020
GoR **A**	Technical and organisational measures to avoid excessive UV exposure, particularly during the midday hours (e.g. provision of shaded areas, structuring of the timetable, consideration of UV radiation protection in the timetabling of sports events), must be an essential part of primary prevention. *Primary Prevention WG*	
LoE **1-** **2+**	[436]; [443]; [500]; [501]	
	Strong Consensus (100%)	

Quéreux et al. [501] showed that teaching eight- to 11-year-old pupils could improve their knowledge of sun effects and -protection but that this did not lead to a change in sun protection behaviour. They therefore recommend that sun safety education be combined with appropriate behavioural preventive measures by schools (provision of shade especially during lunch breaks, avoidance of outdoor activities between 11:00 and 15:00) [501]. Similarly, Hart and Demarco [443], Buller et al. [500], and Gritz et al. [436] recommend timetables be designed to avoid outdoor activities at lunchtime [500]; [436]; [443]. Buller et al. [500] and Gritz et al. [436] complement behavioural preventive interventions with structural and organisational measures such as providing shaded areas [500]; [436].

5.4.5. Side Effects of Primary Prevention Measures

The literature available for this guideline cannot answer the question of what side effects population-based comprehensive UV prevention measures (ratio prevention) have. With regard to potential side effects of sun protection recommendations, reference is made to the comments in Chapter Chapter 5.1.3.

5.4.6. Evaluation of Primary Skin Cancer Prevention Measures

5.50	Consensus-based Recommendation	new 2020
EC	Intervention projects and programmes in the context of primary skin cancer prevention should be evaluated formatively and summatively. The evaluation parameters used should be derived from a theoretically proven model. *WG Information basis of the population*	
	Strong Consensus (97%)	

In order to develop and plan communicative interventions in the context of primary skin cancer prevention in a targeted manner, data collection is necessary even before the actual implementation of the intervention (formative evaluation). This has two aims: collection of information for evidence- and theory-based conceptualization and implementation of the intervention (preproduction research), and a preliminary testing of the finalized intervention and its instruments and materials (product testing). Measurements and monitoring of the entire process are also beneficial in order to be

able to take external and internal disturbance variables into account over time (process evaluation). In addition to surveying aspects of content, process evaluation also includes variables that describe the quality of the intervention organisation (controlling) (e.g. organisational processes). Summative evaluation makes it possible to examine the defined intervention goals of a communicative intervention and to record the effects, effectiveness, and efficiency of the measure. The entire period during and after the intervention must be taken into account. Summative evaluation provides information necessary to identify and, if necessary, quantify possible changes brought about by the intervention. For this purpose, it is at least necessary to collect the relevant variables before (which can already be done within the formative evaluation (preproduction research)) and after the intervention. Furthermore, it is important within the evaluation not only to examine variables that are directly related to the communication, but also to include the relevant health indicators and their changes over time [506]; [503]; [508]; [507]; [504]; [509].

The evaluation parameters used within an evaluation should be derived from a theoretically proven model. According to the Transtheoretical Model, different stages of information processing are passed through before an intervention becomes behaviourally relevant. Continuum models, such as the Health Belief Model and the Theory of Planned Behaviour, also model the process of health behaviour change initiated by a prevention or intervention measure in a differentiated manner. The stage of behavioural change at which the target person or test person is in each case, or which constellations of individual predispositions are present in the members of a target group, also influences their receptiveness to different information and communication offers that are part of an intervention, as well as their evaluation and the resulting mediation potentials. Which end variables are measured and evaluated at the attitudinal and behavioural levels should therefore be derived from the theoretical model on the basis of which the intervention was designed [505]; [510]; [511]; [507].

Research Needs

Research is needed in testing evaluation strategies for reliability and in developing a set of criteria for testing the quality of evaluation measures. In addition, the explanatory power and predictive power of different theoretical models for different objectives and measures should be identified and the model parameters specified for the secondary prevention of skin cancer.

5.51	**Consensus-based Recommendation**	**new 2020**
EC	Evaluations of interventions in the context of primary skin cancer prevention must use empirically proven measurement methods that are specific to the endpoints in question.*WG Information basis of the population*	
	Strong Consensus (100%)	

The evaluation should take place at several measurement points and measure short- and long-term effects. Validated and standardised scales should be used to measure the different endpoints. If these are not available, evaluation findings should be empirically validated by comparing the findings generated by different survey and analysis procedures.

Austoker et al. [468] conclude in their systematic review of prevention measures to increase cancer awareness (which also includes studies on skin cancer prevention) that a higher methodological quality and comparability of study designs is required: "Future research evaluating individual-level interventions to promote cancer awareness should attempt to use study designs that generate high-quality evidence, measure outcomes over a longer term (months/years), and attempt to measure behavioural and stage outcomes, as well as knowledge and attitudes. We also highlight the need for standardised and validated measures of cancer awareness [...]" (p.38 in [468]).

This results in the consequences formulated in the recommendation for the parameters to be evaluated and the way they are measured. This also concerns the choice of survey instruments used for the measurement of attitude- and behaviour-related outcome variables.

It is also important to choose appropriate endpoints to assess intervention effects. To increase validity, objective parameters should be considered in addition to subjective measures. Furthermore, evaluation parameters should be selected that have a proven relationship to clinical endpoints (i.e. risk factors and -indicators of skin cancer). See also Recommendation 5.52.

In order not to underestimate possible effects of an intervention (given the fact that the selected evaluation method may not capture certain effects due to the type of survey), different methods should be used to measure the dependent variables, which are complementary to each other and in their combination allow a more comprehensive picture [451].

There is a need for research into methods to optimise study designs with regard to the evaluation of prevention or intervention measures and the measurement procedures used in this context. The aim is to develop a catalogue of criteria for the evaluation of prevention and intervention measures in order to generate more empirically validated and comparable evaluation findings, e.g. by developing standardised and validated scales.

5.52	**Evidence-based Recommendation**	**new 2020**
GoR **B**	To evaluate the effectiveness of interventions for the primary prevention of skin cancer, skin cancer prevention-specific attitudinal and behavioural parameters as well as indicators on contact frequency/intensity, assessment of communication tools and their mediation quality, and performance should be used.*WG Information basis of the population*	
LoE **1++** **1+**	[451]; [458]	
	Strong Consensus (100%)	

A prerequisite for the unfolding of an attitudinal and behavioural preventive effect of the prevention or intervention measure is how frequently and intensively the individual communication offers and messages are perceived, whether they generate attention, how they are evaluated at the level of content and design, and whether they

are understood, retained, and subjectively perceived as useful. In order to measure the immediate communication success that precedes a longer-term effect at the attitudinal and behavioural level, evaluation parameters are therefore also required that directly address the perception of the campaign message or training measure and measure the dispositions of the test persons in a differentiated manner at the respective stage of behavioural change. Effective interventions must therefore also have a positive influence on the outcome variables upstream of the behavioural change if the behavioural change is to be attributed to the intervention. Only recipient feedback on the actual information or training material provides concrete indications of how information and training offers as a whole or how individual elements as well as the content and design of the information in multimedia interventions are accepted by different target groups and what optimisation potentials result from this.

Need for Research

There is a need for research to systematically evaluate the significance of the parameters directly related to communication (e.g. range and attention-elicitation of the means of communication, comprehensibility and evaluation of the information offered or measure) for the effect of the prevention or intervention measure at the attitudinal and behavioural level. In this context, it is also important to empirically model the different variants of the decision balance and to examine them with regard to their mediatizing effect on sun-protective behaviour in order to draw conclusions about suitable forms of address in prevention campaigns.

Studies in which media messages are used and associated with attitudinal and behavioural outcomes would have to fulfil the necessary prerequisites for drawing conclusions about the effect on the campaign and should only be interpreted as evidence of changes at the attitudinal and behavioural level if it is empirically confirmed that this change results from the contact of the target groups with the campaign content (reach) and the processing of these messages. Previous studies have not yet provided sufficient evidence for this. For example, Del Mar et al. do not provide sufficient evidence that the increased number of excisions by doctors during two TV campaigns can be clearly attributed to these campaigns, so that the assumptions on the effect relationship remain rather speculative, despite a statistical correlation between the campaign period and the number of excisions [512]. Also in Oivanen et al., visits for skin examination cannot be causally attributed to contact with campaign messages [513].

In the evaluation of such measures, detailed information on the disseminated messages and advertising materials as well as a measurement of the contact probability with the campaign and its reach up to the perception and evaluation of the same in the target population should therefore be measured or ensured before evidence of the effectiveness of a campaign can be assumed.

6. Climate Change and UV Radiation

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6.1. Climate Change and UV Radiation

6.1.1. Effects of Climate Change on Global and Regional Air Temperature and on UV Radiation Exposure

6.1	Consensus-based Statement	new 2020
EC	Climate change has an influence on global and regional air temperature. Climate change has an indirect influence on UV radiation exposure. So far, however, no quantitative statements can be made on the associated region-specific impacts.	
	Consensus (95%)	

Climatic changes, such as the current anthropogenic global warming caused by greenhouse gases, are accompanied by a change in meteorological parameters such as precipitation, air temperature, sunshine duration, and UV radiation.

Influence of Climate Change on Air Temperature

Due to the release of greenhouse gases, especially carbon dioxide (CO2), air temperature is rising. According to the Intergovernmental Panel on Climate Change (IPCC) [514], the concentration of CO2 in the atmosphere is now higher than at any time in the past 800,000 years. If the rate of emissions does not change, by the middle of this century there would already be so much CO2 in the atmosphere that the global mean temperature would rise 2°C above pre-industrial levels.

The global average annual near-surface (land and ocean) temperature was 0.83 to 0.89°C warmer than the pre-industrial average from 2006 to 2015, making it the warmest decade on record. Of the 16 warmest years on record, 15 have occurred since 2000. Climate models project a further increase in global average temperature in the 21st century (for the period 2081-2100 compared to 1986-2005) of between 0.3 and 1.7°C for the lowest greenhouse emissions scenario (RCP2.6) and between 2.6 and 4.8°C for the highest emissions scenario (RCP8.5) [515]. RCP stands for "Representative Concentration Pathways." A total of four RCPs are distinguished: RCP2.6, RCP4.5, RCP6.0, and RCP8.5, with RCP2.6 assuming the lowest emission scenarios for greenhouse gases and RCP8.5 the highest.

The average annual temperature for the European land area from 2006 to 2015 was about 1.5°C above pre-industrial levels. The annual average land temperature in Europe is expected to increase in the range of 1 to 4.5°C (RCP4.5) and 2.5 to 5.5°C (RCP8.5) by the end of this century (2071-2100 compared to 1971-2000), which is more than the global average increase in projected temperature. The greatest warming is projected for winter in northeastern Europe and Scandinavia and for summer in southern Europe [515].

With an increase in average temperatures, the probability of so-called heat waves also increases. Internationally, there is no uniform definition of the term "heat wave." According to a definition used for Central Europe by Jan Kysely [516], a heat wave is said to occur as soon as the maximum temperature exceeds 30°C on at least three days in a row, the average maximum temperature remains above 30°C over the entire period, and the maximum temperature does not fall below 25°C on any day.

Studies [517]; [518]; [519] show that the frequency of heat waves has increased in Germany in recent years. The years 1994, 2003, 2006, 2010, 2013, or 2018 can serve as examples. The Intergovernmental Panel on Climate Change [520], [521], [514] points out that an increase in heat days and heat waves must also be expected in the future, according to Coumou (2013) and Robinson [517]; [522] and Coumou et al. (2013) [517]; [522], possibly a fourfold increase by 2040. This is also evidenced by numerous regional studies (see, among others, [523]).

Influence of Climate Change on UV Radiation Exposure

In addition to the state of the stratospheric ozone layer, important determinants of UV radiation at the earth's surface and thus of the UV radiation exposure of humans are indirectly the causes and consequences of climate change (global warming): (i) cloud cover situation, (ii) greenhouse gases, (iii) aerosols, (iv) surface reflectivity (albedo), and (v) human exposure behaviour.

(i) Cloud Situation:

Climate change-induced changes in UV radiation over Northern Hemisphere mid-latitudes caused by global warming appear to be caused by changes in cloud cover scenarios [524].

Consistent with simulations from climate models, several independent satellite data suggest that changes in large-scale cloud patterns have already occurred between the 1980s and 2000s [525]. Between 60°S and 60°N latitudes, observed and simulated changes in cloud patterns are consistent with polar retreat of mid-latitude storm tracks, widespread reductions in aerosol air turbidity between latitudes 30° and 50° of both hemispheres (presumably leading to increases in surface UV radiation), and expansion of subtropical dry zones [531].

Lower cloud cover over the year has an influence on the annual sunshine duration. According to observations of the German Weather Service (DWD), the annual sunshine duration in Germany has increased by about 96 hours (linear trend) over the observation period from 1951 to 2018. An increased annual sunshine duration can in turn result in an increased annual sum of erythema-effective UV irradiance. Initial analyses of data from 1999 up to and including 2018 from one of the measuring stations of the UV monitoring network of the Federal Office for Radiation Protection show that, for example, the summed daily totals for 2018 were significantly higher than the totals for all other years, just as they were for 2003, which was also strikingly sunny and hot [523] – [526].

Clouds have a different impact on UV radiation depending on their type and degree of coverage. For example, according to Seckmeyer [527], thunderclouds (e.g. cumulonimbus congestus) can attenuate incident UV radiation by more than 99% compared to the cloudless case. However, the incident radiation may also be increased compared to cloudless fall due to increased scattering from the clouds [527]; [528]. The

attenuation of UV radiation in general increases with increasing cloud cover and is about 10% to 50% at 7/8 cloud cover depending on the cloud type.

(ii) Greenhouse Gases:

According to current research, greenhouse gases, which are the cause of current global warming, also have an impact on stratospheric ozone destruction and regeneration. A reduction of the stratospheric ozone layer caused by chemicals containing chlorine and bromine (chlorofluorocarbons [CFCs], halons) causes an increase in the erythema-effective UV-B irradiance on the Earth's surface. Due to the ban on halogen-containing substances (Montreal Protocol with amendments [529], a recovery of the stratospheric ozone layer seems to be occurring. Current forecasts indicate that:

- the concentration of stratospheric ozone could return to pre-1980 levels by mid-century. But due to greenhouse gases, the regeneration of the ozone layer could slow down. The interrelationships are complex, however, and are currently the subject of intensive research.
- by the end of the 21st century (2090-2100) compared to the present (2010-2020), the recovery of the ozone layer (due to the decrease of ozone-depleting substances and the interaction with increasing greenhouse gas concentrations) could lead to a reduction of UV radiation, which could be highest over Antarctica (up to 40%). Outside the southern polar region, the reduction appears to be small, less than 10% [530].
- due to the recovery of the ozone layer, the fraction of UV-B radiation could be lower again in 2075- 2095, compared to the period 1955-1975, in all latitudes except the tropics, with unabated emissions of CO2, CH4 and N2O (emission scenario RCP 8.5). Reductions are estimated to be between about 5% and 15% in northern mid-latitudes, with the largest reductions projected for the winter months [531].

In addition, global warming appears to be associated with the occurrence of so-called low ozone events ("Low Ozone Events"), also called "miniozon holes," and thus unexpectedly high UV irradiance levels in the Northern Hemisphere. Detailed explanations are given in Section Chapter 6.1.1.

(iii) Aerosols

Another factor is air pollution from aerosols. The expected improvement in air quality due to air pollution control measures and thus reduction of aerosols in the most densely populated areas of the Northern Hemisphere could lead to an increase of 10-20% in erythema-effective UV irradiance. Aerosols may be the most important contributor to future UV irradiance in densely populated areas, but their projected impacts are the most uncertain [531].

(iv) Surface Reflectivity (Albedo)

The albedo (measure of reflectivity) of, for example, the oceans, ice sheets, deserts, and vegetation zones is another factor that could generate a global and regional change in UV radiation exposure as a result of global warming. Due to the melting of the large ice sheets at the poles, as well as glaciers in high mountain areas, the albedo in these areas decreases, which should reduce the reflectance and thus the UV radiation exposure in these regions. Projections indicate that a reduction in reflectivity due to melting sea ice in the Arctic would result in a decrease in UV radiation of

up to 10%, while the decrease would be smaller (2-3%) at the edge of the Antarctic [530].

(v) Human Exposure Behaviour

Humans base their behaviour, among other things, on the weather, especially in terms of the time they spend outdoors. It is to be expected that weather changes due to global warming will also influence human exposure behaviour, with sunshine duration and thermal sensation being decisive factors (see 6.2.1). In addition, there are individual expectations and preferences, which also depend on the climate zone in which people live. How human behaviour and thus UV exposure will change as a result of climate change can, however, only be predicted with great uncertainty given the current state of knowledge.

6.1.2. Development of Morbidity and Mortality in Society with Increasing Air Temperature and UV Radiation Exposure

6.2	Consensus-based Recommendation	new 2020
EC	Rising air temperatures and changes in UV radiation exposure due to climate change have an influence on the morbidity of society. An influence on mortality can currently only be seen in relation to rising air temperatures. The extent to which climate change, in interaction with processes in the stratospheric ozone layer, has or will have an impact on the incidence and prevalence of skin cancer, can currently only be quantified under simplified assumptions. Adaptation strategies to the health consequences of climate change must accordingly focus on preventive measures for the prevention of UV- and heat-related diseases, especially skin cancer.	
	Consensus (94%)	

The consequences of climatic changes on health are still subject to considerable uncertainty. The reason for this is the multicausal relationships associated with climatic changes, which make it difficult to differentiate which consequences are due to climate change and which are due to other factors (e.g. lifestyle).

Morbidity and Mortality with Rising Air Temperature

Rising air temperatures and heat waves (see Chapter 6.1.1) imply a thermal load. One can speak of thermal stress when the individual thermal comfort zone is left. According to Parsons [532] and Menne and Matthies [533],

the individual thermal comfort zone varies according to geographical location, season, and acclimatisation (physiological adaptability of the body to environmental conditions) or thermophysiological adaptability of the population. When considering health effects of thermal stress, it is important to keep in mind that thermal stress is controlled not only by ambient temperature, but also by additional meteorological parameters such as humidity, wind speed, and radiation patterns.

Numerous studies now show that thermal stress is very likely to have significant effects on human health, well-being, and performance [534]. The effects of thermal stress vary in nature and severity depending on the region, as the effects depend on

the conditions prevailing locally, the population composition and its adaptive capacity, or even the existing health infrastructure [535].

Studies show that high thermal stress in the form of heat waves can be associated with increased mortality (see [536]). For various regions of the world, there are average temperatures that are optimal for health and at which the mortality rate is lowest (e.g. 16.5°C for Amsterdam, 20°C for New York [537]).

During heat waves, increased morbidity occurs, especially for pulmonary and cardiovascular diseases [538]; [539]; [540], as well as increased mortality [541]. A 2008 study suggests that higher temperatures increase the induction of non-melanocytic skin cancers (NMCs, PECs) by UV radiation [542]. However, this evidence could not be confirmed in a more recent study [543].

Infants, young children, the elderly, and the sick are particularly at risk from thermal stress, as the thermoregulatory system in them has limited function [545]; [544]; [546].

An increased mortality due to thermal stress in summer was also demonstrated by Koppe [547], Heudorf and Meyer [548], Schneider et al. [549], and Muthers et al. [550] for Germany. This affected not only southern Germany, but also parts of western and northern Germany, where increased mortality rates were recorded during heat waves [551]. According to Gabriel and Endlicher [552], during the three-week heat wave in 1994, 10–50% more people died in predominantly rural Brandenburg, and in some districts of Berlin even 50–70% more than the average.

In this context, it should be added that the effect of thermal stress on health is intensified by increasing air pollution, especially by nitrogen oxides, ground-level ozone, and particulate matter [553]; [555]; [554]; [556]. Due to the high volume of traffic with corresponding pollutant emissions, people living in cities are particularly affected. Added to this is the fact that cities heat up or store heat more than the surrounding rural areas due to dense development and heat storage. This is significant in that cities often lack the nighttime cooling necessary for health.

Morbidity and Mortality Due to UV Radiation Exposure

Rising skin cancer incidence rates can be shown since the beginning of cancer registration. Possible reasons for this, as well as risk factors, are discussed elsewhere in this guideline (see Section Chapter 4.3).

The extent to which climate change, in conjunction with processes in the stratospheric ozone layer, has or will have an impact on the incidence and prevalence of skin cancer can only be properly quantified in the coming decades, as decades can pass between genetic damage of a general nature or caused by UV radiation and the diagnosis of skin cancer.

Accordingly, at present, only the possible consequences of altered UV irradiances or altered UV radiation exposures due to climate change and changes in the stratospheric ozone layer on human health--in particular on skin cancer--can be discussed. Lucas et al. [557] The authors conclude that in the future there will be a wide variety of interactions of factors related to stratospheric ozone and global climate change. The consequences of global climate change will affect entire populations, including, for example, forced migration that will leave skin types exposed to different levels of UV radiation than they were originally. At the individual level, climate change may

alter behaviour so that individuals may be exposed to more or less UV radiation, depending on acclimatization to warmer temperatures. At this stage, we can only conclude that changes may occur. At the moment, we can only speculate about the possible or probable risks to human health [557].

Besides skin cancer, as the most serious risk of increased UV exposure, other UV-related diseases associated with climate change and UV radiation should not be ignored, such as photodermatoses. These are inflammatory skin diseases that are induced or exacerbated by UV radiation [558] and have a significant negative impact on sufferers in terms of school, work, family, and social activities [559], as well as mental health [560], due to their clinical presentation and the fact that light must be avoided. Photodermatoses are most common in (or even limited to) the spring and summer months. For example, for polymorphous light dermatosis (a photodermatosis that still affects about 18% of the European population [561]), it has been shown that its occurrence follows the annual variations of ambient UV radiation in different European locations. Changes in UV radiation as a result of processes in the stratospheric ozone layer and global climate change may therefore alter the frequency and severity of a number of photodermatoses [557].

Table 21: Summary of possible health impacts of changes in stratospheric ozone (via changes in UV radiation) and due to climate change, and possible interactions. Red arrows show possible impacts of climate change on UV-related health effects.

Health effects of stratospheric ozone depletion due to changes in UV radiation		Influence of climate change and related factors on UV-induced health effects
Skin cancer and photodermatoses: risk increases with increasing UV radiation exposure	←	Warmer temperatures lead to longer time outdoors in cool places and less time outdoors where it is already warm. Warmer temperatures and air pollution (aerosols) can promote skin cancer development.
Eye conditions: The risk of a number of acute and chronic eye diseases increases with increased UV exposure	←	Hotter, drier conditions could increase risk for pterygium; dehydration could increase risk for cataract formation. Removal of snow and ice may reduce incidence of some eye diseases.
Immunosuppression, including reducing risks for autoimmune diseases, such as multiple sclerosis	←	Warmer ambient temperatures worsen symptoms of multiple sclerosis.
Synthesis of vitamin D in the skin and other potential beneficial effects of UV radiation on the skin and eye	←	Warmer ambient temperatures could change behaviour (see above): increase or decrease time outdoors, changes in clothing. Higher temperatures could increase the rate of chemical reactions in the skin, e.g. initiation of vitamin D synthesis. Higher precipitation could reduce time outdoors at high latitudes where vitamin D production is already low. Urbanization, urban "heat islands" and "urban canyons" could reduce UV exposure.
Health protection: sunscreens, hats, protective clothing, umbrellas	←	Warmer temperatures could make it less comfortable to wear hats and use sunscreens and protective clothing. On the other hand, shade could make it more attractive.

Table 22: Summary of possible health impacts of changes in stratospheric ozone (via changes in UV radiation) and due to climate change, and possible interactions. Blue arrows show possible effects of UV radiation on climate change-related health risks.

Impact of changes in UV radiation on the health risks of climate change		Health impacts of climate change and associated factors
UV radiation is potentially insecticidal; lower UV irradiances due to recovery of the ozone layer could lead to an increase in climate change associated effects that increase the risk of infections	→	Change in the spectrum of vector-borne (e.g. malaria) and water-borne diseases
Use of sun protection, e.g. hats, clothing, sunscreens could exacerbate the effects of increasing heat and increase the risk of heat stroke	→	Increase in risks for heat stroke and heat stress as a result of warmer days, warmer ambient temperatures, and extreme heat events
UV radiation plays a significant role in surface water disinfection. Lower levels of UV radiation due to recovery of the ozone layer (or increasing cloud cover) could reduce this effect and increase health risks following extreme weather events	→	Increase in injuries, deaths, and contamination of freshwater reservoirs as extreme weather events increase. Increase in risk of waterborne infectious diseases as a result of reduced availability of safe drinking water
Changes in food quality and quantity due to changes in UV radiation will interact positively or negatively with climate change impacts	→	Food safety challenges
Predicted reductions in UV radiation at higher latitudes will increase the risk of vitamin D deficiency and loss of benefits of higher sun exposure, e.g., for blood pressure and autoimmune diseases	→	Climate change induced migration of dark-skinned migrants, often from low to higher latitudes

6.1.3. Influence of Climate Change on the Development of "Low-Ozone Events" in the Northern Hemisphere in their Relevance for Higher Near-Earth UV Radiation Levels

6.3	Consensus-based Recommendation	new 2020
EC	There is an influence of climate change (global warming) on the processes in the stratospheric ozone layer with the consequence of temporarily and locally increased UV radiation exposure in the northern hemisphere with great significance for the health of the population. Efforts should therefore be made to identify these short-term and temporary events at an early stage and to communicate them effectively so that protective measures can be taken to prevent skin cancer at the moment of the event.	
	Strong Consensus (100%)	

Although the mechanisms of ozone depletion are fairly well understood, several unexpected ozone depletion events [563]; [562] have sporadically occurred in the Arctic during the last two decades due to special meteorological conditions. hese so-called "low-ozone events" (LOEs), also called "miniozon holes" (OMs) [565] ; [564]; [566], are characterized by significantly reduced stratospheric ozone for one to three days over geographically limited regions [567].

According to current knowledge, the reduction of the ozone column (OC) in Antarctica is the result of chemical destruction by photolytic reactions in the very stable polar vortex, which creates favorable conditions for ozone depletion [569]; [568]. Compared to Antarctica, comparatively high ozone concentrations are maintained over the Arctic and the northern hemisphere by the air mass circulation processes prevailing there [570]. In contrast to the conditions over Antarctica, the polar vortex over the Arctic is less stable, which inhibits the ozone depletion by chemical processes over the Arctic [571]. However, long and cold Arctic winters favour the formation of stable polar vortices and thus chemical ozone loss over the Arctic [574]; [571]; [572]; [573]; [562]. One such event in 2011, caused by an extremely cold and stable polar vortex, reached Antarctic proportions in its intensity [563]. Accompanying the seasonal warming in spring, an instability and dissolution of the polar vortex sets in and the ozone-depleted air masses (LOEs or OMs) from the interior of the polar vortex can be transported towards the south, including Europe. LOEs occupy a rather small area compared to the "ozone hole" over Antarctica and lead to unexpectedly high levels of UV radiation in the Northern Hemisphere [524]; [526].

Increased occurrence of these events seems to be related to global warming according to previous knowledge. Due to greenhouse gases, less warming radiation reaches the stratosphere, causing it to cool more. This, in turn, favours the occurrence of LOEs [575]. This increases the likelihood that Europe will be increasingly affected by LOEs, resulting in a high level of UV radiation on the Earth's surface for a few days at the end of March/beginning of April. However, the intricate details of the interactions between the ozone layer and greenhouse gases are not yet fully understood and are therefore the subject of research (such as in the RECONCILE project [576].

In addition, LOEs may occur over Europe in spring and summer as a result of balancing processes of stratospheric ozone concentration between subtropical air masses and those in higher latitudes [577].

The frequency of low ozone events – either due to a local change in atmospheric dynamics or due to an altered transport of ozone-depleted air masses from polar vortices or lower latitudes [578]; [579] - has increased over the European-Atlantic sector in the last two decades [578]; [580].

Need for Research

With regard to the prevention of skin cancer, it is necessary to quantify the effects of climate change on UV radiation exposure. To this end, the influence of the chemical, physical, and meteorological processes of climate change on the stratospheric ozone layer, on the occurrence of low ozone events, and thus on the UV radiation load close to the ground, which is relevant for Germany/Europe, must be described quantitatively. In addition, it is necessary to analyse the current UV radiation exposure in Germany and the region-specific UV radiation exposure recorded in recent decades. Furthermore, as a prerequisite for health policy decisions, projections of the near-surface UV radiation exposure for Germany/Europe are to be prepared in relation to different RCP emission scenarios and supplemented with modelling of cloud cover, aerosol concentration, and, where relevant, albedo.

To estimate the impact of changes in UV radiation exposure on morbidity and mortality due to UV radiation, in addition to an optimized registration of all skin cancer entities in Germany/Europe, an attempt should be made to describe a dose-response relationship between UV radiation/skin cancer. Furthermore, reporting procedures for other UV-related diseases, such as polymorphous light dermatoses, should be established in order to obtain an overall picture of the UV-related disease burden of the population.

There is also a need to conduct appropriate studies to clarify the possible influence of temperature on the effects of UV radiation, especially the carcinogenic effect. There is also a need for research into the possible combined health effects of UV radiation, air pollutants and meteorological factors.

6.2. Status Quo: Perception of Heat and UV Radiation

6.2.1. Temperature-Dependent Behaviour Patterns of Citizens in Different Living Environments

6.4	Consensus-based Recommendation	new 2020
EC	Findings on temperature-dependent behaviour are not yet available independent of the season, and thus daylight duration. The frequency and duration of outdoor activities increase with longer daylight hours and higher temperatures in the range of thermal comfort to mild heat stress. With free choice, temperature-dependent behaviour depends on thermal sensation and internal attitudes toward the prevailing temperature. In hot conditions (severe or extreme thermal discomfort), outdoor activities tend to be avoided. The temperature-dependent behaviour can be influenced by and dependent on specifications and organisational boundary conditions in the various living environments. Temperature-dependent behaviour should therefore be taken into account when designing prevention measures.	
	Strong Consensus (100%)	

Living environments within the meaning of §20 Paragraph 4 No. 2 PrävG and Social Law Book V (Law to Strengthen Health Promotion and Prevention [581]) are social systems that are significant for health and can be delimited; in particular, those of living, learning, studying, medical and nursing care, and leisure activities including sports. Accordingly, living environments are the residential environment (municipality/neighbourhood), day care centres for children, schools and other educational institutions, facilities for the elderly (old people's homes, inpatient long-term care/nursing homes), the workplace, and systems of leisure activities.

With regard to the prevention of skin cancer, behavioural patterns that determine the time spent outdoors and thus the possibility of UV exposure are of particular interest. Studies looking at this issue have almost exclusively related to the living environment "recreational systems." No studies currently exist on temperature-dependent behavioural patterns specifically in kindergartens, schools, training centres, workplaces, and facilities for the elderly, but publications do exist on the prevention of heat-related health damage (see, for example, [582]. In the latter settings, it must be taken into account that behaviour is usually influenced by and dependent on specifications and organisational boundary conditions.

The behaviour or patterns of behaviour of people in their living environments are influenced by the weather. Thermal sensation (the feeling of warmth, comfort, or cold) plays an important role here, along with cloudiness or sunshine, wind speed, and precipitation. One index that can be used to assess thermal sensation based on the human heat balance is the "perceived temperature." It often differs from the measured air temperature, since the sensation is determined not only by the air temperature but also by the meteorological variables of humidity, wind, and radiation, as well as human behaviour (especially activity and clothing) [583]. Subjective internal attitudes towards thermal conditions also seem to determine temperature-dependent behaviour, so that, for example, there are people who find heat pleasant and thus spend more time outdoors [584].

The table Table 20summarizes the information derivable from the studies on weather-dependent behaviour in the lifeworld "systems of leisure" with respect to controlling weather parameters and the behavioural patterns identified in this regard. Beyond the information in the table, it should be noted that the findings on temperature-dependent behaviour are not yet available independently of the season and thus daylight duration. As far as can be seen, the frequency and duration of outdoor activities increase with longer daylight hours and higher temperatures in the range of thermal comfort to slight heat stress. Further studies are needed to make statements on temperature dependence within individual seasons.

The explanatory details of the studies and assessments of their contribution to answering the key question can be found below. The majority of the studies were carried out in other countries, so far without testing the direct transferability of the findings to Germany.

Table 23: Overview of the information that can be derived from these studies regarding the weather parameters that control leisure behaviour and the behavioural patterns that have been identified.

Weather parameters	Behaviour pattern	Reference
Perceived temperature	Increased outdoor activity in thermal comfort, in the warm range to mild heat stress	(Arana, Cabezudo, & Peñalba, 2014; Belanger, Gray-Donald, O'Loughlin, Paradis, & Hanley, 2009; Eisinga, Franses, & Vergeer, 2011; Knuschke, Kurpiers, Koch, Kuhlisch, & Wittke, 2004; Knuschke, Unverricht, Ott, & Janßen, 2007; Spinney & Millward, 2011; Stewart & Kimlin, 2018; Yang, Olofsson, Nair, & Kabanshi, 2017)
	Avoiding outdoor activities in case of severe or extreme thermal discomfort	(Banwell, Dixon, Bambrick, Edwards, & Kjellstrom, 2012; Staiger et al, 2012)
Cloud cover	Increased outdoor activities in cloudless or low cloud weather	(Eisinga et al., 2011; Knuschke et al., 2004; Knuschke et al., 2007; Stewart & Kimlin, 2018)
Precipitation	Avoiding outdoor activities during precipitation	(Arana et al, 2014; Eisinga et al., 2011; Knuschke et al., 2004; Spinney & Millward, 2011)
Wind	Avoiding outdoor activities in high winds	(Arana et al, 2014; Eisinga et al., 2011; Spinney & Millward, 2011)

Arana et al. [585] studied the influence of weather on public transport use in northern Spain during weekends in 2010 and 2011. The number of weekend trips for shopping and leisure decreased when it was windy and rainy and increased when the temperature rose, with a greater influence among occasional drivers than regular drivers. The study region is characterized by a temperate maritime climate with cool summers and mild winters. Average daily temperature maxima have their highest values in August at 22 °C. The statement on the increase of trips with rising temperature should therefore primarily apply to the area of thermal comfort. The range of values of the meteorological variables in the study period was not reported in the paper. The regression model uses the meteorological variables as absolute values, reflecting the annual cycle. It thus provides evidence that more trips are made by public transport (for probably recreational purposes with the possibility for outdoor stays) in temperate climate in summer, and less in rainy and windy conditions.

Banwell et al. [591] conducted interviews and group discussions in Australia (Sydney) with the elderly (> 65 years), a particularly vulnerable group in heat, to shed light on their behaviour in extreme heat or heat waves. The interviews were not directly linked to an acute heat wave. There are various definitions of heatwaves in Australia,

including reaching or exceeding a maximum temperature of 35°C for at least three consecutive days. There was a difference in the behaviour of the elders. In most cases, the pattern of daily activities changed towards reducing physical activities and avoiding spending time outdoors. In some cases, spending time outdoors was moved to the very early morning hours, or physical activity was moved to an air-conditioned area such as a shopping mall. In individual cases, there was no adjustment in daily routine. Consequently, this study gives the indication of predominantly avoidance strategies among elders during extreme heat.

Bélanger et al. [586] used questionnaires to investigate the influence of weather and season on the physical activity of adolescents in Canada (Montreal). Participants were 12-13 years old at the start of the study and were followed for five years. They were able to select applicable activities from 29 in weekly lists that they engaged in for at least five minutes. Because of ties to the school year, data were not collected in July and August, the warmest months on average besides June. No distinction was made between indoor and outdoor activities. Only the frequency of activity was collected, not its duration. In general, the frequency of physical activity was lower in winter and increased in the warmer months. Overall, however, activity decreased with age. Within a season, an increase of 1% in spring and winter and 2% in autumn per 10°C increase in daily mean temperature was reported, as well as a decrease in activity of 2-4% per 10 mm precipitation. The statement regarding the increase in activity with increasing temperature is likely to apply largely to the range of thermal comfort, as the summer months were predominantly not recorded. The actual range of values of the meteorological variables during the study period was not reported in the paper.

Eisinga et al. [587] evaluated the relationship between daily TV consumption and weather conditions in the Netherlands for the period 1996 to 2005. The main meteorological variables affecting TV viewing time were temperature and sunshine duration. More TV was watched when it was colder, cloudier, and wetter, with stronger winds and longer nights. A dependence on the type of TV programme offered was also found, with the conclusion that more broadcast entertainment programmes encourage greater viewing than information programmes in adverse weather conditions. This distinction is now likely to be irrelevant due to the almost unlimited availability of desirable content via streaming services. In the study, a daily mean temperature of 20°C compared to 10°C resulted in 10 to 18 minutes less TV consumption in the entertainment sector. The range of daily mean temperature values during the study period was -12.1 to 25.8°C, with a mean of 10.2°C. It was not investigated whether the interpretation that people actually spent more of their additional TV-free time outdoors when weather conditions were more favorable was correct.

Knuschke et al. [588] and Knuschke et al. [594] ound that meteorological influences, particularly air temperature, sunshine duration, and precipitation play a significant role in individual behaviour with respect to the likelihood of spending time outdoors (and thus the likelihood of individual UV exposures). The leisure time exposures of outdoor workers and indoor workers are largely identical with respect to the mean and distribution of individual UV doses, provided that the same type of leisure time behaviour is involved: the passive share was 70 to 80% while the active share was 20 to 30% of the workers. On the basis of four measurement periods in the months of February, May, September, and December, it was found that the lengths of stay on weekend days vary depending on the season and are influenced by the daily maximum temperature. Since the two variables were not considered independently, it can be assumed that the daily maximum temperature functions primarily as a seasonal indicator in this case. It was assumed that the duration of stay is a linear function of

the daily maximum temperature, although it is rather unlikely that the range of values of the maximum temperature also covered summer values due to the measurement dates. Climatically, the mean daily maximum temperature in Dresden (location of the measurements) is 19°C in May and September, and 4°C in February and December. Consequently, the statement on the increase of outdoor activities with increasing temperature, which is supported by the data, is likely to refer to the range of thermal comfort here as well.

Liu et al. [592] analyzed human planning behaviour in relation to weather using data for coupon purchases in China and visits to public transportation websites worldwide. They conclude that longer-term climate forms the basis for planning responses to current weather. At higher temperatures, the propensity to plan tends to decline. The authors establish a link to social unrest, violence, and societal destabilization in times of climatic change. Within the framework of this model of thought, consequences for outdoor stays would thus also be indirectly possible.

Spinney et al. [589] used time diaries to investigate the influence of weather conditions on leisure behaviour in Canada (Halifax) over the course of a year. Weather data included daily maximum temperature, total precipitation (distinguished between rain and snow), daily maximum wind speed, and total snow depth. The values of daily maximum temperature ranged from -14.8°C to 31.9°C. Additionally, day length was included. While watching television dominates leisure activities with nearly 80% participation rate and a median time of 2.5 hours, only just over 4% of participants engage in outdoor sports, spending nearly an hour (median 58 minutes) outside. A quarter of study participants spend leisure time doing other outdoor activities not classified as sports, most frequently spending three quarters of an hour outside per day. Outdoor activities increase during warm days with more daylight. This confirms the seasonal effect found in the publications of Arana et al., 2014, Belanger et al., 2009, Knuschke et al., 2004 and Knuschke et al., 2007. All weather effects can explain 2.9% of the variation in participation rates in outdoor non-sports activities, and 5.8% in outdoor sports. Temperature (positive) and precipitation (negative) have the strongest influence, and for sports, so does snow depth (positive). The strongest positive influence on time spent on outdoor sports and non-sports activities is day length (season), while precipitation is negatively correlated for time spent on non-sports activities and maximum temperature, wind, and precipitation for sports activities.

Stewart et al. [584] used an online survey of 1400 college students in the southeastern United States to establish a relationship between people's individual liking or disliking of very high temperatures and their exposure to the sun. Mean temperature maxima in Athens, Georgia, ranged from 11.8 to 32.3°C, with values higher than 30°C in all summer months. Individuals who enjoy heat exposure use proportionately less sunscreen than those who avoid heat. A greater proportion of heat-averse individuals spend more time outdoors in the summer months, while this is more likely to be the case in spring and autumn for those who avoid heat. No significant difference was found between women and men in terms of heat preference. U.S. Caucasian types are more likely to be heat-averse, at 51.3%, while the other ethnic types are more likely to avoid heat, at 55.1%.

Yang et al. [590] investigated the relationship between human behaviour related to public park use and thermal comfort in the subarctic climate of northern Sweden (Umea). They combined structured interviews with measurements of meteorological parameters in July and August 2015 for objective thermal assessment of the microclimate. During the interviews from 10 a.m. to 4 p.m., maximum temperatures ranged

from 12.7 to 26.6°C. Under conditions objectively classified as "light heat," most park visitors rated the ambient conditions as "thermal comfort." Forty-nine percent of locals say they prefer even more solar radiation. This example illustrates the overlay of objective measures with subjective expectations and desires, in this case, the solar affinity of people in a subarctic climate. Discrepancies between an objective thermal assessment and subjective thermal perceptions were also found by Becker et al. [593] in a hot-dry climate and were attributed in part to subjective expectations. However, the authors emphasize that it is necessary to test their hypothesis by studies.

Scientific work on temperature-dependent behaviour in other environments is currently pending.

6.2.2. Influence of Climate Change-Induced Changes in Behavioural Patterns on Skin Cancer Incidence

- **The question of whether a climate change-related increase in skin cancer incidence can be expected as a result of changing human behaviour patterns cannot be conclusively answered at present and requires further research.**

Global warming will influence risks and health-promoting effects as a result of climate changes, e.g., ambient temperature and precipitation, through changing sun exposure behaviours [557]. The actual personal UV dose received via sun exposure depends critically on behaviour [557]. Studies have shown that the mean daily UV exposure for adults and children is in the range of 4% to 5% of daily ambient UV radiation [595]; [596]. However, there is considerable variance [531] with a range from one tenth to ten times this mean [597], depending on where one spends time, how long one spends outdoors voluntarily or occupationally, and how one protects oneself from UV radiation. This underscores the importance of individual UV exposure. Most studies on this have been conducted in Caucasian (fair-skinned) populations, so the results may not be applicable to other ethnic groups [598].

The considerations regarding the temperature-dependent behaviour patterns of citizens in different living environments (chapter Chapter 6.2.1) suggest that temperature-dependent behaviour is dependent on thermal sensation and that the frequency and duration of outdoor activities increases with higher temperatures in the range of thermal comfort to mild heat stress. These statements are valid with the caveat that the available studies do not currently allow separation of the influences of daylight duration and thermal conditions.

As stated in chapter Chapter 6.1.1, initial studies indicate that an increased annual sunshine duration, as determined in Germany by the DWD, results in an increased annual sum of the erythema-effective UV irradiance. If, as a result, it can be expected for there to be a greater number of days offering conditions of thermal comfort up to mild heat stress and sunshine, then, according to Knuschke (2004) [588], it can be expected that people belonging to the active leisure behaviour type will spend more time outdoors. For this part of the population, increasing UV personal doses would be expected, which are associated with an increased risk of skin cancer. The measurements and evaluations of Knuschke (2004) [588] also show that the UV vacation dose forms a significant proportion of the annual UV exposure. Changes in holiday behaviour that may result from the effects of climate change on previously preferred holiday destinations would consequently be a not-insignificant aspect in the estimation of UV personal annual doses and the associated skin cancer risk.

In Chapter Chapter 6.1.1 it is described that with a higher number of days with stronger thermal discomfort (heat and heat waves) is to be expected. In this respect, according to the considerations in chapter Chapter 6.2.1.1, there are both indications of avoidance strategies and indications of the fundamental existence of a certain proportion of people with an affinity for heat who would spend more time outdoors despite the heat.

In the scientific literature to date, one indication can be found that the increase in temperature in itself seems to have an influence on the health effects of UV radiation. A study by van der Leun [542] used statistical methods to determine that for the same UV exposure, higher temperatures should increase the carcinogenicity of UV radiation. The authors use data from the US Skin Cancer Registry of the 1970s from ten regions. Because the authors' entire argument depends solely on data from a single region, the results of the analysis do not appear to be very robust. As stated in chapter Chapter 8.2 , the 2015 study [543] did not confirm the effect described above. Piacentini and colleagues [599] conducted studies on the change in non-melanoma incidence associated with temperature increases expected under different emission scenarios for the time horizon 2000 to 2200, based on and extending the study by van der Leun. Assumptions about actual human UV exposure are not directly incorporated in the study by Piacentini [599]. The quantity referred to as exposure in this study is the total available UV dose plus the temperature effect determined by van der Leun [542].

The quantity referred to as exposure in this study is the total available UV dose plus the temperature effect determined by van der Leun [543]. The changes in skin cancer incidence calculated in this study would thus be a direct function of the increase in temperature. However, the study still leaves questions unanswered, so that further investigations would be necessary to consolidate the results, also with regard to the question of whether the possible additional temperature effect is a physiological effect or an effect due to altered exposure behaviour.

Ultimately, the assumption that a warmer climate will lead to significantly increased UV radiation exposure and consequently higher skin cancer incidence cannot be conclusively proven at the present time. This also applies to a suspected additional carcinogenic temperature effect. Suitable studies need to be carried out.

Need for Research

Human behaviour plays a decisive role in real UV radiation exposure. From this derives the need for research to quantify weather-dependent behavioural habits and to clarify the extent to which climate change-induced changes in weather influence behavioural habits of different population groups in the long term in their living environments (kindergartens, schools, training centres, outdoor workplaces, facilities for senior citizens, systems of leisure activities) and on holiday, and how this increases UV radiation exposure and the likelihood of UV overexposure, also during the course of the day. Studies comparing these parameters within individual seasons are needed. On the basis of the knowledge thus gained, quantified statements are to be derived regarding climate change-related changes in the incidence of UV-related diseases, in particular skin cancer, taking into account human behaviour.

6.3. Status Quo: Climate Change and Urban Development

6.3.1. Avoidance of Future Health Consequences/Damage through Urban Development Measures

6.5	Consensus-based Recommendation	new 2020
EC	The primary objective of urban development and planning measures relating to protection from excessive UV radiation and heat must be to protect people in their living environments from unhealthy and unwanted exposure. This requires that the protection offered must be increased.	
	Consensus (95%)	

In order to offer the population protection (beyond the active or behaviour-based self-protection of the individual, e.g. textile and chemical protection) oriented to the conditions against the increasing stresses caused by heat and UV radiation in the course of climate change, the following approaches exist from an urban planning perspective: avoiding the entry of direct and indirect UV radiation, preventing heating, and creating cooling provisions [526]; [600]; [601]. In this context, it is advisable, also due to financial considerations, to implement measures that do not only serve one purpose, but have several benefits at the same time [602]. This allows these measures to be better represented to politicians, taxpayers, investors, and developers. The approach of "Blue-Green-Infrastructures" discussed by Kabisch et al. [601]

as a planning concept for climate impact adaptation with regard to heat avoidance and rainwater retention and its extension to include the aspect of reducing UV radiation input should be highlighted.

In relation to heat and UV radiation, urban planning and the associated spatial planning disciplines are thus required to protect people from unhealthy and unwanted exposure. This means that wherever people go about their daily lives, excessive exposure to heat and UV radiation should be avoided, i.e. specifically when they are inside buildings, when they are going about their daily business (e.g. by shading streets and squares) and when they are outdoors (e.g. schoolyards, playgrounds, sports facilities) [603]. However, even in places where people like to enjoy the sun (e.g. sunbathing areas at swimming pools, beaches, meadows, and paths in parks) [604], it is possible to increase the amount of protection available.

The following measures, which are explained in more detail in Chapter Chapter 6.3.2, appear to be sensible and possible from an urban planning point of view:

- Shading due to building development/structural-technical measures
- Reduction of albedo in built space and open space
- Shading through planting
- Cooling through planting
- Creation of cold air zones

In order for these more technical measures to take effect, measures must be taken at the organisational level. This includes, among other things, the organisation of a

broad political will and the implementation of this political will with the help of appropriate working methods, laws, and regulations at the administrative or implementation level.

6.3.2. Necessities of Technical and Organisational Measures to Avoid Health Consequences of Climate Change Heat Development and UV Exposure

6.6	Consensus-based Recommendation	new 2020
EC	Development, structural engineering measures, and, above all, planting (trees, greening of buildings and lawns), which individually and in combination enable an effective reduction of high solar radiation loads, must be increasingly integrated into climate adaptation strategies of the federal government and local authorities.Particularly for areas with high solar radiation, development must ensure good shading and, where appropriate, canopies with shading elements.Sunlight loads must be reduced through informed planning of daily routines in kindergartens and schools as well as work scheduling.	
	Strong Consensus (100%)	

Shading Due to Buildings/Structural-Technical Measures

Buildings are generally capable of providing shade. Important parameters are the size or height of buildings as well as their orientation, arrangement, and design. However, it should not be ignored that building shadows are considered extremely inefficient, as a study conducted at tourist sites in Paris has shown [605]. According to this study, the least efficient building shading occurs in large squares, which is attributed to a high proportion of diffuse UV radiation, which is higher in such squares than in streets and parks. UV radiation reflected from surfaces may also contribute. Sliney [606] states that a white house paint can reflect up to 22% of UV radiation, whereas an asphalt road reflects only 4% to 9%, depending on age and colour.

Being in the shade of buildings alone cannot provide adequate protection. However, there are other structural/technical measures that provide shade [607]. These can be divided into:

- Permanent systems
- Temporary systems
- Adaptable systems
- Tension membrane structures and sun sails
- Prefabricated shade structures

Permanent systems include stable roofed structures or roof constructions that are erected for a period of at least 10 years. Examples are carport-like canopies, pavilions on playgrounds, or covered pedestrian bridges. Temporary systems such as tents, marquees, and lightweight awnings, on the other hand, are easy to erect and dismantle and are thus well suited when shade is needed only occasionally at certain locations or temporarily at different locations at the same time, or when permanent systems are unsuitable due to activities taking place at the site. Adaptable systems fill a gap here.

Tension membrane structures and awnings can be erected as both permanent and temporary solutions. They are popular because they are versatile in design, require only a few support structures, and can span large areas such as playgrounds and swimming pools as well as shopping streets/pedestrian zones in a filigree manner.

As there are many different types of space and people like to place value on special architectural design, tailor-made solutions are often used. There are also prefabricated shade constructions, where the creative scope is less, but so are the costs. This means that shading measures can be taken on a comparatively manageable budget.

It should be noted with all constructional-technical measures that not every construction or every material offers a high level of protection against UV radiation. In the case of textile solutions, it depends on how closely meshed and thick the material is, what colour it is, and what condition (old/new, wet/dry, loose/stretched) it is in. The tighter-meshed and heavier the material, the higher the demands on the load-bearing structure. Large mesh materials allow better air circulation, but also allow a higher percentage of direct UV radiation to pass through. Light-coloured materials do not heat up as much as dark ones, but scatter and reflect radiation more. Therefore, there is a trade-off to be made in the choice of materials to suit the purpose.

Reducing Albedo in Built Space and Open Space

In addition to house walls and roads, all other relevant surfaces in communities have a specific reflectivity (albedo). From the research of Sliney [606]

it can be seen that grass especially has a low albedo. A high level of protection from UV radiation can therefore be established where structural or natural shading as well as grass-covered areas are equally present. This can also be an argument for more green roofs and facades. The reflective effect of these surfaces is reduced by plant growth. At the same time, a cooling effect is achieved, preventing roof and wall surfaces from heating up and counteracting the heat island effect of cities. Due to the absorption capacity of the vegetation, the usable open space gained by green roofs is better suited for outdoor recreation than, for example, playgrounds laid out with light-coloured slabs.

Playgrounds with a high proportion of sandy surfaces, where the reflectance can be as high as 18%, absolutely require good shading and, if necessary, roofing with shading elements. They are frequented by the youngest children, who require special protection, and should therefore be equipped with special protective measures.

6.7	Consensus-based Recommendation	new 2020
EC	In view of the advancing climate change, surfaces with the lowest possible albedo should be used when creating or redesigning squares (including schoolyards and kindergartens) or streets. In order to reduce the albedo and for the purpose of shading, the majority of all surfaces in residential areas that are not built over must be planted with vegetation.	
	Strong Consensus (100%)	

Grasses are particularly suitable for the greening of areas that are not built over. The creation of such areas can eliminate the need for sealing. They can thus serve as

retention areas for heavy precipitation and thus make a further contribution to climate adaptation.

Shading through Planting

- **Planting (trees, greenery) offers a variety of positive effects and, in terms of protection from heat and UV radiation, can be used to create very efficient structures in urban and rural areas.**

Trees are valuable in adapting to climate change in several ways. Not only do they provide shade depending on the density of their foliage and the size of their canopy as well as their distance from the ground [608], but they can cool their surroundings by up to 30% through evapotranspiration. For example, Streiling & Matzarakis [609] found in a study that temperatures in a city can differ significantly between sites that are heavily shaded by tree canopies and those that are less under the influence of large tree canopies. For example, 30.8°C was measured under a dense canopy, while 34.1°C was measured at a site where there were fewer trees with dense canopies. For the mean radiant temperature, 19.3°C and 21°C were recorded, respectively.

The UV protection factor of trees has been evaluated differently in different studies, ranging from two to 20 [608] depending on various factors. A denser arrangement of several trees into groups of trees usually provides more protection than single trees. Due to these variations, tree shade is not a stable parameter and should only be enjoyed in combination with individual precautions [610]. For urban and landscape planning, however, this means relying more on trees with a particularly high protection factor when creating green infrastructures. As design elements and shade providers, trees are socially accepted and easier to integrate than built structures.

Creation of Cold Air Production Zones

- **By connecting cold air production zones, fresh air corridors can be created that not only have a microclimatic effect, but also serve the entire community. Connected with footpaths and cycle paths, they offer shady spaces for people to move around.**

In combination with other trees and, if necessary, with bodies of water, tree locations can function as cold or fresh air production zones and thus reduce the heat island effect of urban areas. The areas on which the trees stand can, in turn, be used for decentralised rainwater management. In addition, trees store CO2, which in turn serves to reduce the greenhouse effect, and filter dust from the air, which can significantly improve the quality of the air we breathe in communities. If attractively designed, such zones invite people to stay on hot days with high radiation intensity. Buller et al. [611] have shown that cool shaded areas are readily accepted. People walking in the shade of trees are exposed to less UV radiation.

Organisational Measures

According to Knieling et al. [612], climate adaptation requires addressing related tasks along the following categories:

- Cross-sectoral task
- Cross-level tasks
- Intermediary field of action
- Transboundary requirements

- Long-term orientation
- Planning under uncertainty
- Paradigm shift in flood protection

Protection against UV radiation does not yet feature in this report but can and should be included as a task for countering the consequences of climate change. It touches on several sectors (e.g. health, water management and flood protection, urban planning, green spaces and landscape planning) and levels (local and regional) and therefore requires a level that is able to mediate between the different areas of responsibility and to represent the issue appropriately and implement measures, using a broad mix of different formal and informal instruments.

Organisational measures also include all organisational procedures to reduce high UV and heat exposure in the daily routine for each individual. As stated in the policy paper of the UV Protection Alliance [399], daily routines and the organisation of work in people's living environments should be designed in such a way that exposure to UV radiation can be avoided. This is also necessary in the area of occupational safety. Studies show that those who work outdoors have a higher risk of skin cancer than the rest of the population as a result of their activities. Since 01 January 2015, squamous cell carcinomas and their precursors, the multiple actinic keratoses, can be recognised as BK under the number BK5103 (Berufsgenossenschaft Energie). According to the German Social Accident Insurance [613], eemployers should include consideration of suitable sun protection measures in the risk assessment, especially for employees who are regularly exposed to direct sunlight for more than a quarter of an hour. The order of priority of protective measures against solar UV radiation should follow the classic prevention principle "TOP":

- (T) technical measures (shading)
- (O) organizational measures (regulation of time spent under the sun)
- (P) personal measures (clothing, sunglasses, etc.)

According to the DGUV, organisational protective measures are measures such as work planning, start of work, change of activity, rotating work tasks, shift planning, or arrangement of breaks, which must be communicated to the employees in the employer's instruction. If the work task permits, activities should preferably take place indoors around lunchtime. Skilful work planning should reduce daytime exposure. Of course, it is also important to seek shade during work breaks. These statements apply to all insured members of the DGUV and the municipal accident insurers, and also to children and young people in kindergartens and schools.

6.3.3. On the way to a UV-protection optimised municipality

6.8	Consensus-based Recommendation	new 2020
EC	UV protection must be consistently introduced in cities and municipalities as a further line of argument and guiding objective for the implementation of climate protection and adaptation measures. Laws and regulations to implement measures as comprehensively as possible must be enacted or expanded, and funding programmes to optimise UV protection must be launched by municipalities.	
	Strong Consensus (100%)	

UV protection as an argumentation strand and guiding objective can support municipalities in consistently implementing climate protection and climate adaptation measures. The problem of skin cancer is less abstract than the concept of climate change and can thus be better communicated to the public. With guidelines for UV protection optimisation and the coupling of UV protection measures with climate protection and adaptation measures, science can support politics and administration in the implementation of suitable measures. However, this requires funding.

Laws and regulations support municipalities in the largely nationwide implementation of suitable measures because they create legal certainty. In addition, municipalities need funding programmes that make it possible to implement high-quality measures in public spaces and at public facilities.

In order to achieve the goal of largely protecting people from unwanted UV exposure, consistent greening of streets and shading of squares with trees should be aimed for, as explained in chapter Chapter 6.3.2,

which, at best, also take into account requirements of decentralised rainwater management. As a minimum, dark/low-reflective materials are to be provided as floor coverings. It should be noted here that in practice, reflective floor coverings are currently preferred in order to avoid excessive heating. This is understandable, which is why such coverings also require shading. Preferably, however, ground sealing should be avoided as far as possible and grass surfaces should be used, also as roadside greenery and design elements on squares. Here, too, these recommendations lend themselves to combination with rainwater management, because such areas, laid out as retention areas, fulfil another climate change-related purpose. The same applies to playgrounds, schoolyards, and recreational facilities.

Often, however, especially in the case of larger areas, planting cannot provide sufficient protection. In these cases, the structural measures presented (see chapter Chapter 6.3.2) can help to provide shade.

In the future, it should be ensured that all schools, kindergartens, playgrounds, and recreational facilities such as sports fields, open-air swimming pools, etc., have adequate sun protection adapted to the intended use of the facilities. What can be described as sufficient is still to be defined and continuously adjusted.

More thought could be given in future to the roofing of cycle paths and footpaths. Especially connecting routes into and out of centres, which lead through predominantly open and thus unprotected landscape, could be considered for this. Not only do the roofs protect against solar radiation, but the canopies could also keep cycling attractive in rain and snow, thus contributing to climate protection. To make them even more efficient, they could be fitted with photovoltaic systems and used to produce green electricity. Overpasses and pedestrian and cyclist bridges could also be protected and used in this way.

Need for Research

The topic of skin cancer prevention through urban planning and urban development measures still plays a relatively minor role in planning practice in Germany. It is therefore necessary to define effective measures and to create the conditions for their application in combination with existing planning approaches. It is well known that adaptation measures to reduce UV pollution bring synergy effects that are also associated with a reduction in heat pollution. Therefore, it must first be determined in

which subspaces and structures UV radiation (and heat) loads to be reduced occur. Furthermore, it must be clarified which urban structures and which forms of planting are best suited to minimise UV radiation (and heat) under which conditions in different settings. Since not every form of shading or surface design is suitable or desirable for every subspace, the question of which structural-technical measures and which forms of planting can best be integrated into communities must be clarified. For this purpose, it is necessary to determine not only the UV protection factor, but also the effort, costs, design, and acceptance by different stakeholders. Above all, the question of the acceptance of different forms of proportion-related UV protection by the population, but also by politicians and decision-making bodies, is an important field of research. For the necessary planning requirements and security, it must also be investigated whether, and, if so, which, laws and regulations must be created or adapted, how the topic of urban UV (and heat) protection can be integrated into the tasks and decisions of local offices and authorities, and what the handling and routines in this topic area have been to date, possibly also in countries with more experience.

7. Occupational Skin Cancer

Many employed persons work outdoors/in outdoor areas and are thus exposed to UV radiation at work in addition to their leisure activities. Long-term UV radiation exposure, as well as UV radiation exposure acquired during active working hours, is associated with skin cancer risk. That is, UV radiation exposure acquired in occupational life increases the individual morbidity risk on skin cancer. For this reason, multiple actinic keratoses (multiple actinic keratoses are defined as > 5/year individually or confluent to an area > 4cm2) as well as squamous cell carcinoma (including bowen carcinoma) were included by the Federal Ministry of Labour and Social Affairs (BMAS) as BK number 5103 in Annex 1 of the Occupational Diseases Ordinance (BKV), the so-called "Occupational Diseases List," with effect from 01.01.2015. The BK No. 5103 is justified by the knowledge that there is a doubling of the skin cancer rate (squamous cell carcinomas or multiple actinic keratoses) if, in addition to the private (uninsured) natural UV exposure, a 40% occupational (insured) UV exposure is added. This corresponds to about 30% of the lifetime exposure. If this threshold is exceeded, the disease can be recognised as a BK from the point of view of exposure assessment (further information on the subject of BK. DGUV assessment recommendation "Bamberg recommendation" [614].

7.1. Status Quo Outdoor Worker

Dr. Marc Wittlich

7.1.1. Number of Outdoor Workers in Germany

According to the Federal Institute for Occupational Safety and Health, there are 2.4 million outdoor workers in Germany. However, these figures are based on the assumption that outdoor workers are people who spend at least 60% (other sources: 75%) of their time working outdoors.

However, recent studies by the Institute for Occupational Safety and Health of the DGUV (IFA) with GENESIS-UV suggest that the term "outdoor worker," or better, "outdoor employee," should be redefined. Since the definition of outdoor worker is currently of a rather arbitrary nature, it is more expedient to use concrete reference points for this definition. To date, no legally valid exposure limit value has been defined for the protection of employees against hazards from natural UV radiation, either nationally or internationally, so that the standard value from the Second Ordinance amending the ArbMedVV must be used. This states that every employee who works outdoors for more than one hour per day is subject to precautionary measures. Accordingly, an outdoor worker should be defined as a person who works outdoors for more than one hour per day.

If this definition is applied to the data obtained with GENESIS-UV and the employment statistics of the Federal Employment Agency, it is possible to estimate how many outdoor workers there are in Germany. Conservatively, this results in the following figures for the individual categories:

Table 24: If this definition is applied to the data obtained with GENESIS-UV and the employment statistics of the Federal Employment Agency, it is possible to estimate how many outdoor workers there are in Germany. Conservatively, this results in the following fi

Employees subject to social insurance	4,015,691
Part-time employees	935,700
Exclusively marginally employed	614,921
Part-time marginally employed	320,779
Total	5,887,091

Looking at the individual disciplines, the following picture emerges for the main occupational groups:

Table 25: Number of outdoor workers by discipline (Federal Employment Agency, 2019)

Main group (HG)	Designation	Number of outdoor employees within the HG
11	Agricultural, animal husbandry, forestry occupations	466,619
12	Horticulture, floristry	382,983
21	Raw material extraction, glass, ceramics processing	89,315
22	Plastics and wood manufacturing, processing	88,152
24	Metal production, processing, construction	310,170
26	Mechatronics, energy and electrical occupations	7,017
31	Building planning, architecture, surveying professions	44,712
32	Building and civil engineering professions	735,279
33	(Interior) finishing occupations	281,459
34	Building and supply engineering occupations	288,516
42	Geology, geography, environmental protection occupations	9,955

Main group (HG)	Designation	Number of outdoor employees within the HG
51	Transport, logistics (except vehicle drivers)	1,075,438
52	Vehicle and transport equipment drivers	899,322
54	Cleaning professions	8,526
62	Sales occupations	22,086
83	Education, social, domestic professions, theology	1,048,668
84	Teaching and training professions	92,137
94	Performing and entertainment professions	36,737

This estimate is conservative in that occupational groups or sub-groups were only counted if it could be assumed that the largest proportion of employees there fell within the definition of outdoor workers. An example of this is the warehousing industry. There, 1,418,372 employees are active in various occupations. From the measurements of the IFA, it can be deduced that, in particular, warehouse workers in tank farms or external warehouses, as well as shippers, fall under the definition of outdoor workers. However, since it can be assumed that warehousing takes place mainly inside halls, this occupational group was not included in the count.

Overall, it cannot be ruled out that the actual number of outdoor workers in Germany is higher than the figures given above [615].

Need for Research

Institutions such as the Federal Employment Agency, the Federal Statistical Office, and the DGUV should carry out research into the exact determination of numbers of those affected. There is a lack of a scientifically-uniform basis for the question described in this chapter as to what outdoor working time should be used for the assessment of "outdoor activity" in conjunction with the Occupational Health Rules (AMR) 13.3. Personal dosimetric measurements can provide information here.

7.1.2. Level of Additional Occupational UV Exposure for Each Occupational Group

The measurement of exposure to solar UV radiation has already been carried out by several research groups worldwide. Often, the focus has been on irradiation during leisure activities, while relatively few research groups have dealt with irradiation during occupational activities.

In addition, over the years, the measuring technique used has changed fundamentally. At the beginning of the research, mainly polysulfone film dosimeters were used (see e.g. [618]; [617]; [619]; [594]. In current studies, electronic data logger dosimeters are increasingly used, the advantage of which is a time resolution of the

measurements [620], [621]; [622]. In some cases, dosimeters with biological spores are used [623]; [624].

The measurements with GENESIS-UV of the IFA were carried out with a new type of electronic data logger dosimeters, which connects the UV irradiations to be measured with acceleration sensor data. The result is a high reliability of the data. The GENESIS UV measurement system has also been used in international studies [626]; [625].

In Germany, two studies with a larger context have been conducted so far, which deal with the exposure in the occupational environment. While Knuschke [616] monitored some occupational groups in the Dresden area with polysulfone film over a longer period of time, Wittlich (2020) was able to carry out measurements with electronic data logger dosimeters throughout Germany with GENESIS-UV. In the process, 95 occupations with 172 sub-activity groups and 646 sub-activities could be investigated and evaluated. For each occupation, sub-occupation group, or sub-activity, monthly and daily mean values are available in various forms, as well as annual extrapolations. Such a resource is no longer manageable in paper form, so the IFA has created a publicly accessible online database (https://www.dguv.de/ifa/fachinfos/strahlung/genesis-uv/untersuchte-berufe/index.jsp, IFA 2019, https://genesisauswertung.ifa.dguv.de).

For each of the relevant main groups, an annual exposure value of an occupation subsumed therein can be found as an example. It must be taken into account that the standard erythema doses (SED) listed here are acquired in addition to the respective leisure time exposure (measurements show that this is approx. 130 SED per year).

Table 26: Occupationally acquired UV radiation exposure of selected disciplines

Main group (HG)	Designation	Occupation	Annual irradiation in SED* (standard erythema dose, 1 SED corresponds to 100J/m2)
11	Agricultural, animal husbandry, forestry occupations	Farmers	244
12	Horticultural professions, floristry	Gardeners, general	360
21	Raw material extraction, glass, ceramics processing	Blasters (except gunsmiths)	355
22	Plastics and wood manufacturing, processing	Wood preparers	411
24	Metal production, processing, construction	Steel construction fitters	433
26	Mechatronics, energy and electrical professions	Wind turbine service technicians	493

Main group (HG)	Designation	Occupation	Annual irradiation in SED* (standard erythema dose, 1 SED corresponds to 100J/m2)
31	Building planning, architecture, surveying professions	Surveyors	239
32	Building construction and civil engineering	Bricklayers	504
33	(Interior) finishing trades	Plasterers	204
34	Building and supply engineering occupations	Sewage technology specialists	241
51	Transport, logistics (except vehicle drivers)	Delivery persons	309
52	Vehicle and transport equipment drivers	Professional drivers for goods transport	204
83	Education, social, domestic professions, theology	Educators	104
84	Teaching and training professions	Sports teachers	154
The SEDs listed here are exclusively attributable to occupational activities. Accordingly, an average of 130 SEDs of annual irradiation due to leisure time activities, etc. are added per person.			

7.1	Consensus-based Recommendation	new 2020
EC	If employees are exposed to intensive UV radiation outdoors due to their work, targeted technical, organisational, and personal protection and prevention measures must be integrated into everyday working life.	
	Strong Consensus (100%)	

Need for Research

The measurements of UV irradiation in employees initiated by the Institute for Occupational Safety and Health of the DGUV must be kept up to date over the years. Newly occurring or changing activity profiles of occupations lead to different values of irradiation. Accordingly, the findings are subject to constant change, which must be monitored within the framework of research.

7.2. Measures of Behavioural and Situational Prevention for Outdoor Workers

Karina Weinert

The German Occupational Health and Safety Act (ArbSchG) [627] sets out the employer's basic obligations regarding the implementation of occupational health and safety measures to improve the safety and health of employees at work. In doing so, an order of priority must be observed for the measures to be taken.

Proportional preventive measures, i.e., organisational and technical protective measures, are to take precedence over behavioural preventive measures, i.e., personal measures. This is referred to as the hierarchy of the TOP principle:

- Technical
- Organisational
- Personal protective measures ([628])

They are to be recorded in the risk assessment and include the following evidence-based recommendations.

7.2	Evidence-based Recommendation	new 2020
GoR **A**	Technical measure: Workplaces and break areas must offer shading.	
LoE **1-**	[629]	
	Consensus (79%)	

Ruppert et al. [629] conducted a randomized study on skin cancer prevention measures with German vocational school students employed at outdoor workplaces. Six participating vocational schools with a total of 245 participants were randomly assigned into three groups (two intervention groups and one control group). The first intervention group received a 30-minute lecture focusing on workplace sun protection, while the second intervention group was shown a three-minute video produced by the Federal Office for Radiation Protection with comprehensive information on UV radiation and sun protection. The control group received no intervention.

The first intervention group showed a positive association with taking breaks from work in the shade ($p<0.05$). Furthermore, the first intervention group was more likely to seek shade during breaks than the second intervention group as well as the control group (Phi: 0.24). The analysis also confirmed that the provision of shaded workstations increased the willingness to work in the shade by a factor of four in the long term (OR: 4.63, 95% CI: 1.00; 21.51).

7.3	Evidence-based Recommendation	new 2020
GoR **A**	Organisational measure: Employees working outdoors must be informed about UV radiation and the associated health risks as well as the protective measures to be taken.	
LoE **1+** **1-**	[386]; [629]; [630]; [631]; [632]; [633]	
	Strong Consensus (100%)	

Kearney et al. [630] conducted a systematic review on sun protection among farmers and farm workers. A total of 22 studies were included in the review. Two of these included studies conducted interventions aimed at switching to appropriate headwear, for example through a combination of information and action or encouragement. As a result, 25% of the participants in the intervention group in study one switched from a baseball cap to a wide brimmed hat (Burwell et al. 2004. In study two, more participants also wore wide brimmed hats and protective clothing after the intervention than before (p=0.01) (Christensen et al. 2007). Another study intervened by providing a six-month information program on sun protection as well as (early) detection and provided head coverings. The intervention group showed increased sun protection behaviour after the program (p<0.01) (Malak et al. 2011). Another study implemented a community sun protection promoting program. After completing the program, the intervention group had increased sun protection behaviours and a higher number of physician visits for screening and treatment than before the program began (Mullan et al. 1996).

A randomized controlled trial by Mayer et al. [631] aimed at promoting sun protection among United States Postal Service (USPS) letter carriers included 70 postal stations with a total of 2,662 participants. Analyses included 1,183 participants in the intervention group and 1,318 participants in the control group. Participants averaged 43 years of age (SD=8.6), worked an average of 3.9 hours a day outside (SD=1.9), and 77% had skin type III or IV. Over the course of the study, participants were given questionnaires on sun protection behaviours. Furthermore, they were observed and the skin colour of the participants was measured. Follow-ups were conducted after three months, after one year, and after two years. The intervention was based on an ecological behavioural model and a social learning theory as part of the SUNWISE project. At the relationship level, sun protection hats and sunscreen with SPF 30 were provided, as well as visual cues for sun protection implementation using posters, water bottles, key chains, mouse pads, and magnets. At the behavioural level, there were a total of six educational sessions, each lasting five to ten minutes over the two years, with tailored messages about sun protection measures and exposure behaviours. In the intervention group, 27.3% always used a sun protection hat at the beginning of the study. After three months this was 42.7%, after one year 41.1%, and after two years 40.0%. In the control group, 21.0% always used a sunscreen hat at baseline, 21.4% after three months, 24.0% after one year, and 22.3% after two years. Sunscreen was always used before the start of the study within the intervention group by 26.9% and within the control group by 23.5%. After three months, the odds ratio for regular

sunscreen use was 2.8-fold higher in the intervention group (95% CI: 2.2-3.5). In the intervention group 39.4% now always used sunscreen and in the control group this was 23.1%. After one year, 41.6% always used sunscreen in the intervention group and 28.1% in the control group. At the last follow-up after two years, 39.2% (OR=2.9; 95% CI: 2.3-3.6) from the intervention group always used sunscreen and 26.3% from the control group.

As part of a randomized controlled trial in a 2x2 factorial design, Stock et al. [632] studied a total of 148 male Iowa Department of Transportation (DOT) highway workers in an age range of 24 to 64 years. Participants had been working in outdoor occupations for an average of 27 years. During this time, 90% spent five to six hours in the sun per workday, and 60% spent as much as seven to ten hours. Eighty-one percent of respondents never to occasionally used sunscreen at baseline, and 83% never to occasionally wore long-sleeved shirts. Older participants with a history of skin cancer and participants with lighter skin reported higher levels of sun protection behaviours. Interventions were based on the Health Belief Model as well as the Prototype Model of Health Behaviour. Participants were randomly assigned to one of four total intervention groups or the control group. Participants in two of the intervention groups received a UV photo of the face at baseline, and all intervention groups received a 12-minute educational video about skin cancer or ageing due to UV radiation or sun exposure, respectively. The videos included photos of skin wrinkles, age spots, skin cancer, and skin protection information related to sunscreen use, explanation of SPF, recommendation to use a Sun Protection Factor of at least 15, and common sunscreen use mistakes. The control group did not receive any video or UV photo. Follow-up occurred immediately after the intervention, at two months, and at one year. At the post-intervention time point, the knowledge of the intervention groups was better than that of the control group. There was also a significant difference in sun protection behaviour between the intervention groups and the control group at this time point (Fs>7.55, ps<0.01, ds>0.81). There was no significant difference within the intervention groups (Fs<0.63, ps>0.4). Furthermore, a positive attitude towards sun protection was found among the intervention groups (F (1,146) =11.49, p=0.001, d=0.86, Ms=3.6 vs. 3.1). Two months after the interventions, more frequent use of sunscreen by the intervention groups was found (F (1,144) =6.04, p<0.02, d=0.68, Ms=0.78 vs. 1.02). At the last follow-up one year after the intervention was given, the control group had the lowest sun protection behaviour. The intervention groups that had received a UV photo had significantly higher sun protection behaviour after one year compared to the time before the intervention (ps<0.02). Only between the control group and the first intervention group, which did not receive a UV photo and a skin aging video, was no significant difference found. An intervention with a UV photo and/or information on skin cancer was found to be most effective for street workers.

Andersen et al. [633] and Buller et al. [386] examined the long-term effects of the so-called Go Sun Smart (GSS) campaign in a randomized controlled trial beginning in the winter of 2001. In this campaign, embassies in ski resorts in the western USA and Canada recommended sun protection measures for outdoor and indoor workers and guests, for example through posters, newsletters, and a website. The randomized subsample included 3,801 employees of 26 ski resorts after excluding ineligible individuals. At the first follow-up in spring 2002, 2,119 participants still took part and at the second follow-up in autumn 2002, this number was 1,463. The participants were on average 34 years old, 96% light-skinned, and 59% of the participants worked outdoors. The control group was composed of ski area employees without intervention. At first follow-up, a dichotomous scale showed 14% fewer sunburns compared to

baseline in winter 2001, and 8% fewer in the control group (OR=1.63, p<0.05). The number of sunburns was lower in the intervention group than in the control group (difference: 0.25%, p<0.05). There were differences in sun protection behaviour at the second follow-up. Participants in the intervention group were now more likely to wear sunglasses (OR=1.26, p<0.01), more likely to use sunscreen (OR=1.43, p<0.01), and more likely to avoid the sun while working (OR= 1.17, p=0.08). Overall, the intervention group had a higher sun protection behaviour score than the control group (IG: 2.57, CG: 2.63, p=0.04). There were no significant effects for sun protection at the follow-ups. Overall, the results were dependent on the ski resort and its level of implementation of Go Sun Smart (GSS) measures. Through the study, employees were found to suffer more sunburns and take fewer sun protection measures at ski areas that implemented fewer GSS materials. The GSS program reduced excessive UV exposure of employees at ski resorts in the short term. Medium-term effects of the GSS program on skin cancer prevention at ski resorts are at least as large as the short-term effects, especially with respect to sun protection behaviours. The effects are greater in summer than in winter.

The study by Ruppert et al. [629] dealt, as already described in detail above, with the effectiveness of occupational prevention measures on the subject of skin cancer among vocational school students employed at outdoor locations in Germany. In addition to the results already described, a significant correlation between the use of sunscreen products and gender (female) as well as age (>22 years) was also found three months after the baseline survey. Participants' attitudes towards sunscreen were rated as good at this time.

Houdmont et al. [634] addressed sun protection among construction workers in the UK as part of a controlled study. A total of 1,279 participants were included in the study. Follow-up was carried out on 120 participants. A total of 70 outdoor workers were in the intervention group and 50 in the control group. The intervention was delivered during working hours using a 12-minute DVD entitled "Sun Safety in Construction: A Workplace Health Guidance Film." The control group was not shown the DVD. A questionnaire was completed by the participants at the beginning of the study and at the follow-up after approximately one year. Using the questionnaire, participants were asked about ten sun protection measures and an assessment of personal use was made using one of five statements, based on the stages of the Transtheoretical Model (TTM) (stages: lack of intention, intention formation, preparation, action, maintenance, completion).

In terms of sun protection knowledge, there were no significant results for the five items. For sun protection behaviours, however, there was an increase in the Transtheoretical Model for nine measures for the intervention group compared to two for the control group. The nine sun protection measures that improved within the intervention group included using a cover when working in the sun (33% change, p<0.001), checking moles regularly (27% change, p<0.001), job rotation to minimize time working in the sun (24% change, p< 0.001), wearing sunglasses (22% change, p<0.001), minimizing working in direct midday sun (21% change, p<0.01), using sunscreen (17% change, p<0.05), wearing long-sleeved, loose-fitting clothing (14% change, p<0.01), checking the UV index daily (10% change, p<0.05), and wearing a helmet with neck protection (9% change, p<0.05).

7.4	Consensus-based Recommendation	new 2020
EC	Organisational measure: Necessary means (e.g. sun hat with brim and neck protection, sunglasses, covering clothing, sunscreen) to protect against UV radiation must be provided at the workplace.	
	Strong Consensus (100%)	

The study by Ruppert et al. [629] dealt, as described in more detail above, with the effectiveness of occupational prevention measures on the subject of skin cancer among vocational students employed at outdoor workplaces in Germany. In addition to the results already described, a correlation between the provision and use of sunglasses at the workplace was also found (Phi: 0.45).

7.5	Consensus-based Recommendation	new 2020
EC	Organisational measure: In order to reduce UV exposure, working hours including breaks (e.g. avoiding outdoor work at lunchtime) must be organised.	
	Consensus (95%)	

A study by Thieden et al. [635] was able to show that shifting the break times of Irish gardeners towards times of highest UV radiation resulted in reduced UV exposure measured with a dosimeter.

7.6	Evidence-based Recommendation	new 2020
GoR A	Personal measure: The skin and eyes of outdoor workers must be protected from solar radiation. The body must be covered to the maximum with suitable clothing, i.e., in the form of long-sleeved clothing and headgear with neck protection.	
LoE 1+ 2++	[386]; [630]; [631]; [634]	
	Strong Consensus (100%)	

As explained in more detail above, Kearney et al. [630] conducted a systematic review of a total of 22 studies on the topic of sun protection among farmers and farm workers. Two of these included studies conducted interventions aimed at switching to appropriate headgear, for example, through a combination of information and action or encouragement. Twenty-five percent of participants in the intervention group from study one switched from a baseball cap to a wide brimmed hat as a result (Burwell et al. 2004). In study two, more participants also wore wide brim hats as well as

protective clothing after the intervention occurred than before (p=0.01) (Christensen et al. 2007). Another study intervened by providing a six-month information program on sun protection as well as (early) detection and provided head coverings. The intervention group showed increased sun protection behaviour after the programme (p<0.01) (Malak et al. 2011).

As discussed above, the study by Houdmont et al. [634] included an intervention in the form of a short DVD on sun protection in construction, which was played during working hours. As a result, more workers in the intervention group used a cover-up when working in the sun (33% change, p<0.001). Furthermore, more participants in the intervention wore sunglasses (22% change, p<0.001) as well as long-sleeved, loose-fitting clothing (14% change, p<0.001) and a helmet with neck protection (9% change, p<0.05).

Buller et al. [386] and Andersen et al. [633] investigated the long-term effects of the so-called Go Sun Smart (GSS) campaign in selected ski resorts in the winter of 2001. Endpoints on sun protection behaviour included the frequency of use of protective clothing, hats, and sunglasses and goggles. At the second follow-up in autumn 2002, the intervention group wore sunglasses more frequently (OR=1.26, p<0.01) and generally had a higher total score for sun protection behaviour (2.57) compared to the control group (2.63) (p=0.04).

In the study by Mayer et al. [631], interventions took place as part of the SUNWISE project. At the ratio level, sun protection hats were provided, among other things. In the intervention group, 27.3% always used a sun protection hat at the beginning of the study. After three months this figure was 42.7%, after one year, 41.1%, and after two years, 40.0%. In the control group, 21.0% always used a sun protection hat at baseline, 21.4% after 3 months, 24.0% after one year, and 22.3% after two years.

7.7	**Evidence-based Recommendation**	**new 2020**
GoR **A**	Personal measure: Body parts that cannot be covered or shaded by textiles must be covered with suitable sunscreens.	
LoE **1+** **2++**	[386]; [631]; [632]; [633]; [634]	
	Strong Consensus (97%)	

In the study by Mayer et al. [631], nterventions were also carried out within the framework of the SUNWISE project. At the ratio level, sun cream with Sun Protection Factor 30 was provided, among other things. The endpoint here was the amount of sunscreen used with a community pump bottle on display. Before the start of the study, sunscreen was always used within the intervention group by 26.9% and within the control group by 23.5%. After three months, the odds ratio for regular sunscreen use was 2.8-fold higher in the intervention group (95%CI: 2.2-3.5). In the intervention group 39.4% now always used sunscreen and in the control group 23.1%. After one year, 41.6% always used sunscreen in the intervention group and 28.1% in the control

group. At the last follow-up after two years, 39.2% (OR=2.9; 95% CI: 2.3-3.6) from the intervention group always used sunscreen and 26.3% from the control group.

Stock et al. [632] studied a total of 148 male Iowa Department of Transportation (DOT) road workers as discussed in detail above. Eighty-one percent of participants never to occasionally used sunscreen at baseline. Videos shown during the intervention included information on skin protection as it relates to sunscreen use, sun protection factor explanation, recommendation to use a Sun Protection Factor of at least 15, and common sunscreen use mistakes. At the post-intervention time point, there was a significant difference in sun protection behaviour between the intervention groups and the control group (Fs>7.55, ps<0.01, ds>0.81). Furthermore, a positive attitude towards sun protection was found among the intervention groups (F (1,146) =11.49, p=0.001, d=0.86, Ms=3.6 vs. 3.1). Two months after the interventions, more frequent use of sunscreen by the intervention groups was found (F (1,144) =6.04, p<0.02, d=0.68, Ms=0.78 vs. 1.02). At the last follow-up one year after the intervention had taken place, the control group had the lowest sun protection behaviour.

Buller et al. [386] and Andersen et al. [633] investigated the long-term effects of the Go Sun Smart (GSS) campaign in selected ski resorts in winter 2001. Endpoints on sun protection behaviour included the frequency of sun cream and lip balm use. At the second follow-up in autumn 2002, the intervention group used sunscreen more frequently (OR=1.43, p<0.01) compared to the control group.

Ruppert et al. [629] investigated the effectiveness of occupational skin cancer prevention measures among vocational students employed at outdoor workplaces in Germany, as discussed in detail above. Among other things, a significant correlation between the use of sunscreen products and gender (female) and age (>22 years) was found three months after the baseline survey and after the intervention. Participants' attitudes toward sunscreen were rated as good at this time.

The study by Houdmont et al (2016) included an intervention in the form of a short DVD on sun protection in construction which was played during working hours. As a result, more participants in the intervention group used sunscreen compared to the control group (17% change, p<0.05).

7.3. Providing Information and Motivating Employees to Take Protective Measures

According to ArbSchG [627], the employer "has to instruct the employees sufficiently and appropriately about safety and health protection at work during their working hours. The instruction includes instructions and explanations that are specifically geared to the workplace or the employee's area of responsibility. Instruction must be given at the time of recruitment, when there is a change in the scope of duties, at the introduction of new work equipment or a new technology, and before the employee starts work. The instruction must be adapted to the development of hazards and, if necessary, repeated regularly" (ArbschG, §12, paragraph 1).

7.8	Evidence-based Recommendation	new 2020
GoR A	Recommendation grade AProtection and prevention measures must be taught in person.Recommendation grade 0Visual support or reminders of the desired target behaviour can be provided, e.g. in the form of posters, pictures, or videos.	
LoE 1+ 1-	[386]; [629]; [630]; [631]; [632]; [633]	
	Strong Consensus (100%)	

Kearney et al. [630] conducted a systematic review of sun protection among farmers and farm workers. The educational interventions within the 22 different studies produced significant improvements in knowledge, attitudes, and behaviour. Face-to-face contacts were the most effective.

The interventions implemented in a study by Mayer et al. [631] turned out to be successful in increasing sun protection behaviour in view of the results already discussed in detail above. The ease of implementation in institutions also turned out to be positive. These interventions were, at the relationship level, the provision of sun protection hats and sunscreen with Sun Protection Factor 30 with the support of visual cues to implement sun protection measures, for example in the form of posters, water bottles, key rings, mouse pads, or magnets. At the behavioural level, six educational sessions, each lasting five to ten minutes, were conducted over a two-year period with tailored messages about sun protection measures and exposure behaviours.

Stock et al. [632] concluded, based on previous research described above, that a video on skin aging did not make a significant difference to long-term sun protection behaviour. An intervention with a UV photo and/or information on skin cancer was found to be most effective for street workers.

Andersen et al. [633] and Buller et al. [386] examined the long-term effects of the Go Sun Smart (GSS) campaign in a randomized controlled trial beginning in the winter of 2001. In this campaign, embassies at ski resorts in the western United States and Canada recommended sun protection measures for outdoor and indoor workers and guests, such as posters, newsletters, and a website. The GSS program reduced excessive UV exposure and sunburns among employees at the affected ski resorts in the short term. Medium-term effects of the GSS programme on skin cancer prevention are at least as large as the short-term effects, especially with regard to sun protection behaviour. The effects are greater in summer than in winter. (Further studies, for example in other working areas, over longer periods of time, in countries with greater UV exposure, are necessary for generalization).

Based on previous studies, which have already been discussed in detail above, Ruppert et al. [629] concluded that prevention measures and health education on skin cancer protection for outdoor workers should be started at an early age. Information and training on UV radiation and protection should be provided from the first year of training. A lecture intervention is more effective than a video. In addition, the

prevention of the relationship is an important factor. Employers should provide sun protection measures.

7.3.1. Percentage of Outdoor Workers Who Are Subject to Mandatory or Available Preventive Care

The second ordinance amending the Ordinance on Occupational Medical Precautions describes exclusively the introduction of preventive care on offer. Mandatory preventive care is not introduced (cf. Chapter 7.4).

In the explanatory note to Federal Printing Paper 237/19(B), the Federal Council states that a quarter of employees work outdoors but are not exposed to intensive exposure to natural UV radiation of regularly one hour or more per day. Accordingly, approximately 1.8 million workers would fall under the precautionary cause.

In addition, the legislature has mandated that the offer screening must be offered every three years. Accordingly, the precautionary occasion is to be quantified annually with a case number of 500,000 employees.

Detailed data can be derived from the DGUV measurement project on the exposure of employees to solar UV radiation using GENESIS-UV. If the Federal Council's statement that about a quarter of outdoor workers are not covered by the precautionary principle is applied to the figures given in Chapter Chapter 7.1, it follows that about 4.5 million workers are covered by the precautionary principle. If this is spread over three years, then the precautionary event is to be quantified as an annual figure of 1.5 million employees [636].

7.4. Occupational Health Screening for Outdoor Workers

Preventive occupational medicine is intended to contribute to maintaining employability and to the further development of occupational health protection. It serves to determine whether there is an increased risk to health when performing a certain activity and to detect work-related health disorders at an early stage. In this respect, it is an instrument of secondary prevention (early detection – also of risk factors; early intervention, i.e. targeted advice). An essential element of preventive occupational medicine is individual counselling. If there is an appropriate indication, an offer of examination is made, which the employee can accept or reject.

Only doctors with the specialist title of occupational medicine or the additional title of occupational medicine may be commissioned to carry out preventive occupational medicine. As a rule, the company doctor should carry out the preventive medical check-up.

The basic requirements for preventive occupational medicine are regulated in the ArbMedVV and the AMR. A distinction is made between the initiation of mandatory and available preventive medical care:

§ 4 ArbMedVV – Mandatory preventive care

The employer must arrange obligatory preventive care for employees in accordance with the annex. Mandatory preventive care must be arranged before the start of the activity and at regular intervals thereafter. The employer may only allow an activity to be carried out if the employee has taken part in compulsory preventive care.

§ 5 ArbMedVV – Preventive care on offer

The employer must offer the employees preventive care on offer in accordance with the Annex. Preventive care must be offered before the employee starts work and at regular intervals thereafter. Refusal of an offer does not release the employer from the obligation to continue to offer preventive care on a regular basis.

The second amendment to the ArbMedVV, which came into force on 18 July 2019, only provides for offering preventive care for outdoor activities. The employer must offer occupational health care to employees who are exposed to intensive exposure to natural UV radiation of regularly one hour or more per day. In addition, he must keep exposure to hazardous sunlight as low as possible.

AMR 13.3 "Outdoor Activities with Intensive Exposure to Natural UV Radiation of Regularly One Hour or More Per Day," which was published in the Joint Ministerial Gazette (GMBl) on 24 September 2019, specifies outdoor activities with intensive exposure to natural UV radiation based on the following criteria:

For activities in Germany, the following conditions must be met:

(1) For outdoor activities

- "In the period from April to September
- between 10 a.m. and 3 p.m. Central European Time (CET) (corresponds to 11 a.m. to 4 p.m. Central European Summer Time (CEST))
- for a total duration of at least one hour per working day
- on at least 50 working days.

(2) In the case of activities in the shade (e.g. by means of enclosure or other shading measures) which are carried out there permanently and uninterruptedly, a supply precaution is only to be offered from a duration of at least two hours in total due to the lower intensity of the UV radiation. The other criteria set out in paragraph 1 shall remain unaffected.

(3) In the case of outdoor activities on snow-covered surfaces above 1000 metres above sea level, the period referred to in paragraph 1 shall be extended to the duration of one calendar year. This shall not affect the other criteria referred to in paragraph 1 (GMBl No. 36, 24 September 2019, p. 697)."

For activities outside Germany in the equatorial region between 30th degrees north latitude and 35th degrees south latitude, the following requirements for the offer of preventive care on the part of employers shall apply:

(1) For outdoor activities

- all year round
- between 10 a.m. and 3 p.m. local time
- for a total duration of at least one hour per working day
- on at least eight working days.

(2) In the case of activities in the shade (e.g. by means of enclosure or other shading measures) which are carried out there permanently and uninterruptedly, preventive care shall only be offered from a duration of at least two hours in total due to the lower intensity of UV radiation. The other criteria mentioned in paragraph 1 shall remain unaffected.

(3) For activities outside Germany in the entire area of the northern hemisphere greater than 30th degree northern latitude as well as in the entire area of the southern hemisphere greater than 35th degree southern latitude, the criteria specified in section 4.2 shall apply accordingly, whereby the local time shall be decisive instead of the CET and the months of October to March shall be taken into account for the southern hemisphere (GMBl No. 36, 24 September 2019, p. 697). The employer's offer of offer provision must be made on a regular basis and also in the event of the employee(s) rejecting an earlier offer. The maximum time limits, which are regulated in AMR No. 2.1 "time limits for the initiation/offer of occupational health care" (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, 2016), are therefore as follows for outdoor activities:

- The first precaution must be initiated or offered within three months before the start of the activity.
- The second precaution must be arranged or offered no later than twelve months after the start of the activity.
- Each subsequent screening must be initiated or offered no later than 36 months after the previous screening.

Shorter periods are possible if they are considered necessary from an occupational health point of view and can be specified in the risk assessment. The indication of when renewed occupational medical screening is indicated from a medical point of view is part of the precautionary certificate within the meaning of § 6 Paragraph 3 Number 3 ArbMedVV (see AMR 6.3), which is issued to the employer and the employee. In the first years of employment, the focus is on education and the identification of individual risk factors. Early skin cancer detection becomes more important with increasing duration of exposure.

In order to facilitate the organisation of preventive care and individual information and advice on all work-related health hazards, all preventive care occasions should be bundled in one appointment with the company doctor.

7.9	**Consensus-based Recommendation**	**new 2020**
EC	The fact that UV radiation exposure represents the highest occupational cancer risk for outdoor workers in Germany must be the reason for the legislator to prescribe mandatory screening for all highly exposed persons.	
	Consensus (89%)	

UV exposure is by far associated with the highest occupational cancer risk for employees in Germany (Drexler 2017). This should be reason for the legislator to prescribe mandatory screening for all highly exposed persons, as individual counselling can achieve changes in behaviour, especially if counselling is provided at an early stage.

7.5. Reporting Channels, Costs, and Payers of Work-Related Skin Cancer

7.5.1. Reporting Procedure in the Event of Suspicion of the Existence of an Occupational Disease

Suspicion of the existence of an occupational disease can be reported to the relevant statutory accident insurance institution (Berufsgenossenschaften and accident insurance funds) in various ways.

Pursuant to § 193 (2) Social Code VII (SGB VII), employers are legally obliged to report an occupational disease if, on the basis of their personal knowledge, they have indications of the existence of a corresponding occupational disease. It is sufficient for the report that the illness that has occurred could be related to effects at the workplace.

Insured persons may contact the responsible UV institution directly if they suspect the existence of a BK.

According to § 202 SGB VII, doctors are legally obliged to report a BK, even if the insured person objects. This obligation can only be waived if it is certain that the disease has already been reported.

The medical BK notification must be made if there is a reasonable suspicion that a BK within the meaning of the so-called "BK list" (Annex 1 of the BKV) exists. In the case of BK No. 5103 (squamous cell carcinoma or multiple actinic keratoses of the skin caused by natural UV radiation), the suspicion is well-founded if the following have been diagnosed on body parts exposed due to work:

- a squamous cell carcinoma or
- a Bowen's disease/Bowen's carcinoma or
- the preliminary stages, the actinic keratoses.

The precancerous lesions must be multiple in the sense of BK No. 5103, i.e. with a number of more than five within one year or a field carcinization larger than 4 cm2.

In addition, there must have been a relevant work-related UV exposure due to outdoor work. A rough estimate is sufficient for this at the time of notification. The guideline value is a ratio of private and work-related UV exposure (see also convention in Chapter 7.4.4). Since the private dose increases with each year of life, the work-related UV exposure duration required for a BK recognition also increases. Long-term exposure in the sense of this BK is considered to be, e.g. for an age of:

- 50 years - 15 years of outdoor work
- 60 years - 18 years of outdoor work
- 70 years - 21 years of outdoor work
- 80 years - 24 years of outdoor work

The declaration of occupational disease should be made using the statutory form F6000 "Medical Declaration of Suspected Occupational Disease." It must be made immediately, i.e. without undue delay. The notification is remunerated separately by the UV insurer (UV-GOÄ No. 141).

The insured persons must be informed of the contents and of the UV institution to which the BK notification is sent. The responsible UV agency depends on the last hazardous activity of the insured person and is:

- in the case of commercial enterprises, an employers' liability insurance association (broken down by industry),
- in the case of public sector enterprises, one of the regionally subdivided accident insurance funds, and
- for activities in agriculture and horticulture, the Social Insurance for Agriculture, Forestry and Horticulture (SVLFG).

Special regulations apply to civil servants (e.g. in the police service or in the armed forces) and the suspected BK must usually be reported to the employer by the sick person. Further details are regulated in the respective civil servant pension laws of the federal states/federal government.

7.5.2. Cost Unit for Costs of Diagnostics, Therapy, and Aftercare of Work-Related Skin Cancer

The cost bearer for the diagnosis and treatment of work-related skin cancer is the health insurance (statutory or private) until it is recognised as a BK.

If there is a suspicion of the existence of a BK, this must be reported to the responsible statutory accident insurance institution. The notification is remunerated separately by the accident insurance institution (UV-GOÄ-Nr. 141).

After recognition of a BK, the UV insurer assumes all necessary benefits in order to improve the consequences of the BK by all appropriate means. The attending physician will receive a treatment order in which further details on medical reports, aftercare, and the assumption of costs for medical services are regulated. Further detailed information on this subject is contained in the DGUV Guide "Fees in Occupational Dermatology" [637].

7.5.3. Costs of Occupational Medical Screening for Work-Related Skin Cancer

On the occasion of the Second Ordinance amending ArbMedVV, the compliance costs for citizens, for the economy, and for the administration were surveyed. While there are no additional costs for citizens or for the federal administration, additional annual costs of 16.55 million euros are expected for the economy. They include:

- personnel costs for the loss of employees amounting to approximately 6.96 million euros,
- material costs for the use of company doctors of around 7.56 million euros, as well as
- bureaucratic costs of around 2.03 million euros for the employer's efforts to procure and provide information on precautionary measures [636].

7.5.4. Costs of Treatment for Work-Related Skin Cancer

The statutory accident insurance institutions in Germany (Berufsgenossenschaften and public-sector accident insurance institutions excluding the Social Insurance for Agriculture, Forestry and Horticulture) incurred benefit costs for the medical rehabilitation of cases of BK No. 5103 amounting to 5.8 million in 2017 and 3.3 million in

2016 (source: DGUV Occupational Disease Cost Survey, [636]). This results in costs per case of 617 euros (2017) and 560 euros (2016).

Further costs directly related to the disease, such as benefits for participation in working life in the event of a necessary change of job, do not generally arise in the case of BK No. 5103. The average age at the time of notification of suspected BK was 72 years (in 2017), at a time when insured persons are generally no longer gainfully employed.

8. Secondary Prevention

8.1. General Information on the Early Detection of Skin Cancer

8.1.1. Definition of Secondary Prevention, Early Detection, and Screening

Secondary prevention aims at the early detection and prevention of the progression of a disease. Secondary prevention can be described as an umbrella term that is centrally linked to the concept and possibilities of early detection. Early detection of diseases focuses on the timely identification of a disease, disorder, malformation, or other health impairment. In order to be suitable for early detection, it is therefore necessary for diseases to have a long symptom-free phase in which precursors or early stages of the disease are already detectable. By detecting disease at an early stage, secondary prevention aims to reduce or prevent mortality, morbidity, and thereby impaired quality of life.

Screening is a key component of early detection. The term "screening" comes from the English language and means "filter examination." Screening is designed to detect precursors, early stages, and risk factors of a disease. In screening, "undetected diseases or defects are detected using rapid and large-scale tests [...]. Screening tests distinguish between apparently healthy people and those who may have the disease" [638] . Not every screening test takes the form of systematic screening. A screening is part of an overarching program that predefines the target population, examination method, and testing procedures in relation to the target disease. Such a screening programme is characterised by "addressing all persons of a defined target group and specifications for quality assurance from the first invitation to the evaluation of the endpoints" [639]. It complies with defined and verifiable quality standards in that the physicians carrying out the screening not only use a standardised examination method, but also document their examination results, thus making the screening evaluable.

SCS includes the recruitment of apparently healthy participants, collection of medical history and visual whole-body inspection (screening test) for the early detection of malignant skin tumours. As a rule, advice on risk factors and prevention of skin cancer should also be given in this context.

The term **precaution**, which is also frequently used in the context of secondary prevention, is a term used in the legal sense of the coverage of a risk by, e.g., an insurance. However, this term is misleading, as it could give the impression that regular participation prevents the occurrence of cancer. In the context of secondary prevention, the term early detection should therefore be used, as this is also implemented in the Cancer Early Detection Guideline of the G-BA.

8.1.2. Aims of Screening/Basic Principles of Screening Measures

The core concept of screening is the assumption that by diagnosing a disease (e.g. cancer) at an early stage, treatment is more likely to be successful and the risk of morbidity and mortality is reduced. This assumption implicitly assumes that if a disease is left untreated, the prognosis will worsen as it progresses. In the case of MM

and SCC, reduced tumour thickness (i.e. a skin lesion at a less advanced stage) is the most important prognostic factor for improved survival (see, for example, for squamous cell carcinoma [640]). For patients with a BCC, detection of the disease at an early stage means improved quality of life due to fewer necessary therapeutic interventions.

For a cancer entity to be eligible for screening, a (long) "preclinical phase" in which early detection is possible is an essential prerequisite[641]. The disease starts at a certain point in time without being detectable yet. Only later can the disease be diagnosed, e.g. when a solid tumour has reached a minimal (i.e. visible) size. The phase before a disease would be diagnosed even without screening is known as the preclinical phase or "sojourn time" [642]. Accordingly, screening can only lead to an earlier diagnosis during this preclinical phase. The period of time by which the diagnosis is advanced is known as the "lead time." Neither the "lead time" nor the preclinical phase can be determined for single individuals. However, the distribution of these two time periods can be estimated for a population that has been screened. It is expected that in a screened group the average age at the time of diagnosis is lower (by the value of the respective "lead time") than in a comparison group without screening (Spix & Blettner, 2012).

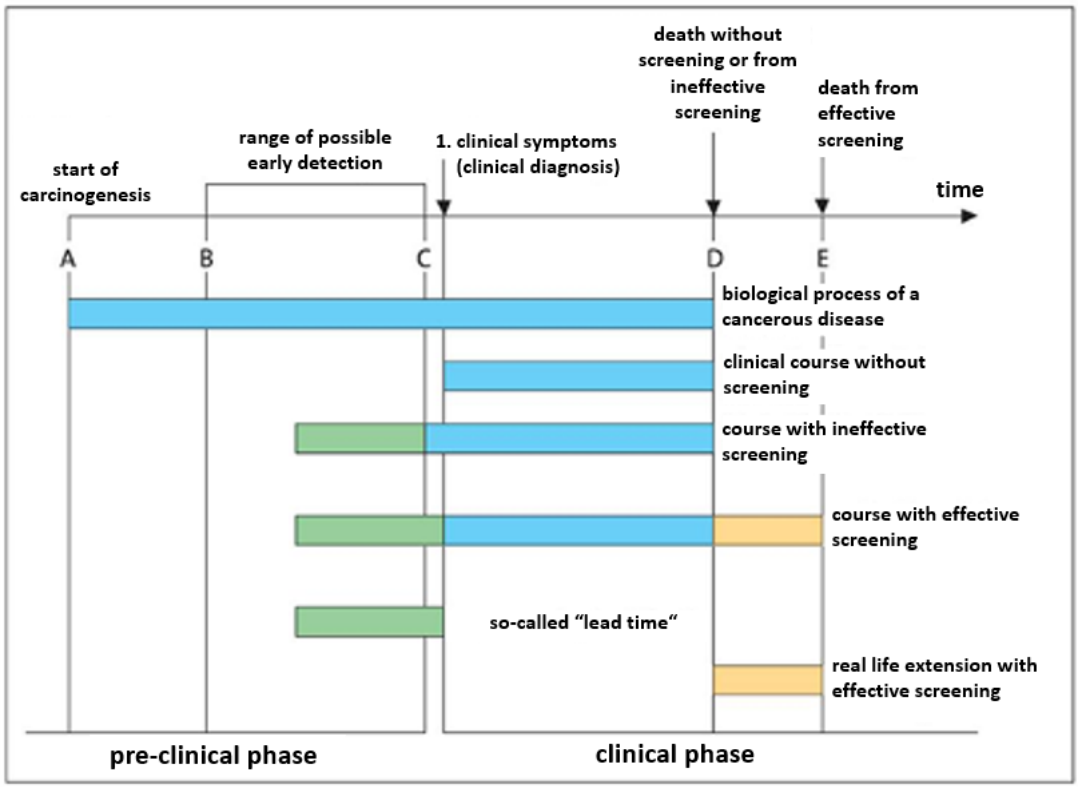

Figure 12: Course of a cancer disease with effective screening (Becker, 2002)

Since the introduction of screening measures, the debate about cancer screening program endpoints has been in flux. Schwartz and others [643] defined increased quality of life and prolonged life span as measures of the effectiveness of the statutory cancer screening examination (CFE) program. Today, however, reduction in mortality is often considered the overriding goal. Therefore, the reduction of unfavourable disease stages, increase of life expectancy, reduction of morbidity, avoidance of unnecessary examinations (e.g. biopsies), reduction of costs of expensive treatments of

advanced diseases, improvement of quality of life, as well as informing the population about the screening measures, are formulated as goals. These goals are also the parameters for the outcome-oriented evaluation of screening measures.

The target group consists of persons who subjectively feel healthy and are also predominantly healthy. The target group does not include persons who come for screening because of complaints or with symptoms or who are in follow-up care. Therefore, few positive test results are to be expected in a screening.

According to Morrison [644], a screening divides the participants into "persons with a low probability of having the disease" and "persons with a high probability of having the disease," whereby the second group is to be submitted to follow-up diagnostics (suspected diagnostics and/or confirmatory diagnostics, see Chapter 8.5)

to confirm the diagnosis. Accordingly, screening refers neither to diagnosis nor to treatment. If the examination is extended to the entire body for the diagnosis of a self-discovered skin lesion, this can also be referred to as "screening."

According to the screening criteria of Wilson and Jungner (1968), screening for cancer should cover the following points [641]:

- The target disease should be a major health problem,
- The natural history of the disease should be adequately understood,
- There should be an identifiable early stage,
- Treatment should be more effective in the early stage than in the late stage,
- An effective test to detect early stages should be available,
- The test should be acceptable,
- Examination intervals should be known/established,
- Adequate health care resources to cover the additional costs arising from screening,
- Both physical and psychological risks should be less than the benefits,
- The costs should be balanced with the benefits.

These were revised by Andermann et al. [645] based on more recent discussion. The following criteria are mentioned by them:

- The screening program should address an identified need/societal problem,
- The goals of the screening should be defined at the beginning,
- There should be a defined target population,
- There should be scientific evidence of the effectiveness of the screening program,
- The program should include as components statements about clinician training, tests used, clinical procedures, and program management,
- There should be quality assurance with a mechanism to minimize potential screening risk,
- The program should ensure informed choice, confidentiality, and respect for the autonomy of the individual,
- The program should ensure equity and provide access to screening for the entire target population,
- Program evaluation should be planned from the outset,
- The overall benefits of screening should outweigh the harms.

Skin cancer meets most, if not all, of these criteria, and is therefore suitable for screening. However, more evidence is needed to evaluate all of these 10 criteria, e.g.

the harms of a SCS, cost-effectiveness, as well as the question of the appropriate screening interval.

In a screening programme, screening is usually carried out by specially trained clinicians. One way to screen is to screen an entire population (population-based or mass screening) without dividing the population into subgroups. Another possibility is a risk group screening only in certain population groups, e.g. in persons who have a higher probability of contracting skin cancer [641].

Given the dependence of the positive predictive value (PPV, see below) on the prevalence of a disease in a given population, and because prevalence is by definition higher in at-risk groups, a screening programme will usually be most productive and effective if it targets high-risk individuals (better PPV in at-risk groups compared with PPV in non-risk groups).

A screening programme may be systematic, by which is meant a highly organised programme with standardised and quality-assured screening. In contrast, a decentralized unsystematic screening is also referred to as "opportunistic" or "grey" screening [641].

Due to the lack of a standardized screening procedure, evaluations of opportunistic screening are difficult to conduct.

A systematic screening program should include the following components [646]; [642]:

- A target population,
- A recruitment strategy (strategies often include mass media campaigns with information specific to the target population and invitation or reminder letters personally addressed to those eligible to participate),
- A screening test,
- A standardized training program for performing physicians,
- A screening interval,
- Follow-up of patients,
- Evaluation.
- To generate evidence regarding the effectiveness of any screening program, the development of a comprehensive evaluation strategy is essential. This includes outcome evaluation in terms of mortality, incidence of stages, morbidity, and quality of life, as well as process evaluation, evaluation of training and evaluation of campaigns and the overall recruitment strategy.

8.1.3. Parameters of a Screening

The sole purpose of a screening test is to identify suspicious findings within a specific target group. Four groups are formed: the true positives (diseased and recognized as such), the false positives (not diseased but diagnosed as diseased), the false negatives (diseased but found to be healthy) and the true negatives (healthy and recognized as such).

The **sensitivity of** a diagnostic test procedure indicates the percentage of diseased patients in which the respective disease is actually detected by the application of the test.

The **specificity of** a diagnostic test procedure indicates the probability that actually healthy persons who do not suffer from the disease in question are also detected as healthy by the test.

The **positive predictive value (PPV)** or positive predictive value indicates how many people who have been diagnosed with a certain disease by a test procedure are actually ill. The PPV is influenced by the prevalence of the disease in the population. The higher the prevalence, the higher the PPV. [647]

The **negative predictive value (NPV)** or negative predictive value indicates how many people who have not been diagnosed with a particular disease by a testing procedure are actually healthy.

Cancer is a progressive disease and screening generally aims to detect cancer at an earlier stage than would be diagnosed in mainstream care - particularly before the tumour has reached an invasive stage.

A screening test, like almost any diagnostic test, is rarely 100% sensitive (i.e. all individuals who have the disease are detected as "true-positive") precisely because it is not a diagnostic test. Typically, no "gold standard" exists for comparing disease status. Most participants in the SCS are "true-negative' (negative test result and free of the disease) or "false-positive," i.e., a positive test result although the disease is not present. Only a fraction of screened individuals are "true-positive," i.e., they have a positive test and are affected by the disease.

8.1.4. Screening in the Context of Cancer Screening Examinations

Various screenings are offered as part of cancer screening examinations. Eligibility for screening is defined by age, gender, and examination interval. For example, in Germany, all women over the age of 20 are eligible for annual screening for cervical cancer. For colorectal cancer-screening, all men aged 50 and over and women aged 55 and over are entitled to two colonoscopies at a minimum interval of 10 years. For mammography screening, women aged 50–69 are invited by letter every two years. Prostate cancer screening is for men aged 45 and over. One can be screened annually.

Table 27: Screening in the context of early cancer diagnoses

Participant Eligibility by Age, Sex, and Screening Interval
Cervical Cancer Screening: Women 20 years of age and older, Annual screening. Women 35 and older, testing for HPV every three years.
Colorectal Cancer Screening: Women 55+ and men 50+, two screenings 10 years apart. Men 50+: entitled to two screening colonoscopies at a minimum interval of ten years. Women 55+: two screening colonoscopies at a minimum interval of ten years. If men and women do not take up the offer until age 65: entitlement to one screening colonoscopy. Women and men 55+: entitled to an iFOBT every two years as long as no screening colonoscopy has been taken up.

Participant Eligibility by Age, Sex, and Screening Interval
Mammography Screening: Women between 50 and 70 years of age. Every two years
Skin Cancer Screening: Men and women aged 35 and over. Every two years
Prostate Cancer Screening: Men 45 years and older. Annual examination

The legal basis for cancer screening examinations is:

- **Act to Improve the Rights of Patients** (Patients' Rights Act), entered into force February 2013. The focus of the Act is on the standardisation of the treatment contract and the associated obligations of those providing treatment (e.g. the structuring of the obligations to provide information or clarification and regulations on the documentation of treatment), the strengthening of the rights of patients vis-à-vis the service providers and in the event of treatment errors in the context of social insurance law, as well as the strengthening of patient participation in self-administration.
- **Act to Strengthen Health Promotion and Prevention** (Prevention Act - PrävG), entered into force July 2015. Amendment of the Fifth Social Code (SGB V), §20. The focus of the Act is to improve the basis for cooperation between social insurance providers, Länder, and local authorities in the areas of prevention and health promotion. In addition, early detection examinations in all age groups are expanded and important measures for vaccination protection are regulated.
- **Act on the Further Development of Early Cancer Detection and on Quality Assurance through Clinical Cancer Registries** (Early Cancer Detection and Registries Act [KFRG]), which came into force in April 2013. The focus of the Act is the creation of the legal and financial framework for the establishment and operation of nationwide clinical cancer registries.
- **Recommendations of the Council of the EU on Cancer Screening,** December 2003. Promotes and supports cancer screening in all states of the European Community and makes recommendations on its implementation.
- **Guideline of the Federal Joint Committee on the Early Detection of Cancer** (Cancer Early Detection Guideline/KFE-RL). The guideline regulates the medical measures for the early detection of cancer, in particular the scope and timing of services, documentation, and evaluation.
- **Guideline for Organised Cancer Screening Programmes** (oKFE-RL). The guideline provides details on the implementation of organised cancer screening programmes. Essential structural elements are a regular invitation, combined with accompanying information for the insured persons about the respective examination, data protection, rights of objection, as well as the performance of the examination and the programme evaluation.

8.1.5. Benefits and Harms

Although screening interventions have the potential to reduce the mortality of a disease and save lives, death will not always be avoidable as an "outcome." Some individuals will die from cancer despite participation in screening because the tumor was not detected at screening, the diagnosed tumor does not respond to treatment, or because it is already at an advanced stage at the time of diagnosis.

In patients with a false-negative test result (they have a negative test result despite having the disease), the deceptive certainty can lead to a delayed diagnosis. In this case, the tumor remains undetected until it leads to symptoms or is discovered during the next screening examination.

Patients with false-positive test results (they have a positive test result although no disease is present) may undergo unnecessary multiple excisions. In addition, the time until the harmless / benign histopathological finding is experienced by many patients as a great psychological burden.

Interval carcinomas, ie tumors that are detected between two screening examinations [648][648] can also occur despite an effective screening program. These are not false-negative results. Interval carcinomas occur either because the screening interval is too long or because the patient is affected by a particularly fast-growing tumour. Missed tumours (false-negative test) are also counted as interval carcinomas. It is not possible to distinguish between the intermediate and the overlooked tumours at SCS.

Finally, during screening, one will also detect very slow growing tumours that, theoretically/statistically, are unlikely to have ever harmed the patient or become life-threatening to the patient at any time, the so-called overdiagnosis. In these cases, further diagnosis or treatment could harm rather than benefit these individuals.

The following must be considered when addressing the issue of overdiagnosis: the current scientific definition describes overdiagnosis as the detection of the early stages of a disease that would not in itself alter the user's lifespan or quality of life. The diagnosis and treatment therefore have a higher impact on the patient's quality of life and generate higher costs than the actual disease would ever have done without the early diagnosis.

Physicians are obligated from a medical ethics perspective to act according to the principle of harm avoidance and principle of care. From the perspective of the definition of overdiagnosis, surgical removal of a carcinoma would be equivalent to harm. Since the aim of screening is to detect tumours at an early and thus symptom-free stage, it is unclear to what extent the tumour would have affected the patient's health in the further course. Therefore, the dilemma exists that physicians act in the sense of care and patient well-being but also in the sense of a high-quality screening program if tumours are removed at this early stage in order to avert possible further harm to the patient, even if they can be described as overdiagnosis from an epidemiological point of view.

8.1	Evidence-based Statement	checked 2020
LoE 2+	Negative consequences of skin cancer screening involve excisions with a benign histology (false-positive tests).The number-needed-to-excise described in studies ranges from 3.25 to 179, i.e. between 3.25 and 179 excisions are needed to confirm one malignant skin tumour histologically.	
	[205]; [649]; [650]; [651]	
	Consensus (91%)	

8.2	Consensus-based Recommendation	checked 2020
EC	With the exception of false-positive tests, there is little evidence to date about potential risks and negative consequences of skin cancer screening. Possible negative consequences are overdiagnosis, overtreatment, negative psychological consequences and possible delays in diagnosis as a result of false-negative tests.These potential risks and negative consequences of skin cancer screening should be reduced as far as possible by appropriate physician training and teaching measures. Physicians should discuss potential risks and negative consequences with their patients before the screening.	
	Consensus (94%)	

Numerous studies have addressed the potential benefits of SCS for individuals as well as for the community (eg, reduction in mortality, morbidity, and increase in quality of life). However, because screening aims to examine and test healthy individuals, potential harms and risks associated with these procedures need to be examined even more carefully.

Despite the rising incidence rates of MM, BCC and SCC worldwide, Germany is the only country with a nationwide population-based skin cancer screening program. Many countries with a higher burden of skin cancer remain reluctant to implement such a program. In order to introduce a screening program, the potential benefits must outweigh the potential risks and harms. Only then can the screening of apparently healthy populations be justified. Because studies are lacking on the burdens of a screening program on individuals and the health care system and because effectiveness has not yet been conclusively demonstrated, many organizations, including the United States Prevention Services Task Force (USPSTF, [652] ; [653] and the Australian Cancer Council (published September 2019) with the New Zealand Guidelines Group [654][654] do not recommend routine SCS.

Many burdens are caused by screening tests because these tests also produce "false-positive" and "false-negative" results.

The following potential risks and harms are associated with **false-positive** test results:

- Many studies showed that suspicious skin lesions turn out to be benign lesions. The proportion of histopathologically confirmed benign lesions ranges from 70% to almost 90% [205] ; [650] ; [651] ; [649] . Only a small proportion of patients receive a "correct-positive" screening result. Sharing this knowledge by physicians with their patients could reduce the pressure and anxiety of patients with potentially "false-positive" test results.
- Superfluous further testing and/or investigation can lead to complications and harm the patient. In the case of skin cancer screening, unnecessary biopsies can cause complications in addition to unsightly and numerous scars. When these scars occur on visible parts of the body, such as the face, it can cause psychological stress to the patient. Different data are given on the number of excisions (NNE) needed to find a malignant skin tumour. For example, a skin cancer screening study showed an excision rate per newly diagnosed MM of 179:1, indicating low diagnostic specificity [649]. In contrast, in the German SCREEN project only 27 excisions had to be performed to detect MM, while the NNE for BCC was 8:1 and SCC 41:1 [205] . In the SCREEN

project, dermatologists and other qualified physicians received additional training on early detection [205] , which was not the case in the study by Schmitt et al [649] . This may have led to the lower NNE and highlights the importance of specific training and education for physicians participating in skin cancer screening.

- Expensive unnecessary excisions can be a burden on the health care system, as can overdiagnosis and unnecessary treatment.
- Quality of life may be affected by worry and stress during the waiting period for the final (negative) examination result. These negative psychological effects depend mainly on the amount of information available to the screening participant and also on the communication skills of the physician.
- Legal action may be taken by those who have been affected by complications during subsequent procedures. This may reduce public confidence in screening.

The following potential risks and harms are associated with false-negative test results:

- False-negative results can lead to a deceptive sense of security; for example, the patient may cancel medical appointments because the earlier screening suggested that everything was fine. In this case, the tumour remains undetected until it becomes apparent on its own or is discovered in the next round of screening. By then it may be too late for treatment or the tumour may be at a more advanced stage than it might have been if it had been diagnosed clinically without a screening offer. This can lead to increased morbidity, expensive therapies, and reduced quality of life due to the delayed diagnosis. In the extreme case of MM, which is associated with a potentially high likelihood of metastasis, a false-negative test result can potentially lead to death. Osborne et al (2003) reported on the accuracy to diagnose "false-negative" in different clinics. They found that the number of "false-negative" was lowest in specialized skin clinics ("pigmented lesion clinics"). They conclude that the experience of dermatologists working in such specialized clinics may be responsible for the improved diagnostic precision [655].
- Legal action may be taken by those affected by late-stage skin cancer despite having attended a SCS. This may also reduce public confidence in screening measures.

Most SCS participants have a "true-negative" test result and benefit from the SCS because physician confirmation that they are healthy is taken as positive. Patients with "true-positive" results may be pressured by the diagnosis because their disease phase is prolonged by the earlier diagnosis due to screening and must wait to see if they benefit from prompt treatment [650] ; [642] . Furthermore, delays in referral of suspicious lesions (through dermatologist consultation or more advanced procedures) may increase potential harms, e.g., increase in tumour thickness of MM and a decrease in survival rates of MM [656] .

Whole-body examination is performed without technical aids. It is a safe, inexpensive, and non-invasive screening test. In addition, it is not painful for patients or excessively time consuming for physicians. To date, there are no known disadvantages that directly result from a full body examination, other than the fact that the participant may be uncomfortable completely undressing for screening.

A skin tumour not detected during a screening may reach a symptomatic stage before the next screening examination is due. These tumours are called "interval

carcinomas." Accordingly, "false-negative" test results may be used to determine the appropriate screening interval for SCS. This would reduce the potential negative consequences "false-negative" results, but increase the "false-positive." A screening interval that is too short, such as every three months for high-risk individuals, could cause long-term psychological distress and adversely affect a person's quality of life.

The possible harms listed are summarized and contrasted with possible benefits in the following table:

Table 28: Potential harms and benefits of screening

Possible Damages:	Possible Benefits
False Negative Results: Patient and doctor reassured, cancer grows, may lead to death. Confidence in doctor and system shaken. False-positive results: False-positive results cause patient and physician to be alarmed and initiate diagnostic steps; physical and psychological distress to patient during waiting period, relief after histologic workup, which can lead to confidence building in physician and system. Overdiagnosis: detection of early stages that do not affect quality and length of life. Diagnosis and treatment would alter quality of life and generate costs. Ethical objections prevent scientific evidence of overdiagnosis.	Early stage detection and treatment Reduction of morbidity Reduction of mortality Reduced impact on quality of life and lower costs. Prevention of further sequelae. Physician gets to know the patient better and may later be able to refer to previous findings. Orient patients (e.g. risk groups) to self-examinations and prophylactic measures. Informing and raising awareness of the user about the disease and possible effects of screening.

Need for Research

Most studies on negative consequences of SCS focus on unnecessary biopsies and the NNE. Further research on other factors that have an impact on potential harms is needed.

The following points should be considered:

- Investigate risk factors for "false-positive" and "false-negative" results in both high-risk groups and individuals without high-risk features,
- Overdiagnosis in SCS needs to be investigated,
- Interval cancer studies to determine optimal screening interval and reduce "false-negative" results,
- the NNE of trained vs. untrained physicians and the resulting consequences for patients,
- the communication skills of physicians and medical assistants to educate participants about potential benefits and risks of SCS,
- the negative psychological effects associated with the uncertainty of potential "false-negative" and "false-positive" results of a SCS,
- the negative impact of screening on clinicians (time, etc.).

8.1.6. Methods of Early Skin Cancer Detection

For the early detection of MM, population-based as well as individual measures are described in the literature. Regarding the effectiveness of these measures, i.e. a shift from late tumour stages to early tumour stages and a reduction in mortality, the evidence is rather low. The existing evidence is based almost exclusively on epidemiological studies rather than RCTs, which would have allowed the generation of higher levels of evidence regarding the effectiveness of population-based screening interventions. The current lack of evidence of efficacy by RCT is the main reason why organisations worldwide [657]; [653] do not recommend such interventions for the early detection of malignant skin tumours [654]; [658].

8.1.6.1. Routine self-examination of the skin

8.3	Consensus-based Recommendation	new 2020
EC	Skin self-examination must be recommended.	
	Consensus (94%)	

In terms of individual measures, routine skin self-examination (SSE) could be a promising method for the early detection of malignant skin tumors, as it is free of charge and free of inconvenience.

Regarding the average melanoma thickness, Titus et al. [659] , who investigated the effect of skin self-examination in New Hampshire, did not observe a significant positive effect (0.68 mm versus 0.91 mm). An association between melanoma thickness (≥1mm versus <1mm) and skin self-examination was shown for a single subgroup (self-examination 1-11x / year: OR 0.39, 95% CI 0.18-0.81) but not overall (OR: 0.68 95% CI: 0.42-1.10) [659] .

Multiple testing is noticeable in the statistics and there is a lack of rationale for grouping the frequency of self-examinations. In addition, they report a possible reduction in melanoma risk from skin self-examination when performed one to 11 times per year (OR: 0.74; 95% CI 0.54-1.02). However, there was no overall association between the frequency of skin self-examination and the likelihood of detecting melanoma (OR: 0.91, 95% CI 0.71-1.16). Furthermore, the authors found a reduced likelihood of a melanoma diagnosis in patients who had self-examined their skin and reported seeing a physician during the past year (OR: 0.54, 95% CI 0.38-0.79).

Paddock et al. [660] failed to demonstrate an association between skin self-examination and melanoma mortality in a 20-year survival study of patients who received an initial diagnosis of malignant melanoma in Connecticut in 1987-1989 (adj. Hazard ratio: 1.12, 95% CI 0.61 –2.06 self-examination versus no self-examination).

The accuracy of the use of "mole mapping diagrams" was tested in an RCT and was more successful in the intervention group than in the control group. The authors describe that increased accuracy in identifying new skin lesions through the use of "mole mapping diagrams" has the potential to reduce mortality from melanoma and that it is a simple and cost-effective intervention [661] .

Further studies suggest that photodocumentation in conjunction with SSE may increase the diagnostic quality of SSE, resulting in a reduced excision rate [662] ; [663] .

In contrast, Muhn et al (2000) concluded from their study that SSE is only a moderately effective method of detecting changes in the size of existing skin lesions. They examined the ability of high-risk individuals to detect changes in the size of their moles on the back. At the beginning of the study, these high-risk patients were trained to perform SSE. The authors report that a large proportion of study participants (25%) did not detect changes, or falsely detected changes when none were present (38%) [664] .

However, the evidence regarding SSE is limited in terms of quality and quantity and it remains unclear whether SSE leads to improved outcomes in terms of morbidity and mortality.

However, differentiating one group "skin self-examination" from another group "non-examination" is difficult. Diagnosis by a physician, whether a dermatologist, general practitioner, or other specialist, is usually based on the detection of suspicious skin florescence by the patient or a relative. Irrespective of this, persons who regularly go for cancer screening or health examination anyway must always be considered.

These remarks explain the difficulty of a scientific consideration and classification of self-examination. For this purpose, in such studies the endpoint should realistically be set at the detection of skin cancer (MM, SCC, BCC) by the pathologist, all later endpoints are scientifically questionable.

If we compare the SSE with the recommended self-examination of the S3 guideline breast cancer and with the S3 guideline of the malignant testicular tumours, a substantial difference is noticeable: here, the proband must palpate himself and not simply look. In both guidelines, self-examination is recommended with instructions. The study situation is not clear either.

Despite the fundamental problems of the studies described, in the absence of evidence from existing studies, self-examination of the skin with guidance (mole mapping diagrams) is nevertheless recommended.

8.1.6.2. The Visual Full Body Examination

Revision by W. Cremer

This chapter deals with the visual whole-body examination performed by health professionals and tested in international studies. It does not refer to the population-based standardized whole-body examination within the framework of the statutory skin cancer screening in Germany. This is discussed in Section Chapter 8.2.

8.4	Evidence-based Recommendation	checked 2020
GoR **A**	To screen for skin cancer, a whole-body examination must be performed.	
LoE **2++**	[205]; [665]; [666]; [667]	
	Strong Consensus (100%)	

8.5	Consensus-based Recommendation	modified 2020
EC	For a whole-body examiantion, the examination room must be sufficiently bright and the examiner must approach the person to be screened close enough to be able to detect skin changes with the naked eye.	
	Strong Consensus (100%)	

The full-body inspection without further aids on the unclothed person represents a simple and inexpensive examination method that has been carried out for decades and with which skin cancer can be detected as part of a screening[205].

In order to achieve optimal results with this method, there are various variable factors, the importance and weighting of which, however, have not yet been tested in studies.

One of these is the illumination of the examination room. Experience shows that daylight and bright white or yellow artificial light are advantageous. According to DIN 12464-1, the illuminance of general lighting in normal examination rooms is between 300 and 500 lux. For a full-body inspection, therefore, a general lighting illuminance of at least 500 lux would appear to be appropriate, while detailed skin examinations require around 1,000 lux. Another factor is the distance between the examiner and the person being examined. In order to be able to detect and assess even small skin changes with the naked eye, a close visual distance is recommended. However, there is a lack of studies on the minimum distance required at what level of visual acuity.

The experience of the examiner is essential for the whole-body inspection. Measurement parameters are sensitivity and specificity in the detection of skin cancer. Different studies have measured the detection of melanoma, the detection of non-melanoma skin cancer (NMSC), or the differentiation between benign and malignant lesions.

The data regarding the sensitivity and specificity of the diagnosis of melanocytic and non-melanocytic skin cancer and its precursors by whole-body inspection is very limited. Diagnosis of non-melanocytic skin cancer (NMSC) by whole-body examination has a sensitivity of 56-90% and a specificity of 75-90%. In a cross-sectional study of Australian GPs, sensitivity in diagnosing various skin cancers by whole-body inspection was 100% for melanoma (n=1), 89% for basal cell carcinoma (n=62), 80% for dysplastic nevi (n=30), 58% for benign nevi (n=69), 42% for squamous cell carcinoma (n=18), and 10% for actinic keratoses (n=31), while the specificity for these entities was 76-99%. For melanoma diagnosis by clinical inspection, the sensitivity of non-dermatologist trained physicians is 86-95% and specificity is 49-77%. Training in melanoma diagnosis did not significantly increase sensitivity and specificity in general practitioners.

In a systematic review, Mogensen and Jemec evaluated all studies between 1990 and 2006 that looked at the diagnostic accuracy of non-melanoma skin cancer (NMSC) using different diagnostic testing methods and technologies. A total of 48 studies were included. In pure clinical examination, according to different studies, the sensitivity for diagnosing NMSC ranged from 56-90% and the specificity ranged from 75-90%, with the best values for basal cell carcinoma (sensitivity 66-89%) [665].

In an Australian monocentric study of 199 consecutive patients with 287 histologically examined lesions, the sensitivity (and specificity) of referring GPs for the diagnosis of basal cell carcinoma was 89% (76%), dysplastic nevus 80% (93%), squamous cell carcinoma 42% (93%), actinic keratosis 10% (98%) and benign nevus 58% (99%) [666].

Kai et al. [668]

made a clinical classification of screened participants into three categories (A: no/very low; B: low cancer risk, follow-up if necessary; C: high cancer risk, further investigation). For patients in category C, a sensitivity of screening of 92.7% and a specificity of 95% for skin cancer of various entities were demonstrated. The recall rate was 6.6%, the finding rate 1.9% and the positive predictive value 26%.

In a comparison of 31 general practitioners with training course and 32 general practitioners without prior training who performed melanoma screening in 109 individuals, sensitivity was not significantly different at 98% and 95% and specificity at 52% and 49%, respectively [669]. However, the results have limited applicability because the selection of general practitioners was not representative and they had been informed in advance that some study participants had suspicious skin lesions. Among surgical oncologists with several years of experience in melanoma diagnosis, sensitivity was 86% and specificity 77% on purely clinical inspection of suspicious pigmented skin lesions [670].

In a single-arm, prospective cohort study, 256 patients at increased risk of skin cancer underwent examination by specially trained nurses to assess whether or not suspicious skin cancer lesions were present [668]. The results were compared with a subsequent assessment by plastic surgeons. Correctly identified by the nurses were 95% of suspicious lesions, while 16% were diagnosed as false positives. Due to some limitations in the design of this study, the results can only be interpreted in a limited way.

8.6	Evidence-based Statement	modified 2020
LoE 2++ 2-	According to a systematic review, the available study data are insufficient to draw conclusions about statistically significant differences between dermatologists and primary care physicians in terms of accuracy in classifying suspected melanoma lesions.	
	[671]; [672]; [673]	
	Strong Consensus (97%)	

A systematic review analyzed all studies from 1966 to 1999 that examined sensitivity and specificity in the diagnosis of melanoma by dermatologists compared to primary care physicians. The studies measured the correct detection of melanoma versus non-melanoma (diagnostic accuracy) or/and the correct determination of whether a lesion could be malignant and thus subject to biopsy or result in referral to a melanoma expert (biopsy or referral accuracy). A total of 32 studies were included in the final analysis. In terms of diagnostic accuracy, sensitivity ranged from 81% to 100% for dermatologists in all prospective studies and from 42% to 100% for primary care physicians. Specificity was not calculated in any study for dermatologists and only in one study for primary care physicians (98%). Regarding biopsy and referral accuracy, sensitivity ranged from 82% to 100% for dermatologists and from 70% to 91% for physician primary care providers. Specificity ranged from 70% to 89% for dermatologists and 51% to 87% for primary care physicians. The authors concluded that the data were not adequate to detect differences in diagnostic accuracy and biopsy or referral accuracy between dermatologists and physician primary care providers [671].

A prospective cohort study examined the outcomes of a screening program conducted as part of a quality initiative in Pittsburgh in 2014. In this study, 53,196 patients had been screened by 939 physicians: 55 clinically active dermatologists and 884 primary care physicians, of whom 155 had completed a corresponding voluntary training (INFORMED: Internet curriculum FOR Melanoma Early Detection) and 729 had not. The extent to which training affected outcomes is not reported. It is only summarily reported that melanomas found in the screening program were thinner (median tumour thickness) than melanomas not diagnosed in the program (0.37 mm vs. 0.65 mm). No difference was observed between the intervention and control groups regarding the probability of finding melanomas ≥1 mm (RR: 0.7, 95% CI 0.2-2.2) [672].

A number of studies showed low evidence on the effectiveness of population-based interventions for early detection of skin cancer. A systematic review examined the effectiveness of interventions to increase cancer awareness and promote early diagnostic workup of possible symptoms (original: "early presentation") at the community level. The researchers found evidence on the effectiveness of educational interventions (brochure, posters and media campaigns), i.e., a reduction in the mean tumour severity of MM and a reduction in the time between detection of symptoms and presentation for clarification [468]. Kai [668] points out that although patients often went for dermatological examination because of self-discovered moles, they rarely went for skin tumours in the genital region, as this region is less accessible to self-examination for various reasons, and plans an educational campaign in local newspapers.

It is recommended by some authors that the SCS should not generally be performed in asymptomatic people as well, but only in high-risk individuals, for capacity and cost reasons, and that instead the population should be instructed in skin self-examination [673].

In a population-based case-control study conducted in Australia, there was an association between whole body clinical examinations and a decrease in the incidence of thick MM [674].

In contrast, a community-based intervention in the UK to promote early detection of MM in the adult general population showed no effect on mortality rates. An implemented health education programme consisted of distributing leaflets on the signs or identifying features of MM and encouraging early presentation for investigation. Skin self-examination was not part of the information. Despite an increase in the incidence of thin melanoma, the researchers found no significant reduction in cumulative mortality in the intervention regions compared with other regions in the UK nine years after completion of the programme [675].

Furthermore, a systematic review on a routine SCS by primary care providers (original: "primary care providers") concluded that there is insufficient evidence to support the effectiveness of such a programme [676].

Other alternative population-based screening approaches are mentioned in the literature. In a randomized controlled trial of a community-based screening program, primary care physicians were trained in the early diagnosis and treatment of skin cancer. Screening was conducted as a whole-body skin examination and local physicians were supported by dedicated "skin screening clinics." The number of whole-body examinations increased in the intervention regions compared with the control regions, which did not have "skin clinics." The authors conclude that the provision of additional "screening clinics" could improve screening participation rates [678]; [677]. Due to low funding, this RCT was never completed and to date there are no comparative data on tumour thickness and/or mortality between intervention and control regions.

Janda et al. [679] reported a significant increase in screening examinations in centrally organized "skin screening clinics" compared to screenings in everyday primary care. Furthermore, so-called pre-screening, i.e. the identification of skin lesions requiring further evaluation by a specialist, performed in hospitals by minimally trained nurses, has the potential to be a cost-effective and reliable screening intervention [667].

Overall, only a limited number of studies exist that provide substantial evidence on the effectiveness of population-based and individual interventions for the early detection of skin cancer. Many do not refer to screening or do not adequately relate to increasing the proportion of early stage disease or mortality reduction.

For example, although information is provided on the extent to which earlier skin cancer stages were found in the screened groups compared to the (not always clearly described) control groups. However, information on whether this has reduced the frequency of later skin cancer stages in the overall population, as well as usable data on skin cancer mortality reduction, overall survival, and quality of life, are missing. A positive effect of the SCS can only be assumed by the fact that earlier cancer stages were found by screening.

The question whether general skin cancer screening can be recommended and whether it is feasible is also answered differently with regard to the limited personnel capacities and the insufficient funding of such projects: yes [672], no for general screening, but only for at-risk individuals [673].

In summary, there is a lack of evidence on the effectiveness of the above screening approaches in terms of mortality reduction. However, given the feasibility, such mass screening programs would not be feasible without such a "gate keeper" approach.

Research Needs

There is a need for research to evaluate the effectiveness of population-based and individual screening for skin cancer. The most urgent need is to demonstrate that screening leads to a decrease in skin cancer mortality, improved overall survival, and improved quality of life.

8.1.7. Screening of Persons at Risk

Revision by G. Mehlhorn

As described in Chapter 4.3, the individual risk of developing skin cancer varies greatly. It depends on environmental, genetic, and acquired risk factors (e.g. immunosuppression in organ transplant patients). This chapter considers individuals at increased risk of skin cancer and reviews scientific evidence on screening these individuals.

High-Risk Individuals and Skin Cancer Screening

- **Targeted SCS of high-risk individuals appears to be more efficient compared with population-based screening. However, the applicability at the population level has been unclear.**

In the systematic review by Watts et al. [680], a total of 34 guidelines were included, with the aim of identifying strengths and weaknesses in the evidence for detecting, screening, and following up high-risk groups for cutaneous melanoma. Thirty-two percent of the studies made recommendations for screening high-risk groups, stating that long-term screening was necessary for patients at high risk, especially if there was a genetic predisposition and a family history of frequent melanoma occurrence. Screening should be done for patients with dysplastic nevi according to 32% of the guidelines and if there is a positive family history in 26% of the guidelines.

Guther et al. [651] attempted to develop a model to identify individuals at increased risk of skin cancer who would benefit from regular SCS. They used an open prospective point-prevalence study of consecutive patients who presented to dermatologists for a complete skin examination. Demographic characteristics and risk factors for skin cancer were documented, as was the histology of skin lesions. Results were analyzed univariately and multivariately, and a risk group model was developed to identify patients most likely to develop MM or NMSC [651]. The sensitivity of the risk model in contrast to the current mass screening in Germany can be described as follows: with a set sensitivity of >92% for melanoma and squamous cell carcinoma, one third of the study population is identified as a risk group and suggested for regular SCS. Overall specificity for the model (MM, SCC, BCC) is 67.24% versus 40.0%, sensitivity for melanoma is 92.3% versus 75.2%, sensitivity for squamous cell carcinoma is 92.4% versus 99.0%, and sensitivity for BCC is 61.8% versus 96.1%. Practical implementation at the population level has not been provided by the authors.

In the cohort study by Rat et al. (2015), recruitment of participants was done by 78 general practitioners in France. Participants are patients with increased risk of skin cancer, determined with a score collected independently of the reason for the visit to the doctor, without previous melanoma (n=3,923). In Rath et al. 2015, the SAM score was used (Self-Assessment of Melanoma risk score). In the score, questions about skin type, presence of freckles, nevian count >20 on both forearms, stay of one year in a country with increased sun exposure, melanoma history, and family history of melanoma are considered. A clinical SCS of the patients was done by the general practitioner, followed by a decision to refer to a dermatologist. At the dermatologist's office, a classification of the suspicious lesion was then performed with possible subsequent removal. This was followed by a telephone survey of patients over the course of treatment from 5 September 2012 to 14 October 2012. The follow-up period for each patient was one year. The cumulative melanoma incidence was 229.4/100,000 for the defined high-risk group. Melanoma occurred in nine of 3,923 patients, all with Breslow index <1. For patient compliance, there was a significant association with age (OR=1.02 per year, 95% CI 1.02-1.03, p<0.001), dermatology physician density high versus low (OR=2.28, 95% CI 1.78-2.92, p<0,001), the designation of a dermatologist by the general practitioner (OR=2.15, 95% CI 1.51-3.09, p<0.001), and the 4.2 times higher likelihood of seeing a dermatologist for 65-year-old patients compared to 20-year-old patients.

A follow-up cohort study of the study just described was done by Rat et al. (2015) in the same year. An invitation was sent by email to re-present to the GP one year after inclusion in the cohort described above. Patients who developed melanoma (n=9) or died (n=11) within one year of starting the original participation were excluded. The melanoma incidence of participants was now 160/100,000. Eighty-three participants had a lesion removed, six patients were diagnosed with melanoma, five with squamous cell carcinoma, and 15 with BCC. The incidence of melanoma was 183.7/100,000 in men and 98.7/100,000 in women. Men over the age of 50 had an increased proportion of lesions removed (21% versus 11.6%, p=0.029) and a higher proportion of malignant lesions identified after removal (66.7% versus 21.5%, p<0.001). Patients over 60 years of age had a higher proportion of identified malignant lesions after removal (66.7% versus 19.4%, p<0.001). Patient compliance is described below. After written re-presentation, 54% of participants consulted the general practitioner, 7% directly consulted the dermatologist, and 31% of participants had no SCS. The proportion of patients who were referred to and saw a dermatologist increased (68.8% versus 59.1%, p<0.001). The proportion of patients who consulted a dermatologist overall decreased (15.8% versus 23.9%, p<0.001). This can be explained by the fact that the proportion of patients who were referred to a dermatologist decreased (12.2% versus 38.8%, p<0.001).

Patients at Risk and Suspected/Confirmed Diagnosis

In the cohort study by Moloney et al. (2014), a total of 311 participants recruited through the Sydney Melanoma Diagnostic Centre and Melanoma Institute Australia outpatient clinic from 2006 to 2009 were allocated to one or more of the following groups. Group 1 (n=219) includes all patients with personal history of at least one invasive melanoma and syndrome of dysplastic nevi (at least 100 nevi, of which at least six have atypical changes and at least one nevi is larger than 8mm). Group 2 (n=52) was assigned to patients with personal history of at least one invasive melanoma and family history of malignant melanoma in at least three first- and second-degree relatives. Group 3 (n=146) included patients with personal history of at least two primary invasive melanomas. For patients with only two melanomas, one of these must have

occurred in the ten years prior to the patient's enrollment. The final group, group 4 (n=17), includes all patients with confirmed CDKN2A (OMIM 600160) or CDK4 (OMIM 123829) gene mutations. At baseline, all nevi were recorded, whole-body skin screening was performed, and suspicious nevi were examined. Dermatologic examination of patients was performed every six months with a median follow-up duration of 3.5 years (2.4-4.2 years). At baseline, 14 melanomas were diagnosed, with a total of 75 during the course of the study. The risk of developing a new melanoma was 12.7% after two years and 18.2% after four years. A comparison of the incidence of new primary melanomas in the last three study years to the first two study years showed the following: Incidence density ratio = 0.43 (95 CI 0.25-0.74, p=0.002). The effect of diagnostic tools in identifying new melanomas revealed the following: 16% of melanomas were detected by dermatoscopic examination of dermatologists without change in whole-body review photography (TBP)/sequential digital dermoscopy SDDI. Eight percent of melanomas were self-discovered by the patient without TBP and 91% of postbaseline detected melanomas had a Breslow tumour thickness of <1mm. Sequential digital dermoscopy (SDD/SDDI) detected 39% of postbaseline melanomas (16% by short-term SDDI, 23% by long-term SDDI). TBP detected 38% (n=23) of postbaseline melanomas (20 by TBP, 3 by TBP alone). None of the diagnosed melanomas were detected solely by changes in TBP by the patient.

In the systematic review by Watts [680], 70% of the guidelines recommend specific training for users of dermoscopy, whole-body photography (for patients with high numbers of nevi, for early detection of lesions), and sequential digital dermoscopy (to improve diagnostic accuracy). Photographic documentation of changes is recommended by ten guidelines. Prophylactic removal of nevi is not recommended by any guideline. The evidence base for targeted screening with dermoscopy and SDDI to improve diagnostic accuracy is considered very good. The evidence base for whole-body photography is lower.

Examination Intervals of Patients at Risk

A guideline from Australia and New Zealand (Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand) states that regular surveillance reduces the average thickness of MM. For high-risk individuals, this guideline recommends a combination of self-examination and screening and advises a screening interval of six months. However, no studies are available that systematically compare alternative methods; these recommendations are based on expert opinion only. The individual frequency of skin examinations in persons at risk should be made dependent on the individual risk factors, i.e. the frequency should be determined in such a way that a reduction of mortality and morbidity as well as a stage shift is achieved.

In the above systematic review by Watts [680], 35% of the included guidelines recommend screening based on prior risk assessment with intervals from six months to annually at regular intervals or for life. Recommendations for screening intervals and -duration for high-risk groups are based on EC.

Overall, there is insufficient evidence regarding optimal screening intervals for individuals at increased risk of skin cancer.

High-Risk Individuals and Skin Self-Examination

8.7	Consensus-based Recommendation	checked 2020
EC	At-risk persons must be taught to carry out skin self-examination so as to be able to identify abnormal skin lesions.At-risk persons must be informed about their individual risk and be regularly examined (at intervals to be defined individually) by a trained physician by means of a whole-body skin examination.	
	Consensus (92%)	

There are different results regarding the benefit of skin self-examination. Because the effectiveness of skin self-examination has already been discussed in sufficient detail in Chapter 8.1.6.1, it is only briefly touched on here in the context of recommending SSE for people at increased risk of skin cancer.

Oliveria et al. [681] showed that regular self-examination has a benefit in detecting thin lesions. Identifying factors associated with performing skin self-examination (gender, age, education, marital status, "skin awareness," previous benign biopsy, presence of atypical moles) will allow health care providers to focus on those individuals who do not perform skin self-examination despite an increased risk of melanoma. They emphasize the importance of identifying factors that increase the likelihood of an individual self-examining their skin, as early detection and excision of lesions has the potential to reduce morbidity and mortality from MM [681].

The review by Watts [680] showed that as part of patient education, skin self-screening is included in 76% of guidelines and specifically named for managing high-risk groups in 38% of guidelines. The intervals for self-screening varied from monthly, trimonthly, six-monthly, to no indication. These recommendations are based on EC.

Need for Research

Studies should be conducted comparing the effectiveness of mass screening with risk group screening for individuals at increased risk of skin cancer and evaluating it in terms of mortality, morbidity, and stage shift. In this context, economic aspects should also be considered.

8.2. Population-Based Skin Cancer Screening in Germany

8.2.1. Scope of Claims and Components

Since 1 July 2008, the SCS has been part of the statutory early cancer detection (regulated by the Cancer Early Detection Guideline of the Joint Federal Committee). Statutorily insured persons over the age of 35 are entitled to participate every two years. A new screening examination for skin cancer is only possible after the end of the calendar year following the previous examination. The SCS is designed as a two-stage mass screening. Either the participant is examined by a general practitioner and, if skin cancer is suspected, is referred to a dermatologist who carries out the standardised visual full-body examination again, or the dermatologist carries out the SCS directly.

The following figure illustrates the screening procedure:

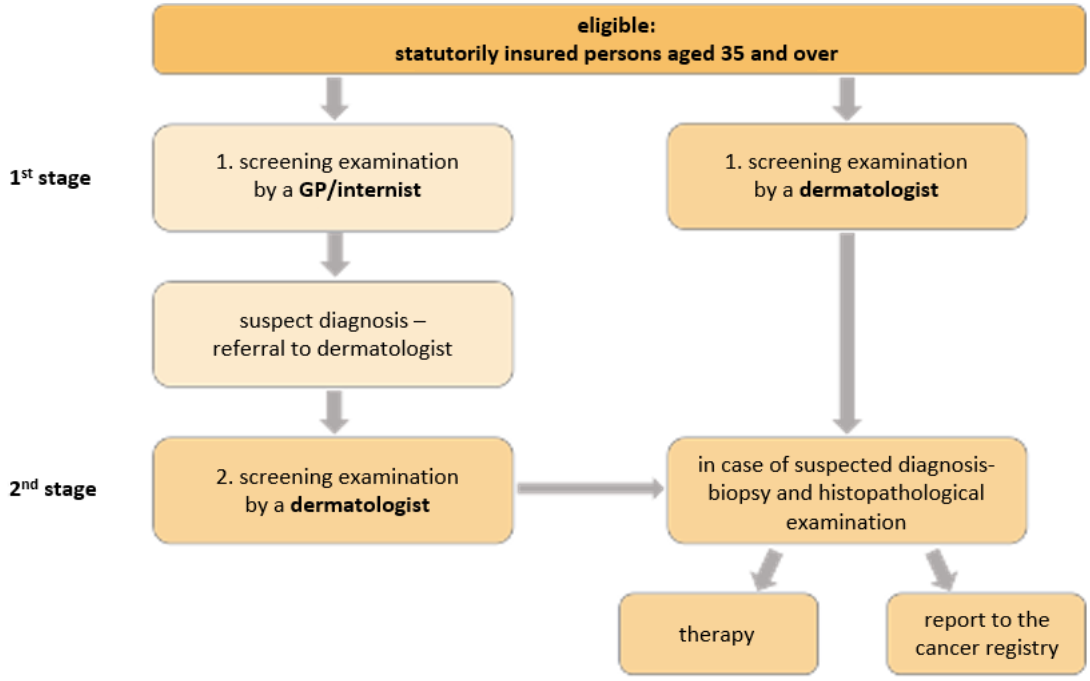

Figure 13: Schematic representation of the multidisciplinary two-stage approach to population-based screening for skin cancer.

The service "Early Detection Examination for Skin Cancer" may only be provided by physicians working within the framework of SHI-accredited medical care who can present an appropriate authorization from the responsible SHI-accredited medical association. The following groups of physicians can receive this authorization after completing the eight-hour continuing education course: general practitioners, internists, doctors without a regional designation, and specialists in skin and venereal diseases.

8.2.1.1. Medical History and Self-Examination

8.8	Consensus-based Recommendation	checked 2020
EC	The person to be screened must be asked about skin changes at the beginning of the screening / presumptive diagnostic procedures.	
	Strong Consensus (100%)	

8.9	Evidence-based Recommendation	modified 2020
GoR **A**	The results of the self-examination of the person to be screened must be included at the beginning of the screening / presumptive diagnostic procedures to identify malignant and benign skin changes.	
LoE **2-**	[663]	
	Strong Consensus (100%)	

In patients with atypical nevi who self-examined their trunk skin, sensitivity for altered or new pigmented moles was 60.2% and specificity was 96.2% [663]. With the addition of digital photographs from the initial examination, sensitivity increased to 72.4% and specificity to 98.4%.

Regarding the medical history, there are only study data stating that it is well reproducible: in a repeated interview of 236 subjects, 116 of them patients with a history of BCC or SCC, after a period of 18-26 months, there was good reproducibility of the answers regarding pigmentation characteristics, sun exposure, and childhood sunburns, while the number of sunburns found the least agreement [682]. A comparison of the diagnosis of difficult to classify pigmented lesions by six dermatologists who were only presented with photographs of the clinical and dermoscopic findings showed low rates of correct diagnosis of melanoma without (38.3%) and with dermoscopy (40.8%) and only 70% of MM and BCC were referred for surgical therapy [683]. The authors speculated that the lack of direct patient examination may have had a negative impact on the results.

Need for Research

In summary, there is a lack of studies comparing the accuracy of the examiner's diagnosis in SCS with and without the aid of history taking and patient self-examination.

8.2.1.2. The Standardized Whole-Body Examination

The SCS includes the standardized, visual full-body examination, in which the entire skin is visually examined without visual aids. This also includes the examination of the scalp, the oral mucosa, as well as the anal and perineal region with the external genitalia in men and women.

8.10	Consensus-based Recommendation	modified 2020
EC	For skin cancer screening, a standardized whole-body skin examination must be performed by physicians who have participated in a special training course on the early detection of skin cancer as defined in the guideline for early detection of cancer.	
	Strong Consensus (100%)	

Performing a standardized full-body examination is the only way to detect skin cancer on an individual. Such a skin examination can be performed by dermatologists or other physicians trained in the early detection of skin cancer.

However, the decision to perform a full body examination must remain with the patient. This means that the person decides for him/herself whether or not to have a full-body examination after extensive information about the potential benefits and harms of screening (see also Chapter 8.3.2).

A large-scale project on SCS, the SCREEN project in Schleswig-Holstein [205]; [206] demonstrated the feasibility of population-based screening using the standardized whole-body examination. In this project, a corresponding training programme for dermatologists, general practitioners and other specialists (gynaecologists, urologists and surgeons) for the early detection of MM, BCC and SCC was carried out. The training included the collection of a targeted patient history, the performance of the whole-body examination and advice on risk factors and prevention. The full body examination was performed in a brightly lit room (or with a bright lamp), an examination couch, and a surface on which the patient could stand. After undressing the patient and possibly removing glasses, the following body parts were examined: the scalp through parted hair, ears, eyelids, oral mucosa, lips, gums, neck, upper body, axillae, arms, hands and interdigital areas, submammary region in women, perianal region, legs, external genitalia, feet including soles, and interdigital spaces between toes (for a detailed description of the screening procedure, see Chapter 8.2.3).

8.2.1.3. Preventive Advice

Another component of screening is preventive counselling, in which the patient is advised on risk factors and UV protection behaviour, adapted to his individual situation. This depends on the congenital and acquired risk factors of the patient, e.g. to which skin type he belongs, and his previous exposure to UV radiation. Then the patient should be instructed for self-examination with the hint that the SCS can only be claimed every two years.

8.2.1.4. Follow-Up Diagnostics and Presentation Period

Within the SCS, some participants are identified who show a suspicious skin lesion on the basis of visual diagnostics. These are now further clarified in the follow-up diagnosis, which no longer takes place within the framework of the SCS. Since 01.04.2020, dermoscopy has been added to the number 01745 in the uniform assessment standard (UAS) catalogue and is therefore no longer billed as an individual health service (IGeL). However, other IGeL-services can be invoiced. This includes, for example, the photo documentation of nevi, which is no longer part of the SCS. It is important to separate the SCS from these individual health services and to offer the screening service defined in the UAS catalogue without costs to be paid by the patient for those insured by the statutory health insurance. The follow-up diagnosis of persons found to be ill at SCS is then carried out by excision and histopathological examination. These two measures can then again be billed via the corresponding figures of the UAS catalogue.

8.11	Consensus-based Recommendation	modified 2020
EC	In the context of skin cancer screening, the period of time until the next appointment for further confirmation of findings following the suspicion of a malignant melanoma or squamous cell carcinoma should not exceed ten days.	
	Consensus (94%)	

Delays in referring patients with suspected skin cancer to a specialist could have an effect on the likelihood of patient survival. The results of a UK study showed reduced tumour thickness and improved survival in patients with suspicious lesions who were referred to a plastic surgeon for consultation and prompt treatment within two weeks. These results support the "two-week rule" for referral for several cancers, which was introduced in the UK in 2000 [656].

8.12	Consensus-based Recommendation	new 2020
EC	Within the scope of a skin cancer screening, the period of time until the next appointment for further confirmation of findings after a suspected basal cell carcinoma can be individually adjusted.	
	Strong Consensus (100%)	

BCCs grow very slowly and do not metastasize, therefore the presentation period for further confirmation of findings can be significantly extended.

8.2.1.5. Examination Intervals

8.13	Consensus-based Statement	modified 2020
EC	On the basis of the current evidence, it is not possible to make any statement about the intervals between screening examinations for skin cancer for people not at increased risk.	
	Strong Consensus (100%)	

8.14	Consensus-based Statement	modified 2020
EC	For people at increased risk for skin cancer, the physician, together with the person to be screened, should define an appropriate interval until the next presentation, based on an assessment of the individual risk profile.	
	Strong Consensus (100%)	

The time interval between screening examinations for skin cancer should be chosen in such a way that the criteria of screening are fulfilled: Identification of early stages, stage shifting and reduction of mortality as well as morbidity.

Considering the age-specific incidence of MM, BCC and SCC and their respective (and different) clinical course, the examination interval in the nationwide SCS was set to two years for persons without risk features. Apart from this practice in Germany, there is insufficient evidence regarding optimal screening intervals both for persons with an increased risk of skin cancer and for persons without specific risk factors.

According to Spix and Blettner [642], the examination frequency (the screening interval) as well as the screening test and the target group from the population have to be determined (see also introduction of this chapter [642]). However, the literature does not provide evidence for confirmed determinations of how to achieve the best effectiveness of a screening programme. The main reason for this is the lack of evidence on SCS of high-risk individuals and individuals without risk characteristics. The available guidelines [654]; [658]; [652]; [653] do not provide information on this.

Need for Research

An evaluation of the SCS in Germany should be carried out, taking into account the clinical long-term course with regard to the screening interval for persons with an increased risk of skin cancer and persons without risk features in order to determine optimal screening intervals. This must include an investigation into interval carcinomas. Preferably, this investigation should be conducted as a randomized controlled trial to determine the possible screening intervals (e.g. one year for individuals at increased risk of skin cancer in one region versus another interval, e.g. three or four years in another region).

8.2.2. Evaluation and Evidence Base

J. Hübner

This chapter reviews and evaluates studies that address the population-based German SCS and the preceding feasibility study "SCREEN" (Skin Cancer Research to Provide Evidence for Effectiveness of Screening in Northern Germany). International studies that deal with screening measures in general can be found in Chapter 8.1.6.2. The reason for this separation is that Germany is the only country with a population-based screening programme and comparability with other, smaller, and more timely screening interventions is limited. In addition, despite some differences in detail, the nationwide screening and the SCREEN project share conceptual similarities, so that the latter provides indirect evidence for the current nationwide SCS of primary interest.

In the one-year pilot project, 360,288 legally insured women and men (about 19% of the eligibile population) were screened by visual whole-body examination. The project was preceded by several years of preparatory activities, including, in particular, publicity measures and training for physicians willing to participate. In contrast to the nation-wide screening, gynaecologists, urologists, and surgeons were also entitled to participate besides dermatologists and general practitioners and internists. Another difference to the current screening is that the intervention was aimed at insured persons already from the age of 20 years. Furthermore, primary screening non-dermatologists were obliged to refer to a dermatological specialist for re-examination not only in case of suspicious cancer findings but also in case of the presence of one of the defined risk factors.

The aim of the screening examination for skin cancer is the early detection of MM, BCC, and SCC. The relevant wording in § 28 sentence 1 KFE-RL deviates in this respect from the normative objective of breast cancer early detection, which exclusively

mentions the reduction of breast cancer mortality (§ 9 para.1 sentence 1 KFE-RL). For the evaluation, this means that a one-sided focus on mortality does not do justice to the intention of the norm setter. On the other hand, early detection is not an end in itself. On the contrary: by bringing forward the diagnosis, healthy people are turned into sick people, which initially represents a harm. The intention is rather that the early diagnosis opens up more effective treatment options, which should not only reduce mortality but also reduce the overall burden associated with skin cancer (cf. § 2 sentence 2 oKFE-RL). This may also include the avoidance of invasive, potentially disfiguring therapies, as well as the detection of precancerous lesions (e.g. actinic keratoses), which may lead to the prevention of cancer.

8.15	Evidence-based Statement	new 2020
LoE 2++	Data on skin cancer screening in Germany show that the population-wide offer of a standardized examination of the skin on the entire body by trained physicians leads to an initially emphasized increase in the incidence of detected cases of melanocytic and non-melanocytic skin cancer.	
	[198]; [205]; [206]; [684]; [685]; [686]; [687]; [688]	
	Strong Consensus (100%)	

8.16	Evidence-based Statement	new 2020
LoE 2++	As a result of skin cancer screening, there is a more marked increase in the incidence of in situ carcinomas compared to invasive tumours. In the case of invasive melanomas, there is a shift in stage with a lower proportion of advanced tumours (stage T2-T4).	
	[205]; [206]; [687]; [689]	
	Strong Consensus (100%)	

8.17	Evidence-based Statement	new 2020
LoE 2+	The incidence of advanced melanoma is declining after the introduction of population-based skin cancer screening.	
	[686]	
	Strong Consensus (100%)	

8.18	Evidence-based Statement	new 2020
LoE 2++	Screening participants with unremarkable results are diagnosed with fewer invasive melanomas (in the sense of interval carcinomas) within two years of screening than would be expected without the intervention.	
	[689]	
	Strong Consensus (100%)	

8.19	Evidence-based Statement	new 2020
LoE 2-	In the temporal context of a feasibility study on population-based screening, there was a significant decrease in documented melanoma mortality.For nationwide skin cancer screening, no decrease in melanoma mortality could be observed in studies covering a maximum period of seven years after introduction.	
	[197]; [198]; [205]; [690]; [691]	
	Consensus (94%)	

Follow-Up Evaluations of the SCREEN Projectt

In the temporal context of the SCREEN project and the preparatory activities, epidemiological trend changes were observed in Schleswig-Holstein, which are to be expected in the case of effective population-based early detection.

Initially, there was a pronounced increase in skin cancer incidence. Compared to 1999, the age-standardized incidence of invasive melanoma (ICD-10: C43) was about 20% higher in 2003/2004 [198], only to fall back below the pre-screening level thereafter [686]; [206]. In the Saarland as a comparative region without systematic skin cancer early detection there were hardly any changes in the C43 incidence in the same period [205]; [206]. Particularly strong increases in incidence were recorded in the SCREEN project for in situ melanoma (+46% (women and men overall, comparison July 2003-June 2004 with July 2001-June 2003) [205] and +133% (women) and +108% (men) (comparison July 2003-June 2004 with 1998-2000) [206]). For invasive non-melanocytic skin cancer (C44), the rate of new cases in July 2003-June 2004 was 47% (women) and 34% (men) higher than in 1998-2000 [685]. This was followed by a delayed slight decline, but not back to pre-screening levels. This could be an expression of a long-term rising screening-independent trend of increase in non-melanocytic skin cancer, as described for Saarland for example [685].

An increase in the incidence of the target disease in the initial phase of a screening programme is a typical consequence of the measure if it cannot be explained by secular trends. It indicates that screening has detected diseases that would otherwise not have been detected or would have been detected at a later time. It also includes diseases that would have been detected in an earlier screening round under the hypothetical assumption of a longer existing programme (“prevalent" cases). The initial prevalence peak, as well as a persistent incidence surplus accompanying the programme, is not as such a suitable indicator of the intended success of the

programme. A remaining incidence surplus indicates diseases that would never have appeared during the lifetime of the affected person without early detection. Such overdiagnoses represent a damage that is in principle unavoidable, although in the case of the one-year SCREEN project it is difficult to quantify.

The crucial indicators for assessing a screening program are incidence and mortality; in the absence of other influencing factors, the age-standardized rate of advanced tumours and the mortality rate should decline.

Indeed, a significant decrease in melanoma incidence rates was observed in the follow-up of the SCREEN project at stage T2 and T3, and also T4 in women (Eisemann et al. 2014b). When these stages are combined, there is a 43% (women) and 40% (men) decrease in the standardized rate when comparing 2006/07 to 1999/2000. Missing stage data have been replaced by multiple imputation in this analysis. A particular contributor to the population-based decline, as suggested by another study, was the reduced burden of disease in participants of the SCREEN project [689]. In this study, the incidence of interval carcinomas was investigated. This refers to carcinomas that occur after unremarkable participation in screening outside the programme within the regular screening interval (here assumed to be 24 months). Invasive interval melanomas were recorded in 150 of 350,307 inconspicuously screened individuals, which is less overall than would have been expected based on incidence rates in the pre-SCREEN era (1999-2002) (age-adjusted relative incidence: 0.71 (95% CI: 0.60-0.84). Among these, in turn, the proportion of T2-T4 melanomas was significantly smaller (16.7%) than in the reference period (28.8%). In addition, it should be taken into account that, on the one hand, the proportion of invasive melanomas with unknown stage (Tx) was higher before the start of the project (42.4% vs. 36.0%), and that, on the other hand, 21.5% of SCREEN participants were recommended for a follow-up examination, which increases the number of interval melanomas compared to a screening-free situation. Both circumstances suggest that the study on interval melanomas underestimates the impact of screening on the incidence of advanced melanomas in a screening cohort. However, it cannot be ruled out in both studies that a change in T classification from 2004 onwards artificially reduced the number of unfavourable stages [686].

In temporal connection with the SCREEN project, there was a significant decrease in melanoma mortality in Schleswig-Holstein [690]; [205]; [198]; [691]. Compared to 1998/99, the age-standardised mortality rate in 2008/09 was 51% lower for women and 47% lower for men, while in neighbouring regions (Denmark, Mecklenburg-Western Pomerania, Hamburg, Lower Saxony, and Germany without Schleswig-Holstein) the rates were stable or increased [197]. The plausibility of the finding has been questioned with different considerations. On the one hand, the significant mortality decline with a SCREEN participation rate of only 19% is unexpectedly high. On the other hand, the decline seems to have started before 2003, although a reliable determination of the time of the trend change is problematic due to statistical noise in the data. Preparatory activities may have contributed to the unexpectedly favourable development, which may have increased awareness of skin cancer early detection among physicians and the population and promoted corresponding examinations already before the actual start of the project. These are not taken into account in the participation rate of 19%. The magnitude of the decrease may also be influenced by the fact that persons with an above-average risk of dying from skin cancer were overrepresented among the project participants [198]; [691]. It is unclear whether and to what extent incorrect coding of cause of death contributed to the observed transient decline in melanoma mortality. During the same period in which the largest decrease in

melanoma mortality was recorded (2008-2010), a significant increase in mortality due to malignant neoplasms of vaguely defined, secondary, and unspecified sites (C76-C80) was recorded [691].

Evaluation Results for Nationwide Skin Cancer Screening

Even after the launch of the nationwide SCS in July 2008, there was a significant increase in skin cancer incidence with a participation rate of eligible persons of approximately 30 percent. For invasive melanoma, an increase in age-standardized incidence of 24% (2006-2010) [690] and 28% (2003/04 - 2010/11) [198] was reported. An analysis of cancer registry data restricted to North Rhine-Westphalia showed an annual percentage change (APC) of 3.8% (95% CI: 0.4%-7.3% (females) or 0.1%-7.7% (men)) and a similar increase for non-melanocytic skin cancer (APC women: 5.2% (95% CI: 2.1%-8.3%,); APC men: 3.6% (95% CI: 0.6%-6.7%) [687]. The increase was more robust for in situ tumours of the skin (in situ melanoma: APC women: 11.2% (95% CI: 5.2%-17.6%,); APC men: 12.0% (95% CI: 5.8%-18.5%); in situ SCC: APC women: 14.3% (95% CI: 8.0%-20.9%,); APC men: 15.1% (95% CI: 8.4%-22.3%) (Stang et al. 2018). In parallel, North Rhine-Westphalia showed an increase in melanoma-associated work disability cases as well as work disability cases and hospitalizations for non-melanocytic skin cancer. A positive association between the nationwide SCS and the frequency of relevant hospital discharge diagnoses (as a surrogate for incidence; C43 and C44 combined) was also found in a study with panel data from 22 European countries over the period 2000-2013 [684]. Only one of the studies identified and appropriately designed found no incidence increase for skin cancer. This was an analysis of health insurance data from Saxony comparing 6-month incidences from the first and second half of 2008 [688]. The negative result is not very meaningful due to the very short observation period, the low participation rates at the beginning of the program, and the relatively small study population.

The same study examined the respective disease severity of cases included in the health insurance data over the period 2008 to 2012. Severe courses (defined as cases with LK and/or distant metastases and/or interferon treatment) were more common in nonscreening participants than in screening participants, although the differences were not significant in each case. Population-based changes in stage-specific incidence of melanoma after the introduction of nationwide screening were examined in the aforementioned study from North Rhine-Westphalia [687].

While the incidence of T1 melanoma increased by 14.6% (95% CI 8.4%-21.2%) annually in women and by 14.3% (95% CI 7.0%-22.2%) in men from 2007 to 2014, the annual increase in advanced melanoma (T2-T4) ranged from 2.9% (95% CI 0.5%-5.4%) (T3 women) to 6.6% (95% CI 2.3%-11.1%) (T4 men). However, it is reasonable to expect that the reported small increases in advanced tumours may actually underlie weaker increases or even declines in new disease rates, as the substantial number of unknown stages (49% of invasive melanomas in women and 50% in men at the start of the observation period) fell to 20% each in parallel. Of note, in the non-modeled annual rates, despite further increasing completeness of staging information at the end of the observation period (2014 vs. 2013), a decline is evident in all advanced stages in both men and women.

Robust evidence for the incidence of overdiagnosis and interval carcinomas is not yet available for the nationwide SCS. None of the identified studies found a decrease in melanoma mortality as a result of the program. The observation periods extend to 2012 [684], 2013 [690]; [198]; [691] and 2015 [687], respectively. The discrepancy with the described mortality trends as a result of the SCREEN project has led to

controversial interpretations, which, in addition to the aforementioned possibility of miscoded causes of death and changes in the population data base (Census 2011), are also based on differences in detail in design, implementation quality, acceptance, and awareness effects of the two interventions (participation of specialists from different disciplines, training measures, motivation of the examiners, age of those eligible, participation rates, self-selection of at-risk individuals, referral of at-risk individuals to specialists, and public relations) [691]). As a result, the SCREEN project [198], in part, and the nationwide screening [690] are rated as questionably more intensive. If one focuses on the initial increase in incidence, neither the one nor the other interpretation can be proven with certainty. The latter interpretation would make the absence of an observed decrease in mortality all the more disappointing. However, it is possible that the time series evaluated so far are too short to detect effects of nationwide screening on mortality [691]. It is generally assumed that mortality-reducing effects of cancer screening do not become visible before five years have elapsed [690]. In the case of the SCREEN project, the second mortality reduction, which was more significant in terms of magnitude, also began with approximately this latency [198]. For the nationwide SCS, this would mean that changes in the mortality trend would only become visible from around 2013.

8.20	Evidence-based Recommendation	checked 2020
GoR **B**	Skin cancer screening should be offered as part of the prevention of skin cancer.	
LoE **2+**	[197]; [198]; [205]; [684]; [685]; [686]; [687]; [688]; [689]; [690]; [691]; [692]	
	Consensus (94%)	

Need for Research

The currently available evidence on the effectiveness of the nationwide SCS is insufficient. Promising results from the SCREEN project have not yet been replicated for the current programme. Harms that counterbalance the presumed benefits have not been sufficiently investigated. The evaluation reports commissioned in accordance with § 35 KFE-RL [693] focus on indicators of structural and process quality and also show weaknesses in this respect, which are largely due to inadequacies in the data basis.

As essential inconsistencies of the last report [693] are to be emphasized [278]:

- For the physician participation rates among dermatologists values of >100% have been mentioned for some KV-districts.
- Due to the lack of an insured person pseudonym, it was not possible to clearly link GP and dermatological screening documentation on an individual level. Therefore, the reported participation rates double-count all insured persons who were screened in two stages, which leads to an overestimation of the utilization.
- Biopsies were documented in only 71.5% of all cases of suspected cancer documented by a specialist. On the other hand, nearly 60,000 cases were documented in which biopsies were ordered without suspicion of cancer. The

authors assume artifacts, which in individual cases were also provoked by incomplete answer options.

Although the documentation requirements that have been in effect since 01/01/2019 suggest certain improvements with regard to evaluability, the most pressing question of whether the SCS provides a net benefit to participants in terms of mortality, morbidity, and quality of life will still not be answered validly by the documentation data.

Randomized controlled trials, which would be most suitable for this purpose, are not meaningful because of the contamination to be expected in the control arm (in Germany) and would require – at least for the outcomes mortality and occurrence of advanced tumours – numbers of participants and observation times that are not realistically achievable.

The most obvious option would be to conduct a cohort study, which, because of the necessary number of person-years to be observed, would most likely be realized as a retrospective cohort study with health insurance data. The main difficulty here is the a priori definition and collection of possible confounders, i.e. factors that are associated with both screening participation and outcome.

Therefore, a case-control study with the possibility of primary data collection is advocated here. In such a study, cases, e.g. individuals with metastatic skin cancer, would be compared in terms of exposure screening participation with control subjects from the general population. Death due to skin cancer could also justify case status, with relevant confounders and exposure collected during lifetime.

High priority continues to be given to conducting ecological analyses, i.e. studies that examine effects of SCS on a group basis and detached from individual uptake of the screening offer. Current figures of the cause of death statistics show that the mortality decline, which was not yet discernible in the cited studies, started in 2013. Since then, age-standardized skin cancer mortality has been declining significantly and steadily. A latency of five to seven years corresponds to what is generally to be expected in the case of cancer screening [690]. However, it can be assumed that improved treatment options for melanoma (immune checkpoint inhibitors and BRAF inhibitors, approved from 2011) may at least have contributed to this development [207].

Therefore, it remains important to monitor the incidence of advanced, particularly metastatic tumours. Declining incidences in advanced stages that cannot be explained by a decline in “natural" incidence reliably indicate successful early detection. Methodological difficulties with respect to lack of completeness in stage data can be addressed by appropriate imputation procedures. When focusing on mortality, possibilities to control the different influences of early detection and therapy should be considered. This can be done, for example, by analysing regional trends in relation to screening participation rates or by making comparisons with other, non-screening countries. Elaborated epidemiological methods (e.g. age period cohort models) can contribute to a deeper understanding of the data. In all group-based analyses, the possibility of ecological fallacy (cross-level bias) should be considered.

Last but not least, the nationwide SCS should be subjected to an in-depth health economic analysis, including harms (including overdiagnosis) and possible modifications, e.g. in the direction of risk-adapted screening.

8.21	Evidence-based Recommendation	modified 2020
GoR **B**	**Dessenting opinion of DEGAM and the DGHNO** The German Society of General Practice and Family Medicine (DEGAM) and the German Society of HNO (DGHNO), Head and Neck Surgery e.V. regard the evidence for the benefit of a general skin cancer screening programme as insufficient compared to opportunistic screening, in agreement with international institutions.Since the introduction of skin cancer screening, the mortality from skin cancer in Germany has not decreased. Therefore, no opportunistic skin cancer screening must be offered. In individual cases, early detection of skin cancer can be performed following balanced information about the pros and cons, especially in people at increased risk.	
LoE **2+**	[197]; [198]; [205]; [684]; [685]; [686]; [687]; [688]; [689]; [690]; [691]; [692]	

8.2.3. Implementation and Quality Assurance of Skin Cancer Screening

8.2.3.1. Education, Training, and Further Education

8.2.3.1.1. Professional Requirements

8.22	Consensus-based Recommendation	modified 2020
EC	Skin cancer screening must be conducted only by qualified physicians who have successfully completed a quality-assured, accredited education course on the conduct of skin cancer screening.	
	Strong Consensus (97%)	

In order to ensure a nationwide population-related skin cancer screening, the G-BA has taken into account the general practitioners (general practitioners, specialists for internal medicine, general practitioners, physicians without regional designation) and the dermatologists for the implementation as well as defined a two-stage SCS.

Independent of these legal requirements, both urologists and gynaecologists have grown experience in early detection and screening measures. This offers the opportunity to include skin cancer prevention in their specialist cancer screening examinations. It is to be expected that women would find it easier when visiting their gynecologist to have the complete skin carefully examined especially also in the intimate area. The same applies to the urologist. In addition, the pilot project of the German SCS (SCREEN), carried out from 2003 to 2004 in Schleswig-Holstein, shows that the design of a population-based SCS with the help of gynaecological support makes sense [694]; [205].

SCREEN also shows that the expansion of physicians' competencies through systematically-developed and quality-assured continuing education is helpful in meeting the

requirements that an SCS places on physicians. These requirements include, for example, the interpretation and communication of the sensitivity and specificity of the screening test, communication skills (e.g. shared decision-making), and the standardised performance of the screening examination [694]. These skills should already be taught and promoted in basic medical training. As part of the "Masterplan Medizinstudium 2020," a revision of the training content and study structure of medical studies is taking place. Doctor-patient communication is of particular importance here (BMBF, 2017). This will be deepened in the skin cancer screening training.

Need for Research

There is a need for research in the sense that, although studies are available that evaluate further education and training courses for their effect (increase in knowledge, diagnostic accuracy, etc.), there is a lack of studies that analyse the professional requirements that are necessary for advising and carrying out a SCS. For this purpose, it would be necessary to conduct a study in which the different specialist qualification profiles are compared with regard to their effect on epidemiological key figures (sensitivity, specificity, positive predictive value, negative predictive value, etc.) related to the screening test as well as with regard to communicative skills. Thus, in a further step, the professional prerequisites necessary for the quality-assured performance of a SCS can be further identified and narrowed down to a competence profile.

8.23	Consensus-based Recommendation	checked 2020
EC	A counselling approach and/or further advice on skin cancer screening cannot be offered and carried out by health professionals who are not medical practitioners (health assistants, practice nurses, nursing professions, other specialist professions within the healthcare system). The precondition for this is: • completion of appropriate professional training and • successful completion of a recognised quality-assured education course on counselling in connection with skin cancer screening.	
	Strong Consensus (100%)	

Personal communication, i.e. the direct conversation between doctor and citizen, plays an important role in health issues. In the pilot project of the German SCS (SCREEN), the special importance of medical assistants (MAs) also became clear in this context. The latter approached potential participants almost twice as often as physicians about their willingness to receive advice on SCS. Direct approach and advice is particularly crucial for promoting decision-making for or against a cancer screening measure (see also Chapter 8.3.2) [694]. To this end, in many cases MAs have more direct access to potential participants in everyday practice; counselling is possible here without a threshold for access. The role of MAs and other health professionals in general and their potential for prevention should also be optimised by participation in a further training course which imparts competences in connection with counselling on early skin cancer detection.

Need for Research

There is a need for research on the formative evaluation of further education and training programmes on SCS for health professionals who are not physicians. The results

of this can provide information on how educational measures for these professional groups should be designed, offered and summatively evaluated.

8.2.3.1.2. Creation of the Technical Prerequisites

8.24	Consensus-based Recommendation	checked 2020
EC	Advanced education/advanced education programmes in skin cancer screening for physicians and other health professionals (health assistants, practice nurses, nursing professions, other specialist professions in the healthcare system) must be extensively offered and carried out by certified trainers.	
	Strong Consensus (100%)	

An important prerequisite for the implementation of a SCS in practice is the quality-assured training of physicians and other health professionals so that they can fulfil their special role in the prevention of diseases.

With the SCS, Germany was the first country in the world to introduce a nationwide, organized, standardized cancer screening examination of the skin. To participate in this SCS, physicians require proof of successful participation in an eight-hour continuing education program recognized by the Kassenärztliche Bundesvereinigung (Federal Association of Statutory Health Insurance Physicians). Initially, a trainer program has been carried out under the direction of the Central Institute for the Panel Doctors: 132 dermatological and 151 general practitioner trainers were trained, who in turn have carried out or are carrying out further training. According to information of the associations of statutory health insurance physicians, about 44,000 physicians (general practitioners and dermatologists) had qualified for the implementation of the SCS by the end of 2012 and 597 pathologists or dermatohistopathologists meet the required quality standards.

Need for Research

There is a need for research in that it must be clarified with the aid of an as-is analysis whether nationwide further training offers exist for the individual professions and whether these are known by the target group. In addition, a target analysis must determine which goals are to be achieved in this regard. If necessary, a concept must be developed so that deficits can be eliminated if there is an incongruence between the actual and the target. Finally, the effects, the effectiveness, and the efficiency of the existing training offers are to be evaluated.

8.2.3.1.3. Contents of the Curriculum

An advanced training course on SCS for physicians or other health professionals (medical assistants, nursing staff, other health care professionals) should impart knowledge and methods on a theoretical and practical level. To this end, the following contents should be included in a curriculum:

- Epidemiology skin cancer (MM, NMSC),
- Aetiology, risk factors and -groups,
- Clinical pictures (MM, NMSC),
- Definition of prevention (primary, secondary, tertiary prevention),
- Early detection of cancer as a screening measure,

- Legal framework,
- Benefits and harms of early detection measures/screening programs,
- Criteria for the evaluation of screening measures,
- Parameters of a screening test,
- Skin cancer screening,
- Measures to address potential participants,
- Requirements for counselling regarding the Informed Decision in the context of a SCS,
- Screening test: standardised whole-body examination,
- Targeted anamnesis,
- Reporting of findings and counselling,
- Quality assurance pathology (histopathological differential diagnoses),
- Quality requirement histopathology,
- Histopathological images,
- Histopathological report (completeness, significance of contents),
- Referral,
- Documentation,
- Billing,
- Reporting to cancer registries,
- Interdisciplinary cooperation,
- Basics of communication,
- Communication between general practitioner and dermatologist, dermatologist and pathologist, physician and patient,
- Communication tools for medical discussion.

Under the coordinating direction of the Arbeitsgemeinschaft Dermatologische Prävention (ADP) e.V. (Dermatological Prevention Working Group) and in cooperation with the Kommission Hautkrebs-Screening Deutschland (German Skin Cancer Screening Commission), which is made up of the ADP, the DDG, the BvDD, the ADO, the DGDC and the ADH, an advanced training programme for the introduction of the SCS was developed in collaboration with the Deutscher Hausärzteverband (German General Practitioners' Association), the Institut für hausärztliche Fortbildung (Institute for Advanced Training in General Practice, IhF), and the DEGAM and published by the Deutscher Ärzte-Verlag (German Doctors' Publishing House), the contents of which are presented here [695]. This program has been evaluated by the Federal Association of Statutory Health Insurance Physicians as being consistent in content with the Cancer Screening Guideline [696]. The contents were taken over from the continuing education program that was successfully carried out within the pilot project of the German SCS (SCREEN).

8.2.3.1.4. Evaluation of Training Programmes/Curricula

The effectiveness of the eight-hour training programme on SCS in Germany has so far only been investigated in the form of pre-post surveys with the participating physicians. The study by Anders et al. [697] served to evaluate the updated training on SCS in Germany since 2015. A total of 573 questionnaires from the training participants (94% GPs; 6% dermatologists) were evaluated. The questionnaire consisted of 34 questions on knowledge about screening and early detection, skin cancer and SCS, and diagnostic accuracy. In addition, surveyed subjective self-confidence in diagnosis and consultation using Likert scales. The evaluation showed a significant increase in knowledge about screening, early detection, and skin cancer and SCS. The participating GPs were more likely to detect skin cancer after the training. In addition, their diagnostic accuracy improved significantly. The number of correctly named diagnoses

increased from 3.89 to 5.27 ($p < 0.001$). Compared to the participating dermatologists, GPs correctly named fewer diagnoses (mean: 10.03 vs 7.45, $p < 0.001$). Basal cell carcinoma was correctly diagnosed by 55.1% of participants in the pretest and 83.1% in the posttest ($p< 0.001$). Furthermore, an increased self-confidence could be observed in the context of the preventive consultation regarding skin cancer. Overall, the participating general practitioners benefited most from the training [697]. However, it has not yet been possible to make any statements about the long-term effects of such training measures or about influences on detection rates, the number of referrals or unnecessary biopsies for the German training programme.

International studies on the benefit of training on SCS and counselling of health professionals on skin cancer are summarized below. It should be noted that in these studies, too, statements on the influence of detection rate, diagnostic accuracy, and avoidance of unnecessary referrals or biopsies in care have hardly been taken into account so far and a clear need for research is evident here. Furthermore, the studies summarized here do not allow any conclusions to be drawn regarding sustainable effects.

The Skin Cancer Screening Education Study conducted in Canada evaluated continuing education on SCS. The structure of the training was based on the SCS training conducted in Germany. The aim of the study was to determine the increase in knowledge and diagnostic accuracy of the physicians as well as patient satisfaction with and well-being during SCS. The intervention group (physicians with skin cancer screening training) showed the highest increase in knowledge as well as confidence in making a diagnosis due to the training. During the subsequent screening period, both values dropped again. The control group (skin cancer screening training only after the screening phase) showed an increase in knowledge both during the screening phase and through the subsequent training. However, these results were not statistically significant. A statistically significant increase in diagnostic confidence was observed after the SCS training. In terms of diagnostic accuracy, both the number of patients who needed to be screened and the number of excisions to detect a skin tumour were significantly lower in the intervention group than in the control group (47.5 vs 221.5; 4.8 vs 28.5). Furthermore, patients showed a higher trust in the physicians of the intervention group (86% vs 78%, $p=0.000$). At 23% compared to 14% of patients, a greater proportion of patients in the intervention group reported feeling shame during the examination, which the authors attributed to the more detailed whole-body examination performed. Thus, more patients in the intervention group reported a more detailed full-body examination, which included examination of the scalp, genitals, and toes. In addition, patients received more information from physicians in the intervention group about UV radiation and skin self-examination, and were asked more frequently about their family history [698].

A randomized controlled trial of 57 general practitioners was conducted to evaluate the effectiveness of a web-based course on early skin cancer detection in the United States. The intervention included a two-hour curriculum aimed at promoting skin cancer diagnosis and preventive counseling. The control group (Attention-Control) was offered a similar course on diet and physical activity. The intervention group performed more whole-body examinations one month after intervention than the control group (4.0 vs. 3.2, $p=0.04$) (1=not performed, 4= performed) and provided informational materials on risk prevention (3.0 vs. 2.1, $p=0.01$) and skin self-examination (2.8 vs. 2.1, $p=0.03$) more frequently. Patients in the intervention group ($n=373$) had a significantly higher biopsy rate than patients in the attention control ($n=663$) one month after intervention (1% vs. 0%), according to the treatment report. However, one

year after randomization, the intervention and control groups differed only in that physicians in the intervention group reported addressing skin cancer more frequently during annual examinations of patients (3.4 vs. 3.0, p=0.2). In addition, patients in the intervention group (n= 307) were less likely than patients in the control group (n=669) to report receiving written informational materials at this point in time (p=0.017). In terms of attitudes, intentions, practice procedures, and knowledge, no difference between the two groups could be observed 12 months after randomisation. Only the personally assessed confidence to perform a whole-body examination is higher in the intervention group at this time (3.7 vs. 3.0, p=0.02) [699].

8.25	Evidence-based Recommendation	modified 2020
GoR **B**	Curricula for the training, advanced education and continuing professional development of physicians or other health professionals (health assistants, practice nurses, nursing professions, other specialist professions in the healthcare system) in primary care provision should include the following subject areas in relation to the primary and secondary prevention of skin cancer: • Epidemiology, • Diagnostic procedures including dermatoscopy and clinical algorithms, aided by photographic images of skin lesions, • Advice (primary and secondary prevention), • Communication, • Treatment. Curricula can be divided into one of more intervention units and incorporate the following educational means and conditions: course attendance, web-based, interactive, multimedia, role play, conveyed theoretically and/or practically.	
LoE **1-3**	[670]; [700]; [701]; [702]; [703]; [704]; [705]; [706]; [707]; [708]; [709]; [710]	
	Strong Consensus (100%)	

Within a systematic literature search (conducted in 2010), 20 publications were identified dealing with 13 different educational programs for health professionals on early skin cancer detection. In addition to the information contained in the respective publications, 12 of the original authors provided further information on the individual analyses. The information compiled provides information on aspects from the areas of curriculum (technical content), forms of training, and the outcomes measured in each case (evaluation). Within the individual training courses, curricula on the topics of diagnostics (in 92% of the studies), epidemiology (97%), treatment (62%), algorithms (46%), and dermoscopy (15%) were developed or adapted, implemented, and finally evaluated. The content was delivered in different forms and with different didactic means: as face-to-face (in 69 % of the studies), interactive (46%), multimedia (23%), or web-based (15%); with one intervention unit (23%), with two (46%), with more than two intervention units (30%). Eighteen out of 20 studies show a significant improvement of the respective outcomes measured by the intervention. Specifically, the endpoints of knowledge, competencies and skills, confidence in diagnostic, treatment, and counselling skills and the proportion of correct diagnoses are increased or

strengthened es and skills, confidence in diagnostic, treatment and counselling skills and the proportion of correct diagnoses are increased or strengthened [707].

In another study evaluating results from 17 general practitioners, whose intervention consisted of a face-to-face session and a booklet with 40 diagnostic images, sensitivity and specificity regarding the detection of different skin lesions improves. Specifically, sensitivity for malignant lesions increases significantly from 63% to 76% (for malignant melanoma from 65% to 81%) and for borderline lesions from 55% to 62%. In addition, a group consisting of six dermatologists was surveyed. In this regard, it can be noted that even after training of general practitioners, the proportion of correctly made diagnoses is often higher among dermatologists (e.g. seborrheic keratosis: dermatologists (100%), general practitioners (54%)) [700]. Twenty-seven medical students with (n=20) and without (n=7) previous knowledge in dermatology who completed the same training also show a significant increase in correct diagnoses. This evaluation shows no significant difference between the group with and the group without prior knowledge [702].

After one hour of training regarding clinical and dermoscopic assessment of skin lesions using 20 pairs of photographic images (each clinical and dermoscopic), the evaluation shows that the confidence in the diagnosis made by the subjects (19 physicians in residency training as dermatologists) was significantly increased by dermoscopic imaging of malignant and benign lesions compared to clinical examination. The exception was the group of dysplastic skin lesions, in which no significant change could be detected. It can also be seen from the results that after training, the assessment shifted significantly towards the respective correct diagnosis (for malignant and benign skin lesions). Again, the result did not change significantly in the group of dysplastic skin lesions. For images that were previously classified as clinically definite to diagnose, no significant improvement is shown by dermoscopic imaging after the intervention[701]. It should be noted that the analysis does not specify a possible control group.

Determination of diagnosis and development of a plan for further diagnosis or therapy based on 36 images in a web-based tutorial significantly increases the proportion of correct diagnoses for some skin lesions in the intervention group after training. No significant changes were observed in the control group (without training). Seventy-one physicians participated in the study (intervention group: n=39; control group: n=32), but only 46 of them (intervention group: n=27; control group: n=19) stayed on until the end of the study [705]).

In a one-week intervention, 32 nurses were trained on clinical decision making, epidemiology, risk assessment, diagnosis, prevention, symptoms and treatment in the context of early skin cancer detection (24 hours theory, 20 hours practice). Among other things, case analyses and photographic images of skin lesions were used for this purpose. In addition to theory, practical training was provided in a clinical setting. Surveys on the outcomes (general knowledge, knowledge regarding prevention, competences regarding early skin cancer detection) took place before the training, after the training and three months after the start of the training. It was found that the knowledge and competence parameters increase significantly, furthermore the self-confidence of the participants regarding the implementation and counselling for early skin cancer detection increases. Overall, the values remain stable over time. Likewise, significant differences in all characteristics were shown with regard to the results of the control group, which consisted of 87 caregivers [708]. It should be noted that the results cannot be completely transferred to Germany, as the job description

of nurses in the USA differs significantly from that of health care and nursing staff in Germany.

Using 252 medical students randomly assigned to two groups and interviewed at three time points, Dolev et al. examined the effect of an intervention consisting of a combination of web-based training in the diagnosis of skin lesions and practical training in a dermatology clinical department. The web-based training consisted of 17 learning units on the diagnosis and, where appropriate, treatment of pigmented and non-pigmented skin lesions (malignant melanoma, non-melanocytic skin cancer, moles and other benign skin lesions). The educational sessions included 85 clinical cases with photographic images and educational texts discussing visual features for the assessment of skin lesions. The practical component included: general dermatology, pediatric dermatology, dermatologic surgery plus teaching sessions, case discussions, and review of relevant literature. Group I completed the web-based training first, then the clerkship; group II completed the clerkship first, then the training. Interviews took place in both groups at the beginning, end, and between each intervention. The students' knowledge of both the diagnosis and treatment of skin cancer was assessed. There was a significant improvement over time in both groups. Overall, the combination of theory and practice results in higher values than only one of the two interventions. In addition, it can be seen that with regard to knowledge in diagnostics the sequence plays a role, i.e. the sequence internship-training provides significantly higher values than the sequence training-internship [704].

A training programme with 65 GPs, 41 of whom fully completed the evaluation, consisted of three learning units: a general three-hour information session (epidemiology, diagnosis, treatment) in which, among other things, different skin lesions were discussed using slides, a practical unit on a melanoma ward (melanoma unit) in a clinic, and a unit focusing on practical skills (e.g. excision methods). It is shown that there is an increase in confidence in medical advice. Specifically, the parameters of advice on the screening interval (increase of 39.7%) and on detection signs of skin cancer (increase of 54.8%) were investigated. In addition, physician diagnostic confidence regarding malignant lesions increased by 43.1%. Within the control group, no significant increase can be detected over time. There was also an increase in the intervention group with regard to correct diagnosis and correct treatment (based on the assessment of photographic images). There is also an increase in the proportion of physicians who independently determine a possible diagnosis before the histological findings are made. In contrast, no significant improvement was achieved in the congruence of the pre-recorded and histologically confirmed diagnosis. Likewise, the training did not lead to an increase in the number of excisions adequately performed from a histological point of view [706].

An intervention conducted with general practitioners and dermatologists in private practice included individual 20-minute face-to-face feedback. This followed the participants' assessment of skin lesions using analogue and digital images and an assessment directly on the patient. In addition, the intervention consisted of a two-hour interactive seminar focusing on pigmented and non-pigmented skin lesions. The subject matter was supported with a slide presentation, videos, and case studies. Also covered was instruction on the whole-body inspection procedure. In addition, other materials were handed out for more in-depth study (colour chart, brochure, “Melanoma Prevention Kit,” magnifying glass, skin colour guide, photographic images). Analysis showed that the intervention significantly increased correct diagnoses and corresponding correct treatment option(s) in the intervention group (n=26) compared

to the control group (n=26). However, training failed to raise the skills of general practitioners in private practice to the level of dermatologists (n=13)[710].

Within a study by de Gannes et al (2004), general practitioners were provided with a twelve-minute video that included information on skin cancer (including risk groups, advice) and photographic images of the different skin cancer entities online. The results showed that only a small increase in knowledge (skin cancer in general, prevention strategies, treatment, suspicious skin lesions) was demonstrated in the intervention group (n=10), which was not significant compared to the control group (n=17). Similarly, there was no significant increase in the frequency of excisions and correctly made diagnoses when comparing intervention and control groups [703].

Bono et al. 2002 showed that the combination of clinical (including ABCD algorithm) and dermoscopic diagnostics regarding the detection of malignant melanoma by experienced dermatologists (professional experience longer than five years) has the most advantageous balance in terms of sensitivity and specificity compared to telespectrophotometric diagnostic procedures. The combination of clinical (86%) and dermoscopic (91%) sensitivity achieved an overall sensitivity of 97%. In comparison, the telespectrophotometric examination had a sensitivity of only 80%; moreover, the specificity was only 49%. In contrast, clinical and dermatologic diagnostics achieved values of 77% and 74%, respectively. A total of 313 suspicious skin lesions were examined in 298 individuals [670].

Although the study did not investigate a direct intervention, it nevertheless gives an indication of possible focal points with regard to the diagnosis of malignant melanoma in the context of early skin cancer detection.

Need for Research

There is a need for research as previous studies on the sustainability and effectiveness of training on clinical patient-relevant outcomes are lacking. Furthermore, recommendations regarding a comprehensive and complete evaluation, which is necessary to attribute effects to specific intervention measures, are not applied. Therefore, it is necessary to place more emphasis on patient-relevant outcomes within the evaluation of existing and future programs and interventions so that programs and interventions can be improved and new programs can be designed in a sound manner.

Regarding the diagnostic accuracy of dermatologists and other trained physicians, the evidence is sparse. Additional studies are needed to support either the “gate keeper" approach or direct access to dermatologists [711]. Future studies comparing dermatologist outcomes with other trained physicians should link diagnostic accuracy with patient outcome data and also include the cost-effectiveness of the two approaches (“gate-keeper" vs direct access to dermatologist). In addition, any weakness in the training and education of physicians for early detection and treatment of skin cancer will be highlighted.

8.2.3.2. Data Documentation and Transmission

A. Katalinic, revision by F. Chenot/A. Waldmann

8.2.3.2.1. Introduction

According to the requirements of the European Union, the German SCS is to be classified as a non-population-based (opportunistic) screening programme. Although it is offered throughout the population as a benefit of the statutory health insurance (SHI)

for insured persons from the age of 35 years, decisive elements of a systematic, population-based screening programme are missing (e.g. invitation procedure for SCS, control of the targeted examination intervals, evaluation of results). In Germany, mammography screening, colorectal cancer screening and cervical cancer screening currently fulfil the requirements of a population-based screening programme.

Although no comparable guideline is available at the European level for the SCS, a development towards a systematic population-based screening programme should also be sought for the SCS in order to ensure a comparable offer situation in the area and high quality of the overall programme. Based on the European Cancer Screening Guidelines, individual elements such as the invitation system (e.g. via residents' registration offices or health insurance funds), monitoring of the examination intervals, documentation of the screening examinations, definition and evaluation of quality indicators and regular feedback on the quality of the examination offer to the participants (benchmarking) are to be implemented.

8.2.3.2.2. Data Collection

In the case of the introduction of an invitation system for the SCS, the following data should be collected to invite the population:

Inviting body (central body or health insurance company):

- Unique personal identification of the person to be screened (screening ID or cancer registry pseudonym),
- Invitation date,
- Age and sex of the invited person,
- Refusal/exclusion (active refusal of SCS or SCS not applicable, e.g. in case of prevalent skin cancer).

Predefined quality dimensions and -indicators are indispensable for monitoring the quality of population-based screening programmes. The assessment of the quality of individual components of a screening programme is facilitated by recourse to normatively defined or empirically determined reference values or reference ranges [712].

The data listed in this guideline recommendation represent a minimal data set for describing skin cancer screening and any clarification of suspected cases, including excisions primarily performed on an outpatient basis. The data set largely coincides with the documentation scope specified by the Federal Joint Committee [696].

In addition, but of crucial importance, the inclusion of a unique personal identification of the screening participants is provided for here. Without such a unique personal identification, neither the screening process (initial examination, second examination if necessary, follow-up by cancer registry if necessary) nor the previous screening history for the participants (determination of the participation rate, transition GP/dermatologist, time interval between initial and second examination), nor the adherence to screening intervals, can be described, nor can a link to the cancer registry data be established, for example, to determine the participant-specific skin cancer mortality and the identification of interval carcinomas.

The administrative availability of baseline data for those eligible (age, sex, etc.) is essential for the implementation of population-based invitations. Non-participants could be reminded of their screening again at defined intervals and individuals not to be invited (patients with skin cancer in follow-up, refusers) could be specifically excluded from further invitations.

Invitation data are also essential to derive indicators of uptake.

With the documentation of the data scope recommended above, the SCS would essentially catch up with mammography screening in terms of process and outcome evaluation.

8.2.3.2.3. Data Transmission

8.26	Consensus-based Recommendation	checked 2020
EC	Data recorded about skin cancer screening must be forwarded by family physicians and dermatologists to an evaluation centre where, together with the invitation data where applicable, they must be collated and evaluated for the quality management of skin cancer screening.In order to determine interval carcinomas and to evaluate mortality, a comparison must be undertaken with the cancer registry. The comparative data must be provided for the purposes of scientific evaluation.When a malignant finding is obtained, the responsible cancer registry must be notified by the examining physicians (including pathologists).	
	Strong Consensus (97%)	

The content of this recommendation is based on mammography screening. In order to determine indicators, the data of the general practitioner, dermatologist, and inviting body are to be merged in an evaluating, quality-assuring body. The pooling of data from one individual is mandatory to determine key quality indicators.

In order to determine how many of the participants with a suspected diagnosis made by the general practitioner are subsequently examined by a dermatologist, the data of the corresponding person from both data sources must be merged. For further indicators (e.g. participation rate [number of participants/number of invited, screening-eligible individuals]), linkage with the invitation data is required.

For the identification of interval carcinomas and for the scientific outcome evaluation of the SCS, the collected data are to be compared and linked with the data of the relevant cancer registry at regular intervals. The procedures for this have already been described for mammography screening.

To support accompanying health services research, defined anonymised data from the SCS should be made available to interested institutions on request. This would take into account the special studies on SCS mentioned in the CS guideline [696].

The reporting of skin cancer cases detected in the screening to the responsible cancer registries enables the population-based evaluation of the SCS.

8.2.3.2.4. Methods of Data Transmission

The CS guideline already stipulates for the SCS that all data must be recorded and transmitted in electronic form (Federal Joint Committee, 2009). The prerequisites for the recording formats and the transmission paths are made binding by the Federal Association of Statutory Health Insurance Physicians in special requirements for the practice management systems [713]. The supplementation of the data record in the sense of the additionally required data fields or procedures for the generation of unique personal identifications (compatible with cancer registries [714] should also be included in these requirements for electronic documentation in the future.

8.2.3.2.5. Data Protection Aspects

The documentation of the examination results for the participants in the SCS should be pseudonymised, taking into account suitable methods and data protection concepts. The additional request for a declaration of consent should be waived. For non-participants, a time-limited pseudonymized data storage of the invitation data for the purpose of outcome evaluation (especially skin cancer-related mortality) should be recommended. All data collection, retention and transmission processes should be closely coordinated with data protection authorities [715].

In analogy to mammography screening, quality-assuring documentation is to be carried out for all participants in SCS. As in mammography screening, a declaration of consent should be dispensed with, otherwise there is a risk of data gaps (see also justification for the CS guideline [646]).

It is particularly problematic that with a consent solution, non-consenting participants could no longer be separated from the group of non-participants. Thus, the comparison of participants and non-participants would not be meaningful.

For mortality evaluation, a comparison of skin cancer mortality between participants and non-participants has to be realized. This is only possible if the data of the non-participants are used for comparison with the cancer registry.

In order to take into account the right to informational self-determination, the personal data of the participants should already be pseudonymised during the primary collection. When using cancer registry-compatible pseudonymization and security procedures [714], re-identification of individuals is virtually impossible. The feasibility of pseudonymised data storage and the comparison of this with other data sources has already been successfully demonstrated by the North Rhine-Westphalia Cancer Registry, even with large data volumes [716].

8.2.3.3. Documentation of Findings

The data collection described above via the practice software within the scope of the billing at the expense of the statutory health insurance is not a documentation of findings. Only the suspicion of skin cancer is documented. The exact findings and localization of skin alterations which are not classified as suspected cancer must be documented separately. Theoretically, pigmented and other skin changes have to be documented so that in case of an accusation of error, if after a skin cancer screening examination without suspicious diagnosis a skin cancer is detected in a short time interval, it can be proved that at the time of the screening examination no skin change was present where the suspicion of a skin cancer should have been detected. Failure to document this regularly leads to a reversal of the burden of proof. Practically, the documentation of the findings of the entire integument is hardly possible without special apparative methods. An average Central European has between 20-30 melanocytic navi, which theoretically should be documented. Lawsuits in connection with overlooked skin cancer after screening are not known to date, according to research as of June 2019. Nevertheless, a free documentation of findings, independent of the sole documentation of the suspicion of skin cancer, in the practice software is recommended.

8.2.3.4. Quality Assurance of Skin Cancer Screening

8.27	Consensus-based Recommendation	checked 2020
EC	Quality assurance measures for skin cancer screening must include structure, process and outcome quality. Because of the absence of scientifically-based quality assurance measures, quality indicators must be confirmed by evidence-based methods and where necessary new indicators developed.	
	Strong Consensus (100%)	

The task of quality assurance is to ensure the quality of the health service *skin cancer screening*. In addition to the targeted *anamnesis* and the *visual standardised whole-body inspection*, this service also includes the *notification of findings* and the *related counselling* as well as adequate *documentation* [646]. Furthermore, a *previous consultation*, a consultation on primary preventive behaviour *(UV consultation*) and *confirmatory diagnostics (histopathology)* must be taken into account within quality assurance.

In addition, quality assurance measures concerning qualification (advanced training programme skin cancer screening) are necessary. Since up to now no sufficient scientific studies on quality assurance in the mentioned areas are available and currently practically no standardized, area-wide measures of static and dynamic quality assurance are carried out, no evidence-based recommendations can be given at this point.

It is therefore necessary to record and further develop any existing individual quality assurance measures, but new procedures should also be developed. These can then be tested, evaluated and, if necessary, implemented across the board. In principle, the quality indicators developed on the basis of these guidelines should be used as a guide. However, since no quality indicators could be developed, it is pointed out at this point that the parameters relevant for quality assurance should be generated from the respective recommendations. An overview or summary of the contents of the recommendations can be taken from the following list. This list contains additions to the advanced training programme for skin cancer screening and is aligned with the Cancer Screening Guideline of the G-BA, the Quality Assurance Agreement on Histopathology for Skin Cancer Screening, and the Objectives Paper 1 of the National Cancer Plan.

Targeted Anamnesis

- Clarification of eligibility
- Completion of the standardized medical history form by the participant
- Collection of family history
- Collection of personal medical history (including possible immunosuppression)
- Collection of the current medical history

Examination

Room equipment

- Examination area is protected from view (privacy screen)
- Use of a surface for the participant to stand on
- Use or presence of good lighting

- Use or presence of an examination couch

Aids

- Presence of spatulas/use of three spatulas per examination
- Presence of examination gloves/use of one examination glove per examination

Visual standardized inspection of the whole body

- Scalp: with two spatulas by parting the hair in strips
- Ears: look behind the ears as well as into the external auditory canal
- Eyelids (for this purpose have glasses removed if necessary)
- With a new spatula, examine the oral mucosa and lips, lifting the tongue and inspecting the gums
- Neck
- Upper body
- Axillae
- Arms
- Hands (especially the interdigital areas)
- Women: submammary region
- Perinal region: person to be screened bends down, pulls glutaen apart
- External female genitalia: lying or sitting down
- Male genital region: can be inspected while standing, the person being screened lifts the testicles and pulls back the foreskin
- Legs and feet, including the soles of the feet and especially the spaces between the toes.

Interdisciplinary cooperation

- Feedback from the specialist in skin and sexually transmitted diseases to the referring doctor (general practitioner, internist, and doctor without a specialist designation) regarding the findings and further procedure

Notification of Findings/Consultation

Notification in case of no clinical suspicion:

- Following the examination, personally by the physician performing the examination
- UV advice
- If necessary, instruction and motivation for self-observation
- Re-presentation after two years

Notification in case of clinical suspicion:

- Following the examination, personally by the physician performing the examination
- General practitioner (general practitioners, internists, general practitioners, and physicians without a regional designation): explanation of further procedure (referral to dermatologist)
- Dermatologist: explanation of further measures for clarification diagnostics, explanation of the modalities of the notification of findings (including possibility of involving a trusted person).

Notification in case of negative skin cancer findings:

- Following the histopathological examination, personally by the physician
- UV counselling
- If necessary, instruction and motivation for self-observation
- Re-presentation

Notification in case of positive skin cancer findings:

- Following the histopathological examination, personally by the physician
- Explanation of the findings with diagnosis, grading, and prognosis
- Explanation of the therapeutic options, if necessary in several sessions
- Explanation of the next steps

Documentation Requirements

General practitioners, internists, general practitioners and physicians without a regional designation must provide the following parameters for complete documentation:

- Physician number
- Unique personal identification of the person examined (screening ID or pseudonym of the cancer registry)
- Age and sex of the participant
- Date of examination
- Suspected diagnosis, differentiated according to skin cancer types:
- MM
- BCC
- SCC
- Participation in connection with health examination

Specialists for skin and venereal diseases provide these parameters for complete documentation:

- Physician number
- Unique personal identification of the person examined (screening ID or pseudonym of the cancer registry)
- Age and sex of the participant
- Date of examination
- Suspected diagnosis, differentiated according to skin cancer types:
- MM
- BCC
- SCC
- In the case of a referral for clarification of an abnormal finding from skin cancer screening, the date of the initial examination and the specification of the suspected diagnosis:
- MM
- BCC
- SCC
- In case of excision: date, histopathological findings, as far as possible tumour thickness or extension, TNM stage, grading
- Notification to the respective cancer registry according to the legal requirements of the respective federal state

Previous Information/Consultation

The following list is based on the checklist of the objectives paper 1 (National Cancer Plan). In this list, the individual points have been summarised, resulting in the following selection of requirements for written and supplementary oral counselling:

- Description of the target disease
- Disease pattern
- Frequency
- Eligibility for the screening service
- (age, interval, authorized service providers)
- Examination procedure
- Reference to guidelines
- Diagnostic accuracy
- Sensitivity
- Specificity
- Positive predictive value
- Negative predictive value
- Benefit
- Side effects of the test
- Risks
- Description
- Probability
- Impact
- Measures
- Procedure in case of abnormal findings
- Symptoms/precursors
- Causes and risk factors
- Guidance and motivation for self-/partner examination
- Primary preventive behaviour (UV counselling)

UV Counselling

UV counselling should include the following points:

- Education on the hazards of UV radiation
- Advice on how to deal with natural UV radiation
- Avoid strong solar radiation exposures
- Avoid midday sun
- Stay in the sun as short as possible
- Seek shade
- Avoid sunburns
- Slowly accustom the skin to sun exposure
- Pay attention to UV index
- Sun protection
- Textiles, headgear, sunglasses
- Sunscreen
- Use sunscreen without prolonging exposure time
- Pay attention to individual skin sensitivity
- Inform about the different skin types
- Advise on individual protective measures depending on the patient's skin type or state of health (immunosuppression)
- Restrictions on sun exposure (cosmetics, medications)
- Protect children in particular

- Limitation of annual sun exposure
- Advice on dealing with artificial UV radiation
- Do not use sunbeds, especially persons under 18 and persons with skin type I (recommendation for non-use: ICNIRP, WHO, EUROSKIN, and NiSG)
- Recommendation of the Radiation Protection Commission for dealing with artificial UV radiation
- Recommendation on behaviour if solaria or other sources of artificial UV radiation are used

Confirmatory Diagnostics (Histopathology)

- Observance of guidelines on methodology and performance of confirmatory diagnostics (excision/biopsy)
- Completeness of the medical documentation of histopathological examinations in particular:
- Indication of the tumour type according to WHO classification
- Indication of histological staging according to TNM classification (UICC)

Contents of the Qualification

- Potential benefits and harms of early detection measures, criteria for the assessment of early detection measures
- Program of cancer screening, health examination, and early awareness of the patient
- Measures for addressing
- Consultation
- Etiology of skin cancer, clinical pictures, frequency, risk factors or -group, anamnesis, visual standardized whole body inspection, gaze diagnostics
- Procedure of the early detection examination for skin cancer
- Presentation and discussion of case studies
- Documentation measures
- Interdisciplinary cooperation

In addition to quality assurance measures, other parameters that serve to evaluate the quality of the results of the SCS should be taken into account:

- Participation rate (differentiated by physician groups, age, and gender).
- Proportion of the combination of SCS and health examination in all SCS performed
- Number of suspected diagnoses differentiated by physician group
- Number of confirmed diagnoses by dermatologists
- Number of false-positive findings
- Detection rate (participation rate/number of detected skin cancers and histopathological grading)
- Overdiagnosis and overtreatment

8.2.4. Knowledge, Perceptions, and Attitudes towards Skin Cancer Screening

E. Grossmann, I.-M. Hübner

- **A high general relevance assessment of free statutory skin cancer screening (gSCS) can be seen among adults with statutory health insurance.**

However, at most half of the eligible persons know about the possibility to make use of it.

The cross-sectional study by Augustin et al. [717], which is representative for Germany, investigates the public perception of the gSCS. The gSCS was introduced in July 2008 as a standard benefit of the statutory health insurance in Germany from the age of 35 and serves the early detection of skin cancer. The study is a standardized telephone survey of 1,014 legally insured adults with German citizenship. Overall, 44% of respondents were aware of the possibility of free gSCS, with a higher level of awareness in eastern Germany, among women and at an older age. Fifty-six percent of respondents consider the possibility of free SCS as personally very important, 32% find it somewhat important. Hope for early detection and good treatment options, physician recommendation, interest in information about skin cancer, and own risk are named as the most important drivers of utilization. For more than half of the participants there is no reason not to go to the gSCS.

Eissing et al. [718]

conducted a representative cross-sectional survey on the public's knowledge and perception of gSCS. For this purpose, 1,004 adult persons with German citizenship were interviewed in standardized telephone interviews. The screening was rated positively overall. Persons who participated rate the advantages of the gSCS higher than the disadvantages. In general, 50% of respondents know about their eligibility for the gSCS, with a higher proportion of women than men. This represents a stagnation compared to previous years.

An American population representative cross-sectional study (Rutten et al., 2009) relates the data collected regarding perceptions of screening to the evidence, and the evidence base here is considered unclear. Nevertheless, 88% of respondents believe that regular checks increase the chance of diagnosing skin cancer at an early stage. This assessment may be due to the fact that despite the perceived lack of clarity of evidence, many organisations recommend SCS.

Sullivan et al. [719], referring to the same population-representative cross-sectional study as Rutten et al. [423], compared knowledge of screening opportunities for different cancers. For skin cancer, the possibility of screening is less known than for colorectal and lung cancer. However, for all three cancers, there is an assumption that screening leads to successful early detection (87-90% of respondents), which is why the value of screening is appreciated.

- **There is a clear gender difference in willingness to participate in SCS. Men are less likely to take up screening and also show a lower willingness to participate.**

Davis et al. [720] investigated attitudes towards skin cancer screening and its uptake among US adults. For this purpose, 1,148 persons were interviewed in standardized telephone interviews. In general, the SCS is perceived as effective by both men and women, but strong gender differences are evident in willingness to participate and participation overall. Men show a lower willingness to participate in the SCS than women. Willingness is higher when specific information on screening is provided. The gender difference is also evident in the uptake of screening: 41% of men have never used screening, compared to only 5% of women.

- **Knowledge of gSCS as well as concern about skin cancer lead to an overall increase in uptake.**

Eissing et al. [718] conducted a cross-sectional survey representative for Germany on the public's knowledge and perception of gSCS. It was found that half of the respondents knew about the gSCS. Thirty-nine percent had participated in screening at least once. Uptake is higher in West Germany and among women than among men and in East Germany. In general, uptake is positively associated with knowledge of screening and concern about skin cancer.

8.2.4.1. Sources of Information on Skin Cancer Screening

The central sources of information on gSCS are health insurance companies, dermatologists, and the media. There are strong socio-demographic and socio-economic differences here. Eissing et al. [718] conducted a cross-sectional survey representative for Germany on the public's knowledge and perception of gSCS. The central sources of information are health insurance companies, dermatologists, and the media (1/3 of respondents each), followed by the dermatologist (20%) and acquaintances and relatives (17%). In East Germany health insurances are more used for information, whereas in West Germany the dermatologist and the family are more used as sources of information. Women are more likely to learn about screening from their dermatologist, whereas men are more likely to be informed by their family doctor. Low-educated and older persons are comparatively more likely to learn about gSCS from media sources, while younger persons are more likely to be informed about gSCS through their private environment.

8.2.4.2. Measures to Promote Informed Uptake of Skin Cancer Screening

8.28	Consensus-based Recommendation	new 2020
EC	Awareness of statutory skin cancer screening should be increased among the population through targeted measures. Different communication channels should be used to reach different target groups.	
	Strong Consensus (100%)	

Eissing et al. (2017) conducted a cross-sectional survey representative of Germany on the public's knowledge and perception of gSCS. It was found that only 50% of respondents were aware of the gSCS and sources of information differed by group of people.

Community-based educational interventions can increase awareness and uptake of the SCS. Janda et al. [721] conducted a community-based intervention tailored to men over 50 years of age to increase uptake of the SCS in Australia. This involved telephone interviews with 559 men over 50 years of age at three measurement time points (before, after and two years after intervention). The education about early detection resulted in a 3.5 times higher participation in the medical examination and a two times higher performance of the self-examination in the target group. At the end of the intervention, the rates were also more than two times higher.

8.29	Consensus-based Recommendation	new 2020
EC	Information about and motivation to take up skin cancer screening should be addressed in a gender-specific way.	
	Strong Consensus (100%)	

Davis et al. [720] investigated the attitude towards skin cancer screening and its utilization of US adults. The cross-sectional study showed a clear gender difference in the (willingness to) take part in SCS. Men showed lower participation than women. However, willingness to participate was higher among men when specific information on screening was provided. In Germany, too, there are gender differences in the use of the SCS: according to the GEDA study 2010, more eligible women than men are aware of the SCS, and it is also used by about more women than men [722]

8.3. Communicative Strategies and Communication Channels of Secondary Prevention

8.3.1. Preamble

A working group of the National Cancer Plan (NCP) dealt with the uptake of cancer screening measures (Goal 1 from Field of Action 1). In the context of this development, a change of direction was made, which places the informed decision for or against a cancer screening measure above the highest possible participation rate [723]. In the following, it was necessary to address the concept of “Informed Decision.” In this context, the members of this working group agreed on the following definition, following Rimer et al. [724] [725] :

An “Informed Decision" occurs when an individual:

- understands the condition being addressed and grasps what the medical service entails, including benefits, risks, limitations, alternatives, and uncertainties,
- has considered his or her preferences, and
- makes the decision in accordance with these,
- believes he or she has participated in the decision to the extent desired, and
- has made the decision voluntarily and with the highest degree of personal autonomy.

Participatory decision-making is present when a decision is made jointly by the health care provider/health professional and the patient and implies the health professional's constructive support of the process at all levels. Overall, a three-stage process is assumed:

1) Conversation about need for decision and communality (Choice/Team Talk):

- Communicate that decision is coming up
- Formulate equal rights of the partners

2) Conversation about possibilities (Option Talk):

- Discuss advantages and disadvantages of the option
- Possibly use of decision aid (Decision Aid)

3) Decision Talk (Decision Talk):

- Determine preferences of the user
- Negotiate decision
- Reach a joint decision

- Reach agreements on the implementation of the decision

In the context of screening measures, the informed decision for or against participation in screening is particularly relevant. If the screening result is found to be abnormal and further diagnostic steps become necessary, the process of participatory decision-making also kicks in.

8.30	Consensus-based Recommendation	modified 2020
EC	Information about the early detection of skin cancer must be guided by the recommendations of the [German] National Cancer Control Plan on an „informed and participatory decision“ to enable the person seeking advice deciding for or against participation in skin cancer screening examination.	
	Strong Consensus (97%)	

8.3.2. The "Informed and Participatory Decision" Regarding Participation in a Screening Examination

Together with representatives of the German Cancer Society (Deutsche Krebsgesellschaft e. V.), German Cancer Aid (Deutsche Krebshilfe e. V.) and the Association of German Tumour Centres (Arbeitsgemeinschaft Deutscher Tumourzentren e. V.), the Federal Government launched the National Cancer Plan in 2008 to coordinate the activities of all those involved in the fight against cancer more effectively and to optimise the care situation for cancer patients in Germany. The goals of the NCP are primarily the further development of early cancer detection and care structures as well as more quality assurance in oncology, ensuring efficient drugs for treatment, and patient orientation. This also includes improving the communication skills of physicians as well as the information, counselling and support services [725].

In this context, Objective 1 (improvement of information and participation in early cancer detection) from Field of Action 1 (further development of early cancer detection) deals with the development of criteria that are necessary with regard to the formal and content-related design of information offers in order to enable citizens to make an “informed decision.” Since cancer screening examinations are aimed at people without symptoms and involve risks as well as benefits, an “informed and participatory decision" for or against participation is particularly important. Therefore, objective, understandable, and comprehensive information about potential advantages and disadvantages must be available to citizens. In order to do justice to this fact, the following checklist for recommended contents of information on screening measures was formulated by the members of Objectives Paper 1. It represents a consensual basis for the production of health information, which will be further tested within research projects [723].

Checklist: recommended contents of information on screening measures (modified) [723]:

- Introduction,
- Target groups,
- Aims of the information,
- Explanation of the disease for which the measure is used:
- description of the disease and its course (without early detection measures),

- health significance/impairment,
- epidemiology (incidence of disease, mortality; it may be helpful to present these risks in comparison with other diseases; presentation of risks in natural numbers and, if possible, graphically),
- treatment options,
- prevention,
- Description of the screening measure:
- objective of the measure (reduction of incidence/morbidity/mortality),
- explanation of the method/description of the procedure of the examination,
- description of further clarification examinations after findings,
- accuracy of the method (frequency of false-positive and false-negative findings; positive predictive value of a finding),
- description of the benefit and quantification (comparative with and without screening),
- level of evidence (or the degree of certainty of scientific proof that the intervention actually achieves its goals),
- description of risks and harms,
- direct risks associated with screening (e.g. radiation, complications),
- indirect risks resulting from a finding,
- … due to false-positive findings,
- … by false-negative findings,
- … due to advance diagnosis,
- … due to overdiagnosis/overtreatment,
- Access to screening,
- Information on costs incurred or cost coverage,
- Information on the quality of the screening measure,
- Description of quality assurance measures (e.g. certification of service providers, training programme, double assessment) and verifiability (quality indicators that the participant can check, e.g. advice on possible findings, need to undress in case of SCS),
- Further information:
- Reference to supplementary information that is missing due to lack of space,
- Reference to the fact that other people who knew this information came to different decisions,
- Reference to the fact that there are no pressures on content or deadlines,
- Reference to patient guidelines or specific further information,
- Decision aids (where validated aids are available for individual decision making),
- Reference to data protection or data use or consent to data sharing,
- Self-examination,
- Reference to the absence of symptoms (i.e. symptoms should and will be clarified irrespective of eligibility for the screening examination),
- Personal responsibility (each person is responsible for taking care of themselves and making decisions for or against preventive measures. The knowledge of one's own risk about effectiveness, benefits, risks, and limits of methods and consequences – even in case of non-use – are the basis for taking personal responsibility),
- Risk groups,
- Imprint/source information/status of information,
- Financing of the information medium, source of information, etc.,
- Information on conflicts of interest,

- Expiry date of the information.

Need for Research

The available studies on the determinants of secondary skin cancer prevention provide little information on the effect of communication measures on informed and participatory decision-making. The focus of the analyses is on participation in screening and knowledge about the risks of the sun or skin cancer and early detection of melanoma, but not on knowledge about the risks and opportunities of using the SCS.

Research is therefore still needed regarding the identification and description of predictors, moderators and mediators acting on the “Informed decision" regarding the secondary prevention of skin cancer, even though studies already provide evidence for this. In this context, the areas of information, context and medium need to be considered. Furthermore, as described, the checklist must be (empirically) tested and further developed, e.g. by means of criteria catalogues or other measuring instruments.

For more general information on the presentation of risks and opportunities of screening, we refer to the guideline evidence-based health information [726]. Although the guideline on evidence-based health information contains only one study on the presentation of risks in information on mammography screening [728], a Cochrane Review compiles the effects of different formats of risk presentations (such as natural frequencies, percentages, absolute risk reduction, relative risk reduction, number needed to treat/screen/harm) on different health topics [727]; [728]. However, these findings may be transferable to the SCS or indicate a need for further research on this topic.

8.3.3. Target Group Approach

8.31	Consensus-based Recommendation	modified 2020
EC	Strategies and measures aimed at enabling the population to make an “informed and participatory decision" for or against participation in skin cancer screening must be tailored to the different target groups. Different characteristics of the target groups (such as their risk perception and self-efficacy) are to be taken into account.	
	Strong Consensus (100%)	

The fact that a decision for or against participation in the SCS is optional and not mandatory for the citizen makes it necessary to offer decision-relevant information and information sources to the target persons. Accordingly, strategic communication considerations are necessary for reaching the different target groups, taking into account the characteristics that influence the accessibility of the respective target group. In this context, it should also be noted that it is often precisely those individuals who are characterised by a low perception of risk and a low sense of self-efficacy despite a rather high-risk status who are to be reached. These groups in particular are often only partially aware of their need for information, communication, and decision-making, have little interest in the topic, and/or do not wish to change their health behaviour and are therefore considered to be difficult to reach target groups [729]. On the other hand, there are also those individuals who show a high level of commitment and a pronounced interest in the topic and whose information and communication

needs are different compared to those of the high-risk groups and must also be taken into account. For this reason, a differentiated and target group-oriented approach and information is of particular importance.

8.32	Consensus-based Recommendation	new 2020
EC	The communication strategy for secondary prevention measures must be oriented towards the information and communication needs and routines as well as the living environments of the respective target group.	
	Strong Consensus (100%)	

This also includes the identification of relevant multipliers (e.g. family members, life partners, doctors, pharmacists, teachers, employers, peers), who can be essential for reaching the actual target group(s).

In the first step, it is necessary to identify the different target groups (segmentation) (e.g. within the framework of the formative evaluation, see Chapter 5.4.6) in order to subsequently describe them and, in a second step, to select, develop and compile suitable strategies and measures (targeting). The function of segmentation is to delineate more homogeneous subgroups from the heterogeneous overall group in order to be able to address and serve them more effectively and in a more targeted manner [731]; [730]. This is possible in particular through digital forms of communication in which the content can be specifically tailored to the user groups.

In this context, it is beneficial if the segmentation is oriented towards health psychology and behavioural science constructs, such as lifestyle, health-related attitudes and motives, risk perception and behaviour, and self-efficacy experience. These factors are in turn linked to information and communication needs, preferences and barriers, to the type and intensity of health-related information search and media use, and to topic perception and processing. With regard to health communication, this means that information and communication objectives, communication channels and message strategies should be developed on this basis in a target group-specific way [732]; [506]; [729].

In addition, it is necessary to record the health literacy and media literacy, the risk status of the persons (e.g. skin type or typical sun exposure duration) as well as life-related settings (e.g. outdoor workplace) of the individual target groups in order to be able to locate and delimit the individual segments and to adapt the contents of the communication measures. Since such comprehensive information is only available through appropriate risk screenings or when using corresponding digital applications, segmentation is in many cases carried out on the basis of more readily available determinants of the aforementioned characteristics.

Here, sociodemographic, socioeconomic, sociological, and psychographic criteria as well as health status, health awareness, and risk profile play an important role. Frequently, the combination of several criteria (hybrid segmentation) is also possible and necessary. In addition, the segmentation should be process-oriented, since a decision is often part of a behavioural change process consisting of several stages (cf. transtheoretical model), the target group differentiation should also take into account that the target persons are to be located at different stages of the health behaviour change and thus have different information needs. In addition, target group

segmentation should constantly adapt to changes in target group characteristics (dynamic segmentation) [730].

Need for Research

However, there is still a need for research to examine how the effectiveness of target group segmented measures differs from those that address the entire population. This applies in particular to opportunities for digital communication measures and instructions for self-examination, e.g. within apps. In addition, empirical evidence is needed to show which criteria applied as part of a segmentation or personalisation strategy have a higher efficiency and effectiveness than others. In addition, strategies and measures for the dissemination of messages and information must be evaluated in terms of their strategy by comparing target groups. In doing so, it is necessary to examine measures in comparison to each other and their suitability for specific target groups.

8.33	Evidence-based Statement	modified 2020
LoE 1++	Informing the adult population in their immediate environment can help to promote skin cancer awareness.	
	[468]	
	Strong Consensus (100%)	

The systematic review by Austoker et al. [468] deals with interventions that promote cancer awareness and early medical consultation in suspected cases. Five studies were included in the analysis that examined interventions targeting individuals and distributing (personalized) information by mail or web-based means. In addition, a further ten studies were analysed, some of which described public education campaigns, but also setting-based (i.e. related to the living environment, e.g. the workplace) interventions. Most studies focused on a specific cancer type. A total of four studies focused exclusively on malignant melanoma. The means of intervention ranged from information leaflets, telephone education, and computer-based learning programmes to mass media education campaigns, educational seminars, lectures, and information stands. As a result, it was found that cancer awareness, attention to possible cancer symptoms, active seeking of help for suspicious symptoms, or knowledge about melanoma risk reduction could be increased by the respective interventions. It can be inferred from the study that interventions tailored to the individual (tailoring) have the highest effectiveness. Embedding or tailoring an information intervention in or to the social setting/immediate lifeworld is one way of target group segmentation [468].

The question at hand is only indirectly examined in the review, so the level of evidence can only be related to the statement of the recommendation in a very limited way. Due to this, the wording “can" has been chosen in statement 8.32.

Need for Research

As the studies show, there are hardly any studies to date that evaluate setting-based interventions (e.g. at the workplace or in the doctor's practice) against interventions

that work without a setting. It would be important to provide evidence for the benefits of setting-based interventions and to generate detailed research results in order to be able to adapt interventions to the respective setting. This is because it is precisely through such interventions that hard-to-reach target groups can be reached.

8.34	Consensus-based Recommendation	new 2020
EC	Family members or multipliers can be involved in measures, for example, to carry out self-examination and to promote informed participation in skin cancer screening.	
	Strong Consensus (100%)	

In the context of information on screening measures, there is evidence that family involvement, such as partner education, can improve self-confidence in self-examination [733] and approaching high-risk patients about family members affected by skin cancer (e.g. siblings) can increase willingness to and participation in SCS [734]; [735]. Robinson et al. [733] show in their study that partner education can improve self-confidence in self-examination in melanoma patients.

Educational videos with information about risk groups or internet training can be offered via GPs and pharmacists. However, there is insufficient evidence on the effect of such educational videos on specific skin cancer risk groups or internet education among GPs [703]; [705] and pharmacists [736].

8.35	Evidence-based Recommendation	new 2020
GoR B	Interventions to promote skin self-examination and inform about skin cancer screening should be multimedia, interactive, integrate multiple communication channels, and be repetitive.	
LoE 1++ 3	[468]; [459]; [451]; [460]; [456]; [458]; [462]; [737]	
	Strong Consensus (100%)	

The knowledge about melanoma and the performance of the self-examination of the skin can be increased by the multiple as well as multimedia approach of adults. These effects were significantly different from the results of the respective control group [451]; [460].

Multiple communication achieves better effects in promoting skin self-examination than handing out a standard brochure once [451]. Repeated multimedia health education with animations, photos, and brief information in clinical settings leads to better knowledge of melanoma and increase in control of moles in at-risk individuals [Glazebrook, C. et al. 2006].

Multimedia communication (e.g., videos) appears to be superior in effectiveness to purely text-based communication [459]. Evidence for the superiority of multimedia forms of delivery (video) over conventional routes via brochures can be found in Idriss et al. and Janda et al. [459]; [462]. Group-based interventions can lead to better risk awareness. Austoker et al. [468] describe an increase in physician consultations within three months of recognition of melanoma symptoms from 16% to 67% [468].

Finally, women and men seem to be equally motivated to visit screening facilities regardless of education level [456]. This is attributed to well-designed promotional materials [737]. Overall, it should be noted that the effects in some studies cannot be clearly related to the attributes multiple or multimedia, as both were applied together and therefore a differentiated view is not possible.

However, on the basis of the available studies, the positive effect of such prevention programmes can only be assumed for complex training programmes that integrate various textual, visual, and audiovisual elements. In the study by Glazebrook et al. [Glazebrook, C. et al. 2006], tthe programmes were not tested against the effect of other programme profiles (other delivery channels or other forms or combinations of information presentation and processing), so that on this basis – despite the partly high level of evidence of the studies – it is not possible to make any statements about which measures or which components of a training programme have an effect and which do not contribute to an improvement in knowledge, attitude, and behavioural parameters. In studies in which different forms and ways of presenting information are compared, e.g. [459]; [462], other biasing factors may have been at work. Moreover, these studies also only provide indications of the effect of a complex and multipart bundle of measures, so that no statement can be made about the potential preventive influence of individual components.

Against this background, the evidence of the use of multimedia interactive training materials for optimizing the cognitive prerequisites necessary for an “Informed Decision" to participate in screening must be regarded as limited.

Need for Research

Accordingly, research is needed to comparatively test the short-, medium-, and long-term delivery performance of different training programs. Conclusions can only be drawn about the mediation potential of individual forms of presentation or programme profiles if the presentation and mediation parameters vary systematically, other parameters (e.g. target group, communication content) are kept constant and confounding variables are controlled or eliminated. Above all, it must be ensured that the information content of the different mediation channels used is comparable. In addition, comparative studies should examine the transferability of findings on the effect of different training programmes in countries and regions with an above-average risk potential from solar radiation (e.g. Australia [678]; [462]) and on specific target groups (e.g. older men [460]; [462]).

Furthermore, in the context of content and design planning and implementation of prevention and intervention programmes, there is a need for research in formative, in-process and summative evaluation (see also the following Chapter 5.4.6). For the strategic planning and conception of campaigns, it is particularly important to determine which communication channels can be used to reach which risk groups and how these should be designed in terms of media in order to also have an attention-grabbing effect in the natural settings of the target groups. In combination with formal

design elements, various message strategies (“message frames") should also be tested for their effectiveness in raising awareness of SCS.

8.3.4. Presentation of Information

E. Baumann, M. Kiehl, Revision D. Reifegerste, I. Hübner

8.36	Evidence-based Recommendation	modified 2020
GoR **B**	Educational and training programmes on secondary prevention of skin cancer should use the simplest, most realistic and vivid forms of visualisation possible in structuring materials and take into account the competence of individual target groups.	
LoE **1-**	[460]; [738]; [739]	
	Strong Consensus (100%)	

A systematic literature review [739] of

25 English-language studies on self-examination and melanoma detection concluded that visual representations improve knowledge, attitudes, and self-efficacy related to skin self-examination, increase frequency and accuracy of examination, and improve melanoma detection in patients. Text descriptions alone prove ineffective. Effective images here include labels of abnormal body sites in the form of diagrams or body sketches, clinical example images of benign and malignant skin lesions, dermoscopy images, and photographs of the patient's own skin and moles as a basis for comparison. The authors concluded that patients should have access to images and a large number of case histories at all times to enhance their visual memory and pattern recognition of melanomas.

However, the potential impact of such information materials as a single intervention should not be overestimated. Even if learning effects on the knowledge level can be demonstrated with appropriately well-designed materials, this can only be transferred to a limited extent to the ability to distinguish benign and malignant lesions in reality [460]). Here, a media communication measure alone does not seem to have a sufficient effect, especially in risk groups with below-average health literacy, so that a combination of such measures with interpersonal counselling and support offers is probably required. King [738] also points to the possibility of unintended effects through visual representations of case studies. He was able to show that visual representations increased perceived informedness about the detection of atypical melanoma, but that willingness to be reviewed by a physician varied.

Research Needed

Accordingly, there is a need for research to find out which depth of information and which type of information presentation is appropriate for which target group, i.e. can be easily understood and transferred into action-relevant knowledge, and to what extent a combination of media and interpersonal training measures is appropriate in each case. In this context, taking into account the target- and risk-group-specific

resources and barriers to information processing, above all the process of directing attention and learning should be analysed in a differentiated manner.

8.37	Evidence-based Recommendation	modified 2020
GoR A	Measures to promote skin self-examination and to inform about the opportunities and risks of skin cancer screening must address the target persons individually ("individual-level-interventions") and include individualized/personalized information and feedback elements.	
LoE 1++ 1+	[468]; [451]; [458]; [734]; [735]	
	Consensus (94%)	

Health information tailored to personal characteristics, behaviour patterns, needs, and beliefs is more likely to be perceived as personally relevant and therefore has a stronger motivating character than information that contains general information and advice. This so-called tailoring should take the form of, for example, personalized feedback on risk status, behavioural recommendations tailored to this, and reminders. This is particularly possible in digital communication formats (e.g. decision-making aids or risk calculators), which can interactively adapt to personal information.

For prevention and intervention programmes that address single individuals via personal contact with a health professional or also in the form of direct media, there is stronger evidence of their effect on the perception of a cancer risk than is the case for interventions that start at the collective level, i.e. do not specifically address single individuals

[468].

The systematic review of studies also provides evidence that individualised targeting or information tailored to individual risk status ("tailoring") is more effective than general information.

Evidence for the effectiveness of "tailoring" is also provided by Glanz et al. (2010). For adults at moderate to high risk of skin cancer, the authors were able to demonstrate a positive impact of personalised feedback in the context of a three-times mailed information package at two-week intervals compared to a non-personalised intervention in the form of general educational material on skin cancer prevention and self-examination as well as a brochure on sun protection measures and behavioural tips. Feedback was personalized based on individual risk status and personal risk factors, as well as on practiced sun protection and self-examination behaviours, behaviour change readiness, and perceived barriers to behaviour change. The constructs "risk perception," "cost and benefit trade-offs of behaviour change," "action-relevant knowledge and skills," and "social norms" were included as mediating variables [451].

A systematic review of personalisation of risk information for informed decision-making about screening participation [740] includes three studies on skin cancer screening [734]; [Glazebrook, C. et al. 2006]; [735]. In two studies, personalized risk

communication in the form of a personalized list of risk factors [735] and in the form of a numerical risk score [Glazebrook, C. et al. 2006] is better suited than generalized risk communication to increase screening participation in high-risk groups. However, in a study [734] this relationship was not found, only a benefit of the personalized list of risk factors on intention to participate in screening. The effectiveness of personalized risk information is also indicated by the successful use of a tool in which individuals were asked to self-assess their risk as part of a self-examination [494]. However, this tool was used in combination with medical advice, so that no conclusions can be drawn about its effectiveness independently of this.

Glazebrook et al. (2006), as part of their interactive PC training for at-risk individuals, worked with individualised feedback on risk status, which, as a fear appeal, aimed to increase perceived threat and, with regard to the practice of protective behaviour, simultaneously provided information to lower barriers and increase perceived benefits. It contributed to an increase in knowledge, particularly among individuals with higher risk status [Glazebrook, C. et al. 2006]. A

gain, however, the programme was not tested against non-personalised training, so the evidence on the evidence of individualised information and feedback elements in this regard remains limited.

Beyond the need for an individualised approach, the studies provide clear evidence that theoretical underpinning of programme designs is important and useful. The elements of the health belief model provide a coherent theoretical framework for personalization that underlies many interventions [734]; [Glazebrook, C. et al. 2006], from which the information to be conveyed individually about the SCS can be derived and which provides explanatory approaches for the target group-specific effectiveness of programs for the prevention of skin cancer as well as starting points for the design of the messages and levels of individualized feedback and evaluation [449]. Glanz et al. (2010) also included the above constructs as mediating variables derived from the health belief model and social cognitive theory to measure the effectiveness of personalized feedback [451]. In addition, the Transtheoretical Model and the Theory of Planned Behaviour are also used as a theoretical basis [741]; [734]; [735].

Need for Research

Accordingly, research is needed to empirically substantiate the short-, medium-, and long-term effectiveness of individualized training programs and feedback elements in intervention measures compared to programs that do not include elements of tailoring and feedback opportunities. In doing so, programs should draw on established theoretical approaches to modeling programs and explaining health behaviour change. Accordingly, the design of such programs should be based on a theoretical foundation and systematically tested against those interventions that do not include tailoring. In this context, the technical possibilities of digital and mobile communication measures in particular should be given greater consideration.

8.3.5. Evaluation of the Communication Process and Success

8.38	Consensus-based Recommendation	modified 2020
EC	Intervention projects and programmes in the context of secondary skin cancer prevention should be evaluated formatively and summatively.The evaluation parameters used should be derived from a theoretically based model.	
	Strong Consensus (97%)	

In order to develop and plan communicative interventions in the context of secondary skin cancer prevention in a targeted manner, data collection is necessary even before the actual implementation of the intervention (formative evaluation). This has two aims: collection of information for evidence- and theory-based conceptualization and implementation of the intervention (preproduction research), and a preliminary testing of the finalized intervention and its instruments and materials (product testing). Measurements and monitoring of the entire process are also beneficial in order to be able to take external and internal disturbance variables into account over time (process evaluation). Process evaluation includes not only the survey of content-related aspects but also the inclusion of variables that describe the quality of the intervention organisation (controlling) (e.g. organisational processes). Summative evaluation makes it possible to examine the defined intervention goals of a communicative intervention and to record the effects, effectiveness, and efficiency of the measure. The entire period during and after the intervention must be taken into account. Summative evaluation provides information necessary to identify and, if necessary, quantify possible changes brought about by the intervention. For this purpose, it is at least necessary to collect the relevant variables in each case before (can already be done within the formative evaluation (preproduction research)) and after the intervention. For an example, see the study by Anders et al. [741] on the SCREEN skin cancer screening project. Furthermore, it is important within the evaluation not only to examine variables that are directly related to the communication, but also to include the relevant health indicators and their change over time [506]; [503]; [508]; [507]; [742]; [509].

The evaluation parameters used within an evaluation should be derived from a theoretically proven model. According to the Transtheoretical Model, different stages of information processing are passed through before an intervention becomes behaviourally relevant. Continuum models, such as the Health Belief Model and the Theory of Planned Behaviour, also model the process of health behaviour change initiated by a prevention or intervention measure in a differentiated manner. The stage of behavioural change at which the target person or test person is in each case, or which constellations of individual predispositions are present in the members of a target group, also influences their receptiveness to different information and communication offers that are part of an intervention, as well as their evaluation and the resulting mediation potentials. Which end variables are measured and evaluated at the attitudinal and behavioural levels should therefore be derived from the theoretical model on the basis of which the intervention was designed [505]; [510]; [511]; [507].

Research Needs

Research is needed in testing evaluation strategies for reliability and in developing a set of criteria for testing the quality of evaluation measures. In addition, the

explanatory power and predictive power of different theoretical models for different objectives and measures should be identified and the model parameters specified for the secondary prevention of skin cancer.

8.39	Consensus-based Recommendation	modified 2020
EC	Evaluations of interventions in connection with secondary skin cancer prevention must work with empirically established measurement procedures geared specifically to the particular outcomes.	
	Strong Consensus (97%)	

The evaluation should take place at several measurement points and measure short- and long-term effects. Validated and standardised scales should be used to measure the different endpoints. If these are not available, evaluation findings should be empirically validated by comparing the findings generated by different survey and analysis procedures.

Austoker et al. (2009) conclude in their systematic review of prevention measures to increase cancer awareness, which also includes studies on skin cancer prevention, that a higher methodological quality and comparability of study designs is required: "future research evaluating individual-level interventions to promote cancer awareness should attempt to use study designs that generate high-quality evidence, measure outcomes over a longer term (months/years) and attempt to measure behavioural and stage outcomes, as well as knowledge and attitudes. We also highlight the need for standardised and validated measures of cancer awareness [...]" (p.38 in [468]).

This results in the consequences formulated in the recommendation for the parameters to be evaluated and the way they are measured. This also concerns the choice of survey instruments used for the measurement of attitude- and behaviour-related outcome variables.

In order not to underestimate possible effects of an intervention by the fact that the chosen evaluation method may not capture certain effects due to the nature of the survey, different methods should be used to measure the dependent variables that are complementary to each other and, when combined, allow for a more comprehensive picture [451].

Research Needs

There is a need for research into methods to optimise study designs with regard to the evaluation of prevention or intervention measures and the measurement procedures used in this context. The aim is to develop a catalogue of criteria for the evaluation of prevention and intervention measures in order to generate more empirically validated and comparable evaluation findings, e.g. by developing standardised and validated scales.

8.40	Evidence-based Recommendation	modified 2020
GoR **B**	In evaluating the efficacy of interventions for the secondary prevention of skin cancer, skin cancer prevention-specific attitudinal and behavioural parameters should be used, as well as indicators of contact frequency/intensity, to assess methods of communication and their quality and effectiveness.	
LoE **1++** **1+**	[451]; [458]	
	Strong Consensus (100%)	

A prerequisite for the unfolding of an attitudinal and behavioural preventive effect of the prevention or intervention measure is how frequently and intensively the individual communication offers and messages are perceived, whether they generate attention, how they are evaluated at the level of content and design, and whether they are understood, retained, and subjectively perceived as useful. In order to measure the immediate communication success that precedes a longer-term effect at the attitudinal and behavioural level, evaluation parameters are therefore also required that directly address the perception of the campaign message or training measure and measure the dispositions of the test persons in a differentiated manner at the respective level of behavioural change. Effective interventions must therefore also have a positive influence on the outcome variables upstream of the behavioural change if the behavioural change is to be attributed to the intervention. Also, only recipient feedback on the actual information or training material provides concrete indications of how information and training offers as a whole, or how individual elements as well as the content and design of the information in multimedia interventions, are accepted by different target groups and what optimisation potentials result from this.

Glanz et al. (2010a) evaluated the assessment of personalized and non-personalized stimulus material by the subjects, although they did not statistically include it as a mediator variable in the impact model. However, it can be shown that all personalized information is rated significantly better than the non-personalized across all items. Also in Glazebrook et al. (2006) the positively rated way of preparation and presentation of the information as well as the perceived user-friendliness of a deployed interactive PC training in the risk group might have contributed to the learning success [Glazebrook, C. et al. 2006].

A relevant concept in this context is also the decision balance derived from the decision-making model of Janis and Mann, which expresses the weighing of positive and negative consequences of an action or behaviour of the target person. It plays an essential role in the context of (health-related) behavioural change according to the Transtheoretical Model. Empirical social research has developed two main ways to capture the concept of decision balance. One way is to contrast the advantages and disadvantages of an action, e.g. a behaviour, i.e. to subtract the disadvantages from the advantages. Another way to operationalize decision balance is to contrast or subtract the advantages of a particular behaviour from the advantages of the opposite behaviour or of not adopting the recommended behaviour [743]; [744].

Accordingly, decision balance should be included as a mediator or surrogate parameter of sun-protective behaviour when evaluating skin cancer prevention interventions.

Need for Research

There is a need for research to systematically evaluate the significance of the parameters directly related to communication (e.g. range and attention-grabbing of the means of communication, comprehensibility, and evaluation of the information offered or measure) for the effect of the prevention or intervention measure at the attitude and behavioural level. In this context, it is also important to empirically model the different variants of the decision balance and to examine them with regard to their mediatizing effect on sun-protective behaviour in order to draw conclusions about suitable forms of address in prevention campaigns.

Studies in which media messages are used and associated with attitudinal and behavioural outcomes would have to fulfil the necessary prerequisites for drawing conclusions about the effect on the campaign and should only be interpreted as evidence of changes at the attitudinal and behavioural level if it is empirically confirmed that this change results from the contact of the target groups with the campaign content (reach) and the processing of these messages. Previous studies have not yet provided sufficient evidence for this. For example, Del Mar et al. do not provide sufficient evidence that the increased number of excisions by doctors during two TV campaigns can be clearly attributed to them in terms of causality, so that the assumptions on the effect relationship remain of a speculative nature despite a statistical correlation between the campaign period and the number of excisions [512]. Also in Oivanen et al., visits for skin examination cannot be causally attributed to contact with campaign messages [513].

In the evaluation of such measures, detailed information on the disseminated messages and advertising materials as well as a measurement of the contact probability with the campaign and its reach up to the perception and evaluation of the same in the target population should therefore be measured or ensured before evidence of the effectiveness of a campaign can be assumed.

8.41	**Consensus-based Recommendation**	**modified 2020**
EC	To evaluate the effectiveness of a communication-based intervention in terms of informed decision-making in connection with secondary skin cancer prevention, at least the following parameters must be determined: • relevant knowledge about opportunities and risks of the measure, • attitude towards the measure, action or behaviour, • participation or non-participation.	
	Strong Consensus (100%)	

Based on the definition, three dimensions can be derived that an “Informed Decision" includes: understanding, preferences, and decision. Mullen et al. also describe a fourth: participation. The individual dimensions can be operationalized in different ways. Understanding, for example, can be mapped by recording knowledge and risk perception. Personal preferences can be assessed with parameters such as perceived benefits or barriers, values, and attitudes. Aspects of participation can be mapped

with the help of concepts such as self-efficiency or shared decision-making. Finally, the decision dimension is reflected in the intention to participate or in participation itself [745]. An assignment of individual parameters to a specific dimension is not always possible in a clear, comprehensive and/or exclusive manner, i.e. in some cases a parameter also captures aspects of several dimensions or only fragments of a single dimension.

Marteau et al. (2001) developed a multidimensional model for the measurement of an "Informed Decision," which comprises knowledge, attitude and behaviour (participation), i.e. proportions of the aforementioned dimensions of understanding, preferences, and decision are taken into account. All three parameters are considered dichotomized in the model: knowledge (high, low), attitude (positive, negative), and behaviour (participation, non-participation). Finally, the resulting combinations of the three variables are used to derive whether a decision is informed or uniformed. It is important for an "Informed Decision" that there is congruence between attitude and behaviour, with a high level of knowledge at the same time (TableTable 25).

Table 29: Informed Decision Algorithm

Knowledge	Setting	Participation	Decision
high	Positive	Yes	**informed**
high	Negative	No	**informed**
high	Negative	Yes	uninformed
high	Positive	No	uninformed
low	Positive	Yes	uninformed
low	Negative	No	uninformed
low	Negative	Yes	uninformed
low	Positive	No	uninformed

Source: (Marteau, Dormandy, & Michie, 2001)

On the contrary, incongruencies between attitude and behaviour are a sign of a uniformed decision (TableTable 25). The model gets its theoretical basis from the Theory of Planned Behaviour [505].

Need for Research

There is a need for research concerning the development of a survey instrument that covers all four dimensions (understanding, preferences, participation, decision) of the "Informed Decision" and thus enables a more precise measurement of it. In addition, predictors, moderators and mediators are to be identified and described that act on the parameter "Informed Decision" as an overall concept. In this context, the areas of information, context and medium need to be considered. Similarly, not only decision-

making processes in the context of secondary prevention (of skin cancer) but also primary prevention are to be evaluated with regard to informed decision-making. In addition, it must be examined whether persons who have made informed decisions actually achieve different short-term and long-term outcomes with regard to primary and secondary prevention behaviours and their consequences in comparison with uniformed decision-makers.

8.4. Doctor-Patient Communication

8.4.1. Structure and Content of Doctor-Patient Discussions

8.42	Consensus-based Recommendation	new 2020
EC	A patient-centered form of communication must take place in doctor-patient conversations.	
	Consensus (95%)	

Doctor-patient communication is a psychosocial aspect of health care. It is important for the accurate communication and understanding of health-related information, the perception and adequate management of emotional distress, the establishment of a respectful and trusting relationship between doctor and patient, and shared decision-making and patient participation in treatment [746].

Patient-centeredness means taking into account patients' values, needs, attitudes, perspectives, preferences, and experiences [746] and patients' abilities and prior knowledge in doctor-patient conversations and the chosen form of interaction.

In general, patient-centered communication is associated with a variety of positive short- and long-term effects for patients [747]; [748]. Using a Randomized Controlled Trial (N = 80 women, aged 18-30 years), Bientzle, Fissler, Cress, and Kimmerle [747] make a comparison of the effects of a physician-centered versus a patient-centered communication style of physicians. The results show that physicians with a patient-centered communication style are perceived as more empathic, socially, and professionally competent. Attitude changes are more likely and influence on decisions is stronger. Only for knowledge transfer do no significant differences between the two communication styles emerge. Findings by Fox, Heritage, Stockdale, Asch, Duan, and Reise [749] also indicate that a patient-centered relationship in combination with a recommendation by the physician to participate in screenings increases willingness to participate. In addition, based on a systematic review of 40 studies, Riedl and Schuessler [750] show that a high degree of patient-centeredness is associated with perceived better emotional health and the use of fewer diagnostic tests.

Relevant components of patient-centered communication that were reviewed include patient activation and active engagement [751]; [752]. Specifically, communication readiness should be encouraged. It describes to what extent the patient feels able and willing to actively engage in the conversation with the physician and to voice his or her concerns [753].

In addition to the patient's experience and skills, willingness is influenced by the physician's communication style. Physicians should communicate to patients that they

can express their needs, attitudes, and opinions. This is both a positive predictor of satisfaction and adherence to treatment recommendations.

Similarly, this includes the physician using clear language that is understandable to laypersons and either explaining or avoiding technical terms. According to a survey of cardiology patients (N = 119) by Thomas, Hariharan, Rana, Swain, & Andrew [754], language that is difficult to understand and uses many technical terms leads to lower patient satisfaction and poorer recall of the physician's information and recommendations. In addition, it is significant to offer the patient the opportunity to ask comprehension questions at any time and to receive answers such as explanations of the relevant information [753].

A high degree of patient-centeredness is achieved when communication is culturally sensitive. This describes that communication should be adapted for different audiences and address individual needs and characteristics of the situation such as person (Betsch et al., 2015; Epstein & Street, 2007).

For the the degree of patient-centeredness, nonverbal communication (including eye contact, gestures, facial expressions, listening) is also taken into account. Especially listening represents a relevant behaviour of the physician, which according to a meta-analysis can also increase patient satisfaction (Henry, Fuhrel-Frobis, Rogers, & Eggly, 2011). Another influencing factor of satisfaction is also an affect-oriented communication of the physician who shows empathy (Schrooten, & de Jong, 2017; Verheul, Sanders, & Bensing, 2010).

8.43	Consensus-based Recommendation	new 2020
EC	The doctor-patient conversation should be divided into two phases. The first phase should serve to clarify the patient's concerns (patient agenda). The second phase of the discussion is the doctor's agenda and should contain precise information for decision-making on examinations, therapies (including the benefits and harms of the various options), and the further course of action.	
	Consensus (82%)	

An effective communication between doctor and patient is supported by a discussion agenda and control. According to Jünger [755] , two phases must be distinguished. At the beginning of a conversation, it is important to clarify the patient's concerns. To this end, physicians should give their patients time to present their concerns, encourage their willingness to communicate and contribute to activating the patient (e.g. in the form of open questions), not interrupt the patient's explanations, instead allow pauses and listen to the patient [755]. Jünger also describes this as the patient-centered phase.

The second phase (physician agenda) should deal with what information, what examinations and therapies are necessary. This is about precise information for decision making. In the course of this, it may seem necessary to ask specific follow-up questions in order to understand the problem and gather information about it (especially in the form of closed questions). In addition, the information is evaluated and information about examinations, therapies is given. Thus, the second phase can also be described as a doctor-centered phase [755].

Finally, it should be noted that basic communicative knowledge and techniques for doctor-centred conversation, as described for example by Schweickhardt and Fritzsche or Jünger (2018), are helpful in the context of the doctor-patient conversation to create successful communication [756]. Jünger describes, for example, the "WRMS" technique (wait, repeat, mirror, summarize) as a central technique of patient-centered communication.

8.4.2. Structure of the Doctor-Patient Conversation Before Screening

8.44	Consensus-based Recommendation	modified 2020
EC	Prior to the doctor-patient conversation, the patient must be issued with evidence-based information on the early detection of skin cancer (skin cancer screening) that provide information about the pros and cons of early detection in comprehensible language without engendering any anxiety. The subject matter must be kept to the checklist agreed in connection with the German National Cancer Control Plan *Recommended content of information about early detection measures* (Federal Ministry of Health, 2010). In addition, reference must be made to the possibility that outstanding queries can be clarified in the subsequent doctor-patient conversation.During the doctor-patient conversation, which must take place in a quiet and undisturbed atmosphere, the checklist must also serve as a guide. Emphasisie must be placed on the following aspects: • Procedure of the skin cancer screening, • Pros and cons of skin cancer screening, • Primary prevention information, • Personal risk profile and resultant consequences (risk communication). A period of time commensurate with the patient's personal preferences must be allowed to elapse between the provision of information and the decision. Associated professional groups and, where applicable, relatives must be included in the communication process.	
	Consensus (82%)	

The doctor-patient interview is important to provide the potential participant with information about primary and secondary measures of skin cancer prevention. This can reduce knowledge deficits and uncertainties on the part of the potential participant regarding behaviour and measures (e.g. full body examination). In addition, the potential participant should be given the opportunity to weigh up the advantages and disadvantages in connection with his or her own preferences, attitudes, and abilities and to make an "informed decision" for or against a measure/behaviour[757]. The information content that is necessary in this regard has been developed by the members of Goals Paper 1 as part of the National Cancer Plan. These are summarised in a checklist. It serves as a basis for informing potential participants in screening examinations. It is planned to supplement this checklist in a further step with a criteria catalogue. This criteria catalogue will be used to review and evaluate information concepts (e.g. brochures, leaflets, verbal communication processes) [757].

Within the doctor-patient discussion, successful risk communication is also important, which shows the potential participant his individual risk and, if necessary, his risk behaviour and allows him to assess it. The recording of individual risk factors is to be determined by self and family history as well as the clinically recordable picture.

In this context, it should be noted that a “positive" family history is sometimes not or insufficiently communicated within one's own family and to health professionals (health care professionals). This may be due to the fact that health professionals, for their part, do not communicate the significance of this risk factor in a clear and comprehensible manner. These findings are presented in a qualitative study using the example of malignant melanoma, in which 22 people from seven families were interviewed. In each family there were persons suffering from melanoma (n=11). They were interviewed about (risk) communication within the family and towards health professionals [758]; [759].

Only one study deals with the recipients' memory of possible risks after an explanatory talk using the example of a dermatological surgical method (Mohs micrographic surgery). The study shows that the general recollection of risks 20 minutes and one week after the explanation does not differ significantly (arithmetic mean of recalled risks: 2.65 (20 minutes) vs. 2.44 (one week – difference: 0.21). In conclusion, it can be assumed that within a period of one week the knowledge base relevant for a decision remains relatively stable [760]. However, these results can only be transferred to screening to a limited extent, since in the study the subjects are already patients, i.e. there is already a disease. This increases the need for decision-making and prioritizes the importance of information differently compared to healthy subjects.

Need for Research

- Clarification of the importance of the time factor in the information and decision-making process with regard to weighing the available facts and memory.
- Studies that assess knowledge and other decision factors multiple times over a longer period of time after being informed.
- Identification and description of predictors, moderators, and mediators acting on the “Informed Decision" for or against participation in SCS. In this context, the areas of communication, information, context and medium should be considered. Questions to be addressed include what competencies and content are necessary to enable health professionals to enable the potential participant to make an “Informed Decision" and how to communicate the content described:
- Studies to identify the physician communication strategies and -pathways (including comparison of different communication styles and modes of delivery) that best succeed in enabling different target and patient groups to make an informed decision for or against participation in SCS.
- Intervention studies that examine the differential impact of an information intervention developed according to the criteria of an “Informed Decision" on different target/patient groups.
- Intervention studies examining the impact of different information channels and mediators in the delivery of an information intervention developed according to the criteria of an “Informed Decision.”
- Instrument development study that captures possible dimensions of an “Informed Decision" and describes their validity in terms of these, in order to review or develop existing or new instruments to quantify an “Informed Decision.”
- Intervention studies, which examine further training courses, which are to convey the criteria of the “Informed Decision" regarding the informing of potential participants, to health professionals in a controlled manner.
- (Empirical) verification of the checklist, e.g. by developing criteria catalogues within validation studies.

- Risk communication within (skin cancer) screening measures.
- Intervention studies in which different types of risk communication and their effects on the decision-making process or on informed decision-making are examined in a controlled manner.

8.4.3. Structure of the Doctor-Patient Conversation After Screening

8.4.3.1. Structure of the Interview When Skin Cancer Is Not Suspected

8.45	Consensus-based Recommendation	modified 2020
EC	If the screening does not reveal any suspicion of skin cancer, this must be communicated to the patient personally by the doctor carrying out the early detection in a counselling immediately after the examination.It must be pointed out that the result of the examination reflects the current status.In addition, the patient's individual risk factors must be explained to him and he must be motivated to practise primary preventive behaviour and skin self-examination. The patient must also be informed that he can visit the doctor again at any time in the event of any uncertainties about self-recorded skin findings.	
	Strong Consensus (97%)	

Even though the results of the study by Karri et al. (2009) do not show any difference in the preference for written notification of findings and face-to-face information, the notification of a negative finding in a personal conversation is recommended. In this way, the patient can be informed about risk factors and risk behaviour at the same time and the physician can better respond to the patient's questions [761].

8.4.3.2. Structure of the Conversation When Skin Cancer is Suspected

8.46	Consensus-based Recommendation	modified 2020
EC	If the screening results in a suspicion of skin cancer, this must be communicated to the patient personally by the doctor carrying out the early detection in a counselling immediately after the examination.Family physicians (specialists in general medicine working in family practice, internal specialists, medical practitioners and non-specialist practitioners): Following the communication of a suspicion, the subsequent procedure must be explained.Dermatologist: The subsequent diagnostic investigations of the clinical suspicion must be communicated and explained.The patient must be informed that the findings will be communicated in a personal conversation and that he has the possibility of including a person of trust in this conversation. The patient must be asked about resources for psychological support during the waiting period and encouraged to practise self-care.The detailed interview must take place following receipt of the histological report.	
	Consensus (88%)	

Although many patients wish to have a detailed discussion already when expressing a suspicion of skin cancer, there is usually not enough time and peace and quiet for this during ongoing practice operations. For this reason, it is recommended to conduct the detailed discussion after receipt of the histological findings [762].

In the conversation it is necessary to address the patient's fears, but at the same time to prepare him for the possibility of a cancer diagnosis.

In addition, it is pointed out that the communication of the diagnosis is done personally in a face-to-face conversation and the patient has the possibility to bring a relative to this conversation [762]. Telephone communications are less appropriate.

Since most patients describe the time until the diagnosis is communicated as very stressful [763], the patient is given suggestions for psychological stabilisation.

8.4.4. Structure of the Doctor-Patient Conversation for Reporting Findings

8.47	Consensus-based Recommendation	modified 2020
EC	The period between the measures to confirm the diagnosis and the communication of the diagnosis must be kept as short as possible.Exclusion of skin cancer: The patient must be told of the histological exclusion of skin cancer. In addition, the patient must be given an explanation about his individual risk factors and he must be encouraged to practise primary preventive behaviour and skin self-examination. The patient must also be informed that he can visit the doctor again at any time in the event of any uncertainties about self-recorded skin findings.Confirmation of skin cancer: The finding of skin cancer must be communicated to the patient in detail with the diagnosis and grading in a personal (face-to-face) conversation. The existing diagnostic and therapeutic steps (including benefits and harms) consistent with the current state of scientific knowledge must be conveyed comprehensibly to the patient.	
	Strong Consensus (100%)	

The breaking of bad news, such as a diagnosis of skin cancer, causes anxiety in many patients. For this reason, sharing the diagnosis should be done in a calm environment, in an understandable manner and within a reasonable time frame. The conversation should be tailored to the patient and his or her intellectual abilities and preferences. Consideration is given to the realization that usually only a small amount of information can be absorbed at one time. Only as little information is given as is compatible with the patient's information needs. Sensitive care is taken to provide education only to the extent that patients signal that they can absorb and process it [762]. In addition, emotional support for the patient is useful. In advance, the patient should be offered the opportunity to include a trusted person in the discussion; this is particularly desired by married persons. The presence of other health professionals is largely perceived as uncomfortable [763].

Depending on the preference or wish of the patient and/or the relative, it may also be useful to address questions about further diagnostic and therapeutic steps, the effects of the disease and treatment on everyday life, and possibly also questions about the prognosis of the further course of the disease. For the discussion about the prognosis, it should always be taken into account that in the general population cancer is often associated with death and dying and that it is important to address this association and the fears associated with it. A sound source of information should be chosen for prognosis. In addition, patients prefer a brief information sheet with answers to the most important and frequently asked questions, as well as references to other support services.

The above recommendations for the educational interview are based on a standard publication on the delivery of serious diagnoses [764].

The general goals of the educational interview are to convey information to the patient in a way that is understandable, to provide psychosocial support for the patient, and to design strategies for action together with the patient. The conversation can be divided into six steps according to the SPIKES model of Baile et al. (2000):

At the beginning, an appropriate atmosphere is to be created and important persons are to be involved (e.g. partners). This is followed by an elicitation of the patient's attitude and clarification of the level of information about the previous diagnosis. After obtaining permission to communicate findings, this is done in adequate language (no technical terms) and by not communicating too much information at once. The understanding of the communication of findings and information is checked regularly during the interview. After communicating the findings, it is useful to address the patient's feelings, identify reactions, and acknowledge them appreciatively. At the end, further planning is discussed [764]. Patients are encouraged to ask further questions themselves [762]. In particular, at the end of the interview, the patient is asked if any questions remain unanswered. The patient is also offered the possibility of seeking psychosocial support from cancer counselling centres or self-help groups [762].

Need for Research

There is a need for research on how long patients wait on average to be informed of a confirmed diagnosis. This can be determined by the retrospective collection and analysis of data from patient files, compiled by personnel within the medical practice, with due regard for data protection. The quality of the patient interview should also be recorded, but this may prove difficult due to the sensitive nature of the situation. Qualitative and quantitative interviews with affected patients may play a role.

8.5. Diagnostics

8.5.1. Suspicious Diagnostics

T. Eigentler, C Berking, G. Mehlhorn/ Revision: C. Berking, M. Felcht, P. Mohr

8.5.1.1. Introduction

The subject of the secondary prevention of skin cancer includes the performance of a screening test and the clarification of a clinical suspicion of malignancy in the context of the suspected diagnosis.

The screening test is at the beginning of the early detection chain and involves the use of a simple, valid test on healthy individuals.

Morrison (1992) defines screening as the examination of asymptomatic individuals with the aim of classifying those examined into two groups with regard to disease: those with a high probability of disease and those with a low probability. In this context, the screening test represents a filtering method that makes it possible to identify persons with a high probability of disease in a collective. These individuals can then be further examined and, if necessary, treated in a procedure that follows the screening test [644].

For the screening test for skin cancer, only those measures are suitable which can also be carried out on larger population groups and are time and cost effective. As a means of screening test, the whole-body inspection with the naked eye on a completely undressed person is the appropriate measure (see also Chapter 8.1).

As soon as the examiner clinically suspects malignancy during the screening, the screening test is completed and the diagnosis of suspicion begins.

In the context of the diagnosis of suspicion, various methods and techniques have been investigated and published as aids to clarifying clinical suspicion of malignancy, and these are discussed below. These measures include:

- dermoscopy,
- ddition of algorithms,
- photography,
- teledermatology,
- spectrophotometry,
- near-infrared spectroscopy,
- confocal laser scanning microscopy,
- multiphoton laser tomography,
- optical coherence tomography,
- electrical impedance spectroscopy,
- high-frequency sonography,
- multispectral analysis,
- raman spectroscopy.

If malignancy of a skin change is still suspected, confirmation diagnostics are then performed (see Chapter 8.5.2).

8.5.1.2. Dermatoscopy

8.48	Evidence-based Recommendation	modified 2020
GoR **A**	Dermatologists must offer dermoscopy in the presumptive diagnostic procedure of pigmented and non-pigmented skin and nail lesions. Guideline adaptation: Australian Cancer Network Melanoma Guidelines Revision Working Party (2008).	
LoE **1+**	[765]; [766]; [767]; [768]; [769]; [770]; [771]; [772]; [773]; [774]; [775]	
	Consensus (86%)	

8.49	Consensus-based Recommendation	new 2020
EC	Dermatologists must be trained in dermoscopy for the presumptive diagnostic procedure.	
	Strong Consensus (100%)	

8.50	Evidence-based Recommendation	checked 2020
GoR 0	Dermatoscopy can be performed in people at increased risk undergoing an individualised check-up.	
LoE 2++	[772]	
	Strong Consensus (100%)	

Dermatoscopy (synonyms: incident light microscopy, epiluminescence microscopy, dermoscopy) is a non-invasive diagnostic procedure for the evaluation of skin lesions. The principle is based on a magnified image of the skin structures, which are usually illuminated with a light source. The dermatoscope is placed directly on the skin lesion to be examined. To avoid reflection of the light, either a contact medium (immersion oil, disinfection spray, ultrasound gel) or a light source with polarizing light must be used. Dermatoscopy can thus be used to evaluate structures down to the upper dermis. Dermatoscopy can be used to visualize diagnostic features of skin lesions that are not visible to the naked eye.

Dermatoscopy devices function with either an analog optical unit or photosensors. With both procedures, depending on the device used, there is in principle the possibility of documenting the findings.

Dermatoscopy of Melanocytic Lesions

Dermatoscopy is suitable for the examination of melanocytic lesions, especially for the diagnosis of melanoma [766]; [767]. Kittler et al (2002) performed a meta-analysis of 27 papers on the diagnostic accuracy with and without dermoscopy. The accuracy of melanoma diagnosis with the aid of dermoscopy was found to be significantly higher (log odds ratio 4.0 (95% CI: 3.0–5.1) vs. 2.7 (95% CI: 1.9-3.4); 49% improvement, p=0.001). Diagnostic accuracy was dependent on the level of practical training of the physician. Only with increasing training and experience was dermoscopy superior to the classic purely ocular diagnosis [767]. This systematic review did not show any significant advantage of an algorithm for evaluation (pattern analysis vs. ABCD-rule of dermoscopy vs. point systems (3- and 7-point list)).

There are individual studies on the diagnostic validity of dermoscopy in general medical care. These show improved sensitivity of the diagnosis “melanoma" or at least the identification of suspicious lesions requiring biopsy with the use of dermoscopy [768]; [769]. It should be noted, however, that these studies were all conducted with

clinicians trained in dermoscopy (although in some cases only through seminars or literature).

Some publications also suggest a reduced excision rate of benign lesions with the use of dermoscopy (reduced ratio of excised benign to excised malignant lesions; reduction in the number of patients referred for biopsy) [776]; [771].

For people at increased risk of skin cancer, the physician, together with the person to be screened, should determine an appropriate time interval based on an assessment of the individual risk profile (see also chapter Chapter 8.1.7).

Dermoscopy of Non-Melanocytic Lesions

In contrast to melanocytic lesions, the number of studies on dermoscopy of non-melanocytic lesions is significantly lower. In some studies on pigmented lesions [773]; [774]; [665], non-melanocytic lesions are listed in the margin. In the work of Lorentzen et al. (2008) the diagnostic specificity of dermoscopy for BCC is given as 99%.

In principle, dermoscopy is suitable for non-melanocytic lesions. In addition to typical features of individual lesions, attention should be paid to vascular structures [775].

8.51	Consensus-based Recommendation	checked 2020
EC	For all lesions of the skin and the adjacent mucosae in the facial, genital or anal region that would be insufficiently investigated by diagnostic procedures involving the use of dermatoscopy, the patient must have a consultation with further specialist diagnostic procedures.	
	Strong Consensus (97%)	

For melanocytic and non-melanocytic lesions of the skin, such as spinocellular precancerous lesions or carcinomas in the genital or anal area, which would be insufficiently clarified by the diagnosis by dermoscopy, consultation for further gynaecological or/and surgical diagnosis should be made. The diagnosis should primarily be made clinically by means of a precise inspection and, in addition, by means of a differentiated vulvoscopy, vaginoscopy or anuscopy. In case of abnormal findings, tissue sampling should be performed.

If melanocytic or non-melanocytic (squamous) precursor lesions or tumours of the oral mucosa are suspected, further ear, nose, and throat and/or oral and maxillofacial surgical consultation and diagnosis should be performed. Tissue sampling should also be performed in case of suspicious findings. The same applies to lesions in the facial region which can only be inadequately clarified by diagnostics using dermoscopy.

In this regard, reference is made to the currently existing interdisciplinary S2k guideline for the diagnosis and therapy of vulvar carcinoma and its precursors of 2015 (AWMF register number: 015/059) and to the S2k guideline for the diagnosis and management of precursor lesions of oral squamous cell carcinoma in dentistry, oral and maxillofacial medicine (AWMF register number: 007/092).

Findings at the eyelids should be further clarified by an ophthalmologist, since due to the specificity of the eyelids (protective function of the eye, glandular tissue for the

tear film, special innervation as well as tear duct guidance, etc.) the spectrum of diseases is significantly broadened and the functional preservation of the eyelids is of importance.

8.5.1.3. Algorithms and Photography

8.52	Consensus-based Statement	modified 2020
EC	Computer-based algorithms for the classification of (pigmented) skin lesions are currently being developed and investigated in many cases, but the guideline group is not yet in a position to make any statements in this respect.	
	Strong Consensus (97%)	

8.53	Evidence-based Statement	checked 2020
LoE **2-**	The value of whole-body photography in melanoma risk patients remains unproven.	
	[777]; [778]	
	Strong Consensus (97%)	

A problem in the diagnosis of suspicion is the relatively low specificity in the clinical diagnosis of melanoma, that is, against a background of a relatively low incidence of melanoma, a proportionate number of benign lesions are unnecessarily excised. For example, this ratio is 10-35 nevus cell nevi and seborrhoeic keratoses to one melanoma in general practices in Australia [779]. In a randomised controlled trial of 468 participating GPs in Australia, the provision of an algorithm (describing morphological changes and clinical symptomatology) and a photocamera (for follow-up within four to eight weeks) to assist in the detection of melanoma as distinct from other pigmented lesions (nevus cell nevi, seborrheic keratoses) did not reduce this ratio between excised benign lesions and melanomas [779]. In an older, very similar study of around 100 Australian primary care providers, these aids resulted in a 4.8% lower ratio of excised benign lesions, although this study had methodological flaws [780].

Guitera and colleagues have presented two algorithms for use in combination with confocal laser scanning microscopy for the diagnosis of BCC and MM [781]. The diagnostic accuracy of the algorithm for diagnosing BCC in the training set demonstrated a sensitivity of 100% and specificity of 88.5%. In contrast, the diagnostic accuracy of the melanoma algorithm demonstrated a sensitivity of 87.6% and specificity of 70.8%. Serial, automated, digital whole-body photography with 48 images per patient was presented in a historical cohort study as a new method for regular screening of high-risk melanoma patients, allowing earlier detection of melanoma as measured by the average thinner Breslow tumour thickness compared to other patient cohorts [777]. he combined use of whole-body digital photography and digital dermoscopy at an average interval of five months in patients with atypical nevus cell nevus syndrome resulted in higher diagnostic accuracy with the detection of even early and small melanomas and a saving in biopsies [778].

However, these conclusions of the authors are based on inaccurate data of their study results with only a small number of histopathological findings in relation to the total cohort as confirmatory diagnosis and the lack of a control group.

Specialized image processing programs for melanoma detection have been developed, but their value remains an open question. An editing program of digital images to distinguish melanoma from melanocytic nevi based on 3 variables of geometry, colour, and colour texture was presented with a sensitivity of 60.9% and a specificity of 95.4% in terms of predicting the diagnosis of melanoma and an overall accuracy of 89.4% [782]. Due to lack of information on study details, the results and their transferability can only be assessed to a limited extent.

8.54	Evidence-based Statement	modified 2020
LoE **2b**	Sequential digital dermoscopy can improve the early detection of malignant melanomas in follow-up control that do not have specific dermoscopic malignancy criteria. Guideline adaptation: Australian Cancer Network Melanoma Guidelines Revision Working Party (2008). Guidelines Program Oncology (German Cancer Society, German Cancer Aid, AWMF): Diagnosis, Therapy and Follow-up of Melanoma, Long Version 3.2, 2019, AWMF Registry Number: 032/024OL, http://www.leitlinienprogramm-onkologie.de/leit-linien/melanom/ (retrieved on: 2020-05-25).	
	[765]; [783]; [784]; [785]; [786]; [787]; [788]; [789]	
	Strong Consensus (100%)	

SDD is based on the principle of dermoscopy. By storing and digitally analysing the image material, it enables additional statements to be made about the recorded pigmented lesions. Thus, short-term changes in conspicuous lesions (1-3 months) can be detected, on the other hand, a medium- to long-term screening can be performed. Compared to dermoscopy alone, sequential dermoscopy has the advantage of being able to detect changes over time that do not show typical dermoscopic malignancy criteria but do have morphological or colour dynamics.

The Australian guideline evaluated four studies in different clinical settings on sequential digital dermoscopy [654].

Haenssle et al demonstrated a 17% improvement in early detection of malignant melanoma compared with routine dermoscopy with a mean follow-up of 32 months. The rate of excised melanomas among all excised data was 8.3% [783]; [784].

In the study by Kittler et al., histopathological examination of 499 pigmented lesions was performed after different lengths of follow-up (1.5–4.5 months, 4.6–8.0 months and > 8 months) [785].

A total of 92 melanomas were detected among the excidates; 61.8% and 45% and 35.1% of these melanomas, respectively, each had no typical dermatoscopic features for melanoma with increasing follow-up time, but had changed in SDD during the course. According to the results of this study, the time frame for follow-up of a lesion should be 1.5–4.5 months or for control 6–12 months.

In other studies, the additional use of sequential digital dermoscopy detected early invasive melanomas that were unremarkable by purely dermoscopic criteria [786]. The ratio between excised nevus and melanoma was decisively dependent on the selection of criteria, especially a moderate increase in size (< 5%) was only associated with a low risk of melanoma detection.

In addition, the value of dermoscopy and sequential digital dermoscopy was investigated in a study in which 63 general practitioners in Australia and New Zealand received training [790]. The use of dermoscopy alone achieved a 19.3% reduction in the excision rate, and the additional use of sequential digital dermoscopy achieved a 70.6% reduction (inclusion of a total of 374 pigmented lesions). However, the results are biased (identification bias), as not all lesions were examined histologically.

8.5.1.4. Teledermatology

8.55	Consensus-based Recommendation	checked 2020
EC	Teledermatology can be used to assess benign and malignant skin tumours.	
	Strong Consensus (100%)	

Teledermatology makes use of digital photographs of suspicious skin findings, which are sent to medical colleagues via the Internet and evaluated by them. This should improve the diagnostic quality (second opinion), reduce the number of personal medical consultations, and reduce the time required for diagnosis or therapy. Ferrandiz et al. (2007) were able to demonstrate the latter in a study of 134 preoperative patients with clinical suspicion of non-melanocytic skin cancer or fast-growing vascular tumour and 784 teleconsultations. They found a significant reduction in dermatology consults and waiting time to surgery compared with the conventional referral process [791]. The concordance rate between diagnoses made via teleconsultation and those made via histopathology was 0.86, with 12 of 20 mismatched lesions corresponding to diagnoses not originally included in the study.

In another study, 2,009 patients with benign or malignant skin tumours presenting to primary care centers each had two digital photographs (panoramic and close-up) of their skin tumours sent to and evaluated by dermatologists at a skin cancer center via the internet [792].

Teleconsultation filtered out 51.2% of patients, while 48.8% of patients presented in person at the skin cancer center. Referral times were significantly reduced compared to conventional methods. Concordance of diagnoses via teleconsultation with the same dermatologist was 0.95 and between two dermatologists was 0.85. Concordance between general practitioner and teleconsultation dermatologist was 0.46. Sensitivity of teleconsultation-based diagnosis was 99% and specificity was 62%.

In a prospective controlled study, a dermatologist was presented with a digital survey photograph, a close-up photograph, and a dermoscopic photograph of the lesion in question in 451 patients, through which he assessed the urgency of presenting the patient in person to the clinic [793].

This reduced waiting times for patients with urgent tumours, i.e. melanoma or squamous cell carcinoma, to present to clinic by a mean of 10 days compared to the conventional referral process.

A UK study tested the diagnostic accuracy of a dermatologist who initially made the diagnosis after conventional clinical examination of referred patients with pigmented lesions and repeated months later using anonymised stored photographs of the same lesions [794].

There were no differences in diagnostic accuracy, which supported the possibility of using teleconsultation. However, the authors suggested that this method only examines a snapshot rather than the whole patient, does not allow palpation of the lesion, and that the results depend on the quality of the photographs. They also call for a cost-benefit analysis before recommending the methodology for implementation.

Teledermatology received a negative evaluation in the study by Warshaw et al. (2009) of 519 patients with pigmented lesions, in which diagnostic accuracy was significantly worse compared with clinical examination in the patient (sensitivity 64% vs. 80.3%) and could not be improved by additional evaluation of dermoscopic images [795]. However, the study population was limited to men of an average age of 66 years with a range of 23 to 94 years.

A comparison between the evaluation of conventional photographs as slides and of compressed digital photographs showed no differences in sensitivity and specificity in the diagnostic accuracy of pigmented skin lesions [796].

8.5.1.5. Spectrophotometry

- **Spectrophotometric analysis of pigmented lesions has not been able to show an improvement in sensitivity and specificity in melanoma diagnosis** [797]; [798]; [799].

Telespectrophotometry involves measuring the reflectance of a lesion at wavelengths between 420 to 1,040 nm using a CCD camera with 17 interference filters. The 17 spectral images are stored in a PC and further processed. In a study of this method, four descriptors were defined according to the clinical characteristics of the lesions using the ABCD rule: roundness (asymmetry), flatness (boundary), average reflectance (colour/colouring), and size (diameter) [798]. One hundred eighty-six patients with 195 pigmented lesions were evaluated. All variables were significantly different between melanomas and non-melanomas, with colour being the most important parameter. Due to shortcomings of the study design and an unclear potential for bias, the significance of the results is unclear. By the same research group, 313 suspicious skin lesions in 298 patients were examined by clinical inspection, dermoscopy and telespectrophotometry [670]. Regarding the correct diagnosis of the 66 histologically confirmed melanomas, the sensitivity was 86%, 91% and 80%, respectively, and the specificity was 77%, 74% and 49%. Thus, telespectrophotometry did not provide any advantage.

In another recent study, spectrophotometric analysis of 881 skin lesions in 860 patients was performed by a dermatologist [799]. Compared to his assessment using clinical inspection and dermoscopy, there was no improvement in sensitivity (94% vs. 91%) and specificity (87% and 91%) with respect to melanoma diagnosis.

8.5.1.6. Near-Infrared Spectroscopy

- **The value of near-infrared spectroscopy in distinguishing melanocytic and non-melanocytic skin lesions from each other and from normal skin remains open.**

Near-infrared spectroscopy with wavelengths between 700-2,500 nm measures absorption by hemoglobins, cytochromes, water (O-H groups), lipids (C-H groups), and proteins (N-H groups) in tissues for each wavelength, which can provide inferences about tissue composition and oxygenation [800]. In one study, images were taken in vivo in the visible and near-infrared range (400-2,500 nm) of a total of 195 benign and malignant skin tumours, of which 130 could be evaluated [800]. Significant group differences could be shown, such as between dysplastic nevi and other skin lesions (e.g. actinic keratoses, BCC, lentigines) and between basal cell carcinomas and common nevi as well as seborrheic keratoses. Malignant melanomas were not investigated in this study.

8.5.1.7. Confocal Laser Scanning Microscopy (CLSM)

- **CLSM has high resolution in the assessment of pigmented and non-pigmented lesions of the skin. After appropriate training, CLSM can improve the diagnostic accuracy of single-cell lesions. CLSM can be used for the tentative diagnosis of AK and SCC in clinically indeterminate findings. CLSM can be useful for the diagnosis of BCC.**

The CLSM is a modern technical procedure in which focused laser light and its reflection from the various structures of the skin can be used to produce sectional images of the epidermis and papillary dermis in near histological resolution. In this process, the different media act as endogenous chromophores, so to speak, due to their different refractive indices (examples of refractive indices: water 1.33, keratin 1.5, melanin 1.7). The standard wavelength of the laser is 830 nm, with so-called multi-wave devices wavelengths of 400-1,064 nm are available. The lateral resolution is 0.1-1 µm, the axial resolution 3-5 µm and the maximum penetration depth, depending on the wavelength, ranges up to about 250-300 µm, at the nail organ also up to 450 µm. The in-vivo examination on the patient is performed in real time by placing the device on the lesion to be examined by means of coupling through a coupling medium such as gel and oil, similar to dermoscopy.

There are now over 300 publications as well as an S1 guideline ([801]) in the field of non-invasive dermatological diagnosis. There is also a meta-analysis on the value of CLSM in the diagnosis of BCC. The analysis of six studies showed a sensitivity of 0.97 with a 95% CI of 0.90-0.99 and a specificity of 0.93 (95% CI 0.88-0.96) [802]. However, these results are critical due to a high risk of bias and a small sample.

A systematic review identified a total of 11 studies whose results could not be pooled due to heterogeneity of individual studies [803]. The review demonstrates that CLSM can improve the diagnostic accuracy of malignant melanoma compared with dermoscopy. For BCC, the authors also concluded high diagnostic accuracy despite limited data, whereas no conclusions could be derived for squamous cell carcinoma. Further meta-analyses on the value of confocal laser scanning microscopy in the diagnosis of non-pigmented skin lesions are not yet available [806]; [805]; [804]; [665]. Data from meta-analyses are available on the value of confocal laser scanning microscopy in the diagnosis of pigmented skin lesions. The systematic review by Stevenson et al. included a total of five histologically controlled studies in which 909 lesions were examined [807]. The focus of this work was on the identification of malignant

melanoma from clinically indeterminate lesions. The authors demonstrated a sensitivity of 93% [95% CI 89-96] and a specificity of 76% [95% CI 68-83] per lesion. The rate of histologically proven malignant melanoma ranged from 29 to 37% in the studies. In another meta-analysis with n=21 retrospective and prospective studies, CLSM was evaluated for its value in the evaluation of malignant skin tumours [808],

with eight of the 21 studies examining malignant melanomas exclusively (n=1400 lesions). In these studies, sensitivity was 92.7% (95% CI: 90-95) and specificity was 78.3% (95% CI: 76-81). In eight other studies with a total of 1,825 lesions, BCC and SCC were examined in addition to MM. Here, the sensitivity was 94.5% and the specificity 85.4%. The studies differed in the number of participating centers (monocentric, multicentric) as well as in the number (1-5) and expertise of the investigators.

However, the results of the meta-analyses should be viewed critically because the studies were subject to verification bias: not all lesions were subjected to histological examination or CLSM was compared with dermoscopy. Some studies also examined overlapping patient collectives. However, the QUADAS-2 test showed a high study quality for malignant melanoma. Sensitivity (91.4-94.5%) and specificity (76.0-85.4%) were at similar levels in all meta-analyses.

A study by Alarcon investigated whether CLSM can reduce the “number needed to treat" (NNT: number of treatments needed) for suspected melanoma [809]. A total of 343 patients who had at least one suspicious lesion were included in the study and examined in three groups (dermoscopy alone, CLSM and dermoscopy, CLSM alone). There were statistically significant differences between the groups with a decrease in NNT from 3.73 to 1.12, especially the significantly higher specificity argued for adding CLSM to dermoscopy to reduce the rate of unnecessary excisions.

Another study by Pellacani et al. also showed a significant reduction in the number of excisions required for the diagnosis of malignant melanoma (6.8 vs. 14.6) by adding CLSM [810]. A total of 1,005 patients were studied for this purpose. Another publication of this working group additionally demonstrated that CLSM would also lead to a relevant cost reduction by avoiding resections of benign lesions [811].

8.5.1.8. Multiphoton Laser Tomography (MLT)

- **The value of multiphoton laser tomography in melanoma diagnosis remains open.**

MLT is a non-invasive examination technique that can assess both cellular and extracellular structures with subcellular resolution. MLT is based on the excitation of biogenic fluorophores by two or more low energy long wavelength photons and the induction of “second harmonic generation." A resolution of up to less than one micrometer is achieved. Studies are being conducted to determine the extent to which the technique is helpful in melanoma diagnosis:

A prospective study is available on MLT in which 83 melanocytic lesions were examined. The examination was performed both in vivo and ex vivo, but not all lesions were examined in parallel. Using four independent investigators in a blinded experimental design, sensitivity ranged from 71 to 95%; specificity ranged from 69 to 97%. Another study investigated a “fluorecence lifetime imaging" measurement in addition to MLT [812]. After a training phase, a total of 125 lesions were examined; a sensitivity of 100% and a specificity of 98% were demonstrated with regard to the diagnosis of malignant melanoma (n=25). In a study by Balu et al., a nine-point score was

developed on a small number (n=15) of melanocytic lesions with and without dysplasia as well as malignant melanoma, which showed a high discrimination potential [813].

8.5.1.9. Optical Coherence Tomography (OCT)

- **The value of OCT to distinguish melanocytic skin lesions from each other and from normal skin remains open. Optical coherence tomography can be used for the diagnosis of non-melanocytic skin cancer in clinically unclear findings.**

OCT is a modern optical technique that allows non-invasive, real-time imaging of the epidermis and upper dermis. The basis of OCT is white light interferometry. The travel time of a signal within the tissue sample is compared with a reference signal of known optical path length. OCT is analogous to B-mode in the ultrasound pulse-echo technique, measuring optical rather than acoustic reflection. The examination technique allows a penetration depth of up to one millimeter and a resolution of 3-15 µm. The image is displayed vertically, as in histological sections, and newer devices also allow display in the horizontal plane. Both melanocytic and non-melanocytic skin tumours have been imaged using the method and the results published, with the most convincing results being for BCC and systematically evaluated [815]; [814]; [816]; [817]; [818]; [819]; [820]. A systematic review identified the following features for the diagnosis of BCC with OCT in all 17 included studies: rounded/rounded dark structures in the upper dermis surrounded by a hyperreflective halo, which may still be surrounded by a hyporeflective border, and disruption of the epidermal layer [817]; [384].

Several studies are available on OCT for the evaluation of melanocytic lesions, describing potential differentiation criteria. In a multicenter, prospective study by Gambichler et al on a “high definition" OCT system, a total of 93 lesions (27 of which were malignant melanomas) were examined [821]. A sensitivity of 74.1% (95% CI: 54–89) and a specificity of 92.4% (95% CI: 83–98) were achieved.

However, larger controlled and high-quality studies are still lacking, so the value of the diagnosis cannot be conclusively assessed at present [815]; [665].

8.5.1.10. Electrical Impedance Spectroscopy

- **The value of multi-frequency electrical impedance spectroscopy (EIS) in distinguishing melanocytic and non-melanocytic skin lesions from each other and from normal skin remains open.**

Multi-frequency electrical impedance spectroscopy (EIS) is a technique that uses a small probe to send electric current at different frequencies from different electrodes into the superficial skin and measures and evaluates the change in current, frequency, and electric field. The electrical properties of biological material reflect cellular properties of the tissue such as cell density, architecture, cell shape, and the content of intracellular and extracellular water. Pilot studies found significant differences between BCCs and normal skin, and differentiation of BCCs from benign nevi with a sensitivity of 96% and a specificity of 86% [665].

In addition to this, an international multicenter study was published in which 22 clinics participated [822]. A total of 2,416 lesions in 1,943 patients were evaluated, among which 265 malignant melanomas were diagnosed (112 in situ, 153 invasive).

The method had a sensitivity of 96.6% (256 of 265 melanomas) and a specificity of 34.4%.

8.5.1.11. High-Frequency Sonography

- **The value of high-resolution sonography in differentiating melanocytic and non-melanocytic skin lesions from each other and from normal skin remains open.**

High-resolution sonography of the skin (synonym: ultrasound) is a non-invasive diagnostic procedure for the evaluation of skin lesions. The principle is based on the visualization of house structures with the help of high-frequency sound waves. The sound waves are reflected by structures of the skin, reabsorbed by the transducer and then converted back into electrical pulses by means of the piezoelectric effect. Images are generated from the electrical impulses. Water or ultrasound gel serve as contact medium.

According to Lassau et al (1997), high-frequency ultrasound is a simple, reliable, non-invasive method for accurate preoperative evaluation of skin tumour dimensions. The correlation between ultrasound and histologic measurement of tumour thickness (Breslow index) of 13 melanomas was very strong (R2= 0.9959), but there were no differences in the sonographic characteristics of melanomas and nevi. Thirty-one of the 32 BCCs were detected with high-frequency ultrasound. One lesion was not a BCC, but an actinic keratosis. Resection was complete in 24 cases and incomplete in seven cases [823].

Krahn et al (1998) were able to show sensitivity in determining the tumour thickness of melanomas (± 0.2 mm): < 0.76 mm: 79.3%, 0.76 – 1.5 mm: 42.9%, > 1.5 mm: 100%. The technique allows surgical planning and avoids reexcisions. However, its use is limited to differential diagnoses of malignant and benign skin lesions [824].

Wortsman and Wortsman (2010) studied the value of ultrasound in differential diagnosis. The proportion of correct clinical diagnoses at referral was 73%, whereas after diagnosis by ultrasound the proportion of correct diagnoses was 97%. Diagnostic accuracy for ultrasound is reported as 99% sensitivity (95% CI: 98.9-99.5) and 100% specificity (95% CI: 96.4-99.9). However, the inclusion criteria are not described and not all patients received a biopsy with histopathological confirmation. Also, the investigators knew the previous clinical diagnosis (lack of blinding). Due to the study design and the lack of description of the patient population, the results can only serve as a very limited basis for recommendations for action [825].

8.5.1.12. Other Methods: Multispectral Analysis and Raman Spectroscopy

Several studies are available on multispectral digital dermoscopy. In a study by Elbaum et al. a total of 63 malignant melanomas and 183 nevi were examined [826]). Here, depending on the evaluation mode, a sensitivity between 95-100% and a specificity between 68 and 84% could be shown. In another multicenter, prospective study, a total of 1,383 patients with 1,831 lesions were examined [827]. A total of 127 melanomas were identified. The sensitivity in this study was 98.4% (125/127 melanomas) and the specificity was 9.9%. A group of experienced dermatologists evaluated 130 single-cell lesions in the study by Hauschild et al. [828]. Here, sensitivity was higher by multispectral analysis than by evaluation of clinical and dermoscopic images by the experts alone. Specificity was also low in this study.

Raman Spectroscopy

Raman spectroscopy involves the study of inelastic scattering of light by molecules and solids. In a study, Lim et al. investigated several spectral investigation methods, including Raman spectroscopy [829]. The authors were able to demonstrate 100% sensitivity and specificity of Raman spectroscopy in a small group of patients (12 melanomas, 17 benign pigmentary lesions). Significant differences between nevi (n=41) and malignant melanomas (n=15) were also shown by Philipsen et al. [830]. However, the authors did not provide data regarding specificity or sensitivity for the method.

8.5.2. Confirmatory Diagnostics

Christian Rose and Michael Flaig

8.5.2.1. Methods of Confirmatory Diagnostics

8.56	Consensus-based Recommendation	checked 2020
EC	The histopathological examination of a suitable tissue sample is the standard confirmatory diagnostic method. The histopathological diagnosis must be used to confirm a suspicious lesion.	
	Strong Consensus (100%)	

8.57	Consensus-based Recommendation	checked 2020
EC	At the time of tissue sampling, consideration must be given to the relevant specific functional features in each case (e.g. in the facial and genital region) to prevent a functional disorder (e.g. ectropion, facial nerve paralysis) simply as a result of the tissue sampling.	
	Strong Consensus (100%)	

The histopathological examination of the tissue sample is performed by a trained pathologist (specialist standard) or dermatohistologist (additional qualification). In the quality assurance agreement for the SCS [831], a minimum number of personal findings on skin samples is additionally required of the examiner, which must be proven.

As a rule, the skin tissue is processed after formalin fixation. In rare cases, histological examination is performed using the frozen section technique. In this case, appropriate experience with the technical execution and evaluation of these preparations is necessary [832].

The availability of a suitable tissue sample is a prerequisite for histopathological examination. The procedure for tissue sampling depends on the clinical findings and the suspected clinical diagnosis (see also chapter 3.2.3 in the S3 guideline “Diagnostics, Therapy and Follow-Up of Melanoma” [831]; [789]).

Special anatomical conditions must be taken into account, taking into account the expertise of the relevant specialist areas (e.g. ENT, oral and maxillofacial surgery, ophthalmology, gynaecology), already during tissue removal with regard to function and

cosmetics, so that no injury to nerves (e.g. of the facial nerve) and scarring distortions and possibly stenoses (e.g. of the lacrimal ducts, eyelids, genitals) occur.

8.5.2.2. Carrying Out Confirmatory Diagnostics

8.5.2.2.1. Confirmatory Diagnostics in Malignant Melanoma (MM)

8.58	Consensus-based Recommendation	checked 2020
EC	On clinical suspicion of a malignant melanoma, this lesion must first of all be completely excised with a small safety margin.	
	Strong Consensus (100%)	

8.59	Evidence-based Statement	checked 2020
LoE 2+	The optimal tissue sample for histopathological assessment of a skin lesion suspected of being malignant melanoma is the complete excision (excision biopsy) with a safety margin of 2 mm, including the removal of fatty tissue.	
	[658]	
	Strong Consensus (100%)	

Following SIGN Guideline No. 72 “Cutaneous Melanoma“ (2003) and “Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand” (2008), MM should be excised completely with a small safety margin of 2 mm [654]; [658]. A larger excision distance, on the other hand, destroys lymphatic drainage pathways and possibly impedes the finding of sentinel lymph nodes [833].

8.60	Consensus-based Recommendation	checked 2020
EC	In the case of large, extensive tumours on the face or acral skin that are suspicious for melanoma and for which a primary diagnostic excision is difficult, a sample biopsy or partial excision can be performed.	
	Strong Consensus (100%)	

In special situations, especially with large, melanoma-suspicious tumors in the face or in acral skin, where a primary diagnostic excision is difficult, a trial biopsy or partial excision can also be performed [654]. Studies have shown that this procedure does not worsen the prognosis for patients [834].

For tissue sampling, a general distinction is made between incisional and excisional biopsies. For incisional biopsies, punch biopsies and flat biopsies are available; for excisional biopsies, spindle-shaped excision is available [835]. Superficial shave biopsy of suspicious lesions is not appropriate [658]. The various biopsy techniques each have advantages and disadvantages. A properly performed flat biopsy (shallow incision) is wider than a punch biopsy. It reaches the middle corium and allows a

better assessment of the architecture. A punch biopsy usually exposes deeper portions of the corium [836]; [833].

Communication between clinicians and histopathologists is of particular importance in a specimen biopsy. To avoid misdiagnosis and delay in diagnosis, the histopathologist must be informed that a specimen biopsy from a larger tumor is available. The sampling site from the lesion must be precisely indicated (e.g., marginal area, nodular portions, regression zone). The transmission of a clinical image can be helpful here.

8.5.2.2.2. Confirmatory Diagnosis of Basal Cell Carcinoma and Squamous Cell Carcinoma

8.61	Evidence-based Recommendation	modified 2020
GoR **0**	On clinical suspicion of a basal cell carcinoma or a squamous cell carcinoma, the tumour can undergo complete primary excision or a sample biopsy can be taken beforehand.	
LoE **3**	[837]	
	Strong Consensus (100%)	

Depending on the clinical situation, a punch biopsy, a shallow ablation (shave excision), or an excision biopsy may be appropriate in cases of suspected SCC or BCC. The histopathological diagnosis can usually be reliably established from this [837].

8.5.2.3. Histopathological Diagnostics

8.62	Consensus-based Recommendation	checked 2020
EC	Each histopathological report (cf. quality assurance agreement) must contain a description of the microscopic findings and the formulation of a diagnosis. The type of tumour must be stated in accordance with the WHO classification and the histological staging in accordance with the currently valid TNM classification (UICC).	
	Strong Consensus (100%)	

The most important component of every histological report is the correct diagnosis of a tumour including clinical-pathological correlation. In the case of a malignant tumour, the growth pattern, the degree of differentiation and cytomorphological characteristics of a malignant neoplasm must be described. The tumour is to be typed according to WHO. The staging is to be determined according to the valid TNM classification, whereby a grading is given at the same time for squamous cell carcinomas.

When diagnosing a malignant tumour, information on the incision margin must be provided. The lateral and deep incision margins are assessed for the absence or presence of tumour dressings (residual tumour (R) classification).

If applicable and reasonable, a micrometric measurement of the safety distance to the sides and to the depth can be performed. In the S3 guideline “Diagnostics, Therapy, and Follow-up of Melanoma," parameters of the histological report of findings in malignant melanoma were elaborated and consented in chapter 3.2.5 [789].

In the valid AJCC classification of malignant melanoma (8th edition) of 20016/17, the determination of the maximum tumour thickness according to Breslow (measured at the bottom of the stratum corneum to the deepest tumour cell) and an ulceration of the primary tumour (epidermis interrupted by melanoma growth) are included. In contrast to the previous classification, the determination of the Clark level is no longer relevant for the classification. The histopathological findings of malignant melanoma should include the following criteria:

- indication of whether the excision margins are microscopically tumour-free,
- the determination of the maximum tumour thickness according to Breslow (measured from the underside of the stratum corneum to the deepest tumour cell),
- the ulceration of the primary tumour (epidermis interrupted by melanoma growth),
- information on histopathological features such as vascular invasion and on morphological features (e.g. desmoplastic melanoma parts).

In addition to the diagnosis, the histological report should also contain information on risk factors for tumour recurrence or distant metastasis.

In the S3 guideline "Actinic Keratosis and Squamous Cell Carcinoma of the Skin," parameters of the histological report of findings in squamous cell carcinoma were elaborated and consented in chapter 4.6 [384].

The following information should be included:

- histological tumor type (for specific subtypes of SCC).
- description of the histological depth extension in relation to the anatomical stratification (especially from Clark level V, corresponding to infiltration of the subcutis)
- measurement of the depth extension from an invasion depth of 2 mm (corresponds approximately to the diameter of a 10x field of view)
- in case of a positive result, indication of the presence of a perineural spread, a vascular invasion or a slight differentiation
- completeness of resection of the invasive tumor part

In the S2k guideline "Basal Cell Carcinoma," risk factors for a recurrence of the BCC were defined in chapter 5. These are the localization of the BCCC (nose, eyelids and ears), the maximum tumor diameter, whether it is already a recurrence, the histological subtype (especially sclerodermiform), the development on a radioderm, and perineural growth [385].

Further contents of the histopathological findings of a malignant skin tumour within the scope of the SCS 2008 were regulated in the associated quality assurance agreement for the histophathological examination, which are legally binding for the pathologists and dermatohistologists in this context [831]. As stipulated therein, the size of the specimen to be examined and the type of sampling technique are to be documented in the histological findings and/or OP report (Annex 1 of this quality assurance agreement).

8.6. Skin cancer related quality of life

Yvonne de Buhr, Elisa Grossmann & Jessica Achter

A methodical assessment of the quality of life of skin cancer patients to derive targeted interventions to improve the overall situation does not currently take place in the German health care system. There is evidence that interventions can positively influence individual dimensions of quality of life (QoL) [838]; [839].

A generally binding definition of the term “health-related quality of life" (“Health-Related Quality of Life,” HRQoL) does not exist. Here, we adopt an operational definition as a multidimensional construct that incorporates physical, emotional, mental, social, spiritual, and behavioural components of well-being and functioning.

There is a general consensus that health-related quality of life can only be captured in a meaningful way from the subjective perspective of those affected [840].

Quality of life is essentially determined by the presence or absence of problems that are individually experienced as burdensome.

Instruments for assessing quality of life can be divided into cross-disease (generic) and disease-specific procedures. Frequently used instruments to assess the quality of life of skin cancer patients are, for example: “European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30,” “Short Form-36" (SF-36), “Brief Symptom Inventory" (BSI), “Global Quality of Life Scale" (GLQ-8), and “Quality of Well-Being Self-administered Questionnaire" (QWB-SA). Further instruments are the questionnaire for general health-related quality of life for melanoma patients (FACT-M), FACT-BRM for cytokine therapy and FACT-F for “Fatigue,” “State Trait Anxiety Inventory" (STAI), and “Hospital Anxiety and Depression Scale" (HADS) for anxiety and depression as well as the “Cancer Therapy Satisfaction Questionaire" (CTSQ), for the assessment of QoL under therapy.

Influence of Skin Cancer on the Quality of Life of Affected Patients

- **Patients with advanced melanoma (stages III and IV) suffer from severe psychological distress.**

The systematic review by Dunn et al. [841]

examined quantitative and qualitative psychological outcomes in patients with advanced melanoma (stage III/IV). The literature search was conducted in five databases (Medline, PsycINFO, Ovid, CINAHL, ScienceDirect) for articles from January 1980 to January 2016. Fifty-two English-language articles were included, of which 48 were quantitative and four were qualitative.

The qualitative studies reported the psychological distress of patients due to the uncertain future, the inability to make long-term plans, which causes a sense of loss of control, anxiety, and frustration and hopelessness, especially in stage III patients. In 75% of patients this leads to emotional distress, in half to panic, despair, and a sense of shock, and in 25% there is a sense of injustice.

Patients who relapsed were less likely to feel the shock, but found the check-ups frightening, reminding them of their mortality, and reported anger and resentment (one article).

In quantitative studies, 20-28% of patients had clinical anxiety (score according to HADS) and 16-19% had clinical depression (two articles). Approximately half of stage III and 56-58% of stage IV patients are considered highly or seriously stressed (two articles).

Two articles identified significantly lower emotional functioning of stage IV compared with stage III patients and of patients in whom the lymph glands are affected compared with others (one article) [841].

- **Melanoma patients with lymphedema have lower health-related quality of life than patients without lymphedema.**

A Danish cross-sectional study [842]

examined the HRQoL of 431 patients with melanoma of the extremities at Herlev Gentofte Hospital between January 1997 to February 2015 using standardized assessment tools.

Melanoma patients with lymphedema (n=109) showed significantly lower HRQoL than patients without lymphedema. This was particularly true for the subscales general health/quality of life (OR=1.7; 95% CI: 1.1-2.5; p= 0.008), role function (OR=2.8; 95% CI:1.7-4.4; p<0.0001), social function (OR=2.2; 95% CI: 1.2-3.8; p=0.006), fatigue (OR=0.5; 95% CI: 0.3-0.7; p=0.0005), pain (OR=0.6; 95% CI: 0.4-0.9; p=0.01), and body image (OR=0.4; 95% CI: 0.2-0.6; p<0.0001).

When stratified by age and gender, younger patients with lymphedema are more likely to experience financial difficulties, younger patients and women with lymphedema report poorer social function, and women report poorer body image. When stratified by affected limb, type of treatment, clinical stage, and duration of lymphedema, no statistically significant differences were seen [842].

- **Non-melanocytic skin cancer has a rather small impact on the quality of life of the majority of affected individuals.**

A systematic review by Waalboer-Spuij and Nijsten [843]

investigated HRQoL in patients with skin malignancies using a search in Embase, MEDLINE OvidSP, PubMed publisher, and Chochrane Central. The aim was to identify relevant quality of life problems and to summarize the instruments used for the study in patients with keratinocytic carcinoma.

A study regarding the impact of BCC on quality of life showed little impact with only a small difference before and after therapy. Measurements were made using the UK Sickness Impact Profile (UKSIP), a measure of general health status, and the Dermatology Life Quality Index (DLQI), a dermatology-specific questionnaire. In this study, the authors found very low scores, including a small impact on quality of life, with only a minimal increase one week after therapy. This leads to the preliminary conclusion that BCCs cause little impairment.

Another study focused on distress and coping strategies using the HADS and the Ways of Coping – Cancer Version (WOC-CA) questionnaire. Nineteen percent of patients with non-melanoma skin cancer experienced significant levels of distress (HADS score > 13).

In a cross-sectional study of 52 German patients diagnosed with actinic keratosis, BCC, and SCC, the majority reported no to low levels of quality of life impairment

using the DLQI. One third of the patients reported moderate to great impairments, especially in the subscales “symptoms and feelings,” “leisure time," and “daily activities.”

In a prospective US cohort study, FCK were associated with low DLQI scores, indicative of low quality of life impairments. Four months after initiation of therapy, only items focusing on physical improvement and embarrassment decreased significantly [843].

- **The more severe the actinic damage to the skin, the worse the health-related quality of life was rated by those affected**.

Part of the observational cross-sectional study in a multicenter setting by Tennvall et al. [844]

was an analysis of HRQoL of patients with different severities of actinic keratosis (AK), using general and disease-specific measurement tools. Included patients were a total of 312 AK patients attending a dermatology clinic in Denmark. Eighty-nine percent of the patients had current AK lesions, and the remaining 35% had follow-up appointments for previous AKs. Patients completed the Actinic Keratosis Quality of Life Questionnaire (AKQoL), the DLQI, and the EQ-5D-5L (included EQ-VAS) after prior physician grading of disease severity.

Patients reported impairment in HRQoL on the AKQoL. The mean score on the AKQoL for the 286 patients who completed the questionnaire was 6.7 (scale: 0-27). Respondents with severe actinic damage had a worse HRQoL (10.07) than those without severe actinic damage (6.3) ($p<0.001$). Women reported a higher AKQoL score (7.9) than men (5.3) ($p<0.001$), with a higher AKQoL score here representing a lower quality of life. Participants under 60 years of age reported a worse HRQoL (8.1) than older subjects (5.0-7.3) ($p=0.004$) [844].

The mean score of those who completed the DLQI questionnaire (n=209) was 1.99 (scale 0-30). Patients with severe actinic damage had a higher DLQI score (4.6) than patients with mild AK (1.7) ($p<0.001$), with a higher DLQI score corresponding to a lower quality of life. Respondents with current AK had a higher DLQI (2.1) than respondents without current AK lesions (0.9) ($p=0.009$). Patients who already had squamous cell carcinoma (SCC) scored higher DLQI (3.4) than those who did not have squamous cell carcinoma (1.7) ($p=0.016$). Respondents who were treated with immunosuppressants had a higher DLQI score (4) than respondents without this treatment (1.9) ($p=0.023$). The DLQI categories in which most impairment was perceived were "symptoms and feelings" (37%) and "daily activities" (25%) [844].

Two hundred seventy-six patients completed the EQ-5D-5L questionnaire and formed a mean score of 0.88 (scale 0-1). Patients with comorbidities reported lower HRQoL (0.86) than those without comorbidities (0.93) ($p<0.001$). Respondents with squamous cell carcinoma (SCC) had a lower HRQoL (0.85) than respondents without prior SCC (0.89) ($p=0.038$). Patients reported most problems in the domain of pain/discomfort (38%) [844].

9. Health Economic Evaluation

9.1. Health Economic Evaluations of Measures for the Primary Prevention of Skin Cancer

9.1.1. Effect Measures of Primary Prevention Measures of Skin Cancer

Ulrike Helbig

Various effect measures and calculation tools are used in the literature. They are listed here to illustrate the common practice and to approach the question of cost-effectiveness analysis and cost-utility analysis in the health care sector.

Table 30: Effect measures and calculation tool of preventive measures

Effect measures:
Disability adjusted life-years/Health adjusted life-years/ quality-adjusted life-years
Life-years gained through death averted (death averted life-years saved)
Prevented deaths/deaths averted
Preventable skin cancer incidences/cases prevented
ROI (Return on Investment)
Indirect productivity costs (Years of potential life lost)
Government cost savings (net benefits and cost effectiveness)/Major economic burden (cost of medical care/lost productivity)
Total economic loss over the lifetime of the individuals effected
Calculation tools:
Markov model
Univariate and multivariate (probabilistic) sensitivity analysis.
Cost-effectiveness analysis
Standard cost/profit and standard cost/effectiveness
Incremental cost per quality-adjusted life-year (QALY)

Effect measures:
Annual medical cost on a per case basis
Total medical care
Population Attributable Risk (PAR)

9.1.2. Health Economic Evaluations of Primary Preventive Measures for Tanning Bed Use

Inga-Marie Hübner and Jessica Achter

- Model calculations based on international data and a retrospective cost-of-illness study indicate an economic benefit/cost-effectiveness of reducing tanning bed use

9.1	Consensus-based Recommendation	new 2020
EC	The less sunbeds are used, the fewer sunbed-induced illness costs arise; therefore, the use of sunbeds must be avoided.	
	Strong Consensus (100%)	

The study by Guy et al. [845]investigated the impact of a reduction in tanning bed use in the USA on melanoma prevention and treatment costs. The estimates were made using a Markov model. A cohort of 61.2 million individuals aged 14 years or younger was studied at annual intervals over their lifetime. Five different scenarios were examined: restricting tanning bed use among minors and reducing use by 20%, 50%, 80% and 100%. Compared to the no age restriction case, banning tanning bed use for minors was estimated to prevent 61,839 melanoma cases (4.9% reduction) and 6,738 melanoma deaths (4.7% reduction).This would result in a gain of 142,659 life years and elimination of treatment costs over the lifetime of the 61.2 million adolescents aged 14 years or younger of approximately $ 342.9 million. The estimated health and economic benefits increase with greater reductions in the prevalence of tanning bed use, according to the model. For a 20% reduction in prevalence compared to 100%, the estimated number of melanoma cases prevented increases from 40,410 to 202,662, as does the estimated number of melanoma deaths prevented from 4,286 to 23,266. In addition, the number of life years gained increases from 91,229 to 458,592 and the therapy costs saved increases from $ 219 million to $ 1.1 billion over the lifetime of the cohort.

Hirst et al. [846] provide a prediction of preventable skin cancer cases and associated cost savings to the government associated with regulation of the tanning industry in Australia. For this purpose, a Markov model was set up in order to map the future costs and health effects of sunbed use at the current standard compared with the enforcement of regulations. Regulations are understood here as a ban on sunbed use for minors and for people with very light skin. The Markov model used comprises a hypothetical cohort of 100,000 individuals aged 15 years who go through various

cycles until they reach the age of 85 years.Health effects were measured using the number of new melanoma and squamous cell carcinoma cases and life years gained. With stricter regulations, it is estimated that between 18 and 31 melanomas, 200 to 251 squamous cell carcinomas, and associated costs of $ 256,054 per 100,000 people could be prevented. This would result in the prevention of melanoma deaths with a gain of 31 life years.

Waters and Adamson [847] studied the health and economic consequences of using tanning devices. To do this, they estimated the number of health problems associated with tanning device exposure in the United States and calculated the cost of medical care in the form of therapy. The major unit of analysis for the study represented the number of individuals living in the US who sought therapy for BCC, SCC, or melanoma. To estimate the percentage of these cases attributable to tanning device exposure, a population-attributed risk (PAR) was calculated for each disease. YPLL (years of potential life lost) was also used to calculate annual medical costs on a per case basis and indirect productivity costs. The analysis shows that in 2015, there were 8,947 incidences of melanoma in the US, including 5,176 invasive and 3,771 in situ, as well as more than 86, 600 cases of SCC and 168,000 cases of BCC attributable to tanning device exposure. The cost of indirect medical care for these cases is $ 343.1 million annually and will result in an economic loss of $ 127.3 billion over the lifetime of the affected individuals. In summary, the use of tanning devices represents a significant contribution to disease and premature mortality in the United States. Furthermore, use represents a significant economic burden in terms of medical care costs and lost productivity. the use of tanning devices represents a significant contribution to disease and premature mortality in the United States. Furthermore, use represents a significant economic burden in terms of medical care costs and lost productivity. the use of tanning devices represents a significant contribution to disease and premature mortality in the United States. Furthermore, use represents a significant economic burden in terms of medical care costs and lost productivity.

In a retrospective cost-of-illness study, Pil et al. [848][848] used a Markov model to analyze the current and future economic burden of skin cancer in Belgium and the cost-effectiveness of primary prevention of skin cancer. The health-related burden of skin cancer was estimated based on the registered prevalence of skin cancer lesions in therapy or follow-up. To estimate the total economic burden of skin cancer on the population, retrospective data in the form of questionnaires completed by patients between March and June 2015 were used. A total of 287 patient-completed questionnaires were included. The median age of the participants was between 61 and 70 years. Based on the questionnaires, costs per skin cancer type were calculated for six months each, separately for the diagnosis and treatment, intensive follow-up, and long-term follow-up phases. In order to calculate the future health and economic costs of skin cancer, a Markov model with a time horizon of 20 years was set up. Costs were expressed separately as costs to the health care payer, costs to the patient, and costs due to productivity losses. The total economic cost of skin cancer in 2014 in Belgium was estimated at 106 million euros. The total cumulative costs over a 20-year period were estimated at 3.2 billion euros and over 50 years at 8 billion euros. The Markov model simulation over 50 years showed that of the 8 billion euros, 238 million euros (2.9%) could be saved by a complete ban on sunbeds. Furthermore, the budget impact analysis showed that each euro invested in an awareness campaign would save the health care payer 3.6 euros in the long run. After a period of 50 years, a ban on sunbeds would lead to a reduction in prevalence of 8.6% (absolute number: 9,491 in men and 11,335 in women). Banning the use of sunbeds would further lead to a reduction in the prevalence of squamous cell carcinoma by 22.7% (absolute

number: 35,934 in men and 52,565 in women). By reducing the prevalence of squamous cell carcinomas and ma-lign melanomas, fewer tumors would subsequently develop to later stages, and therefore a reduction in skin cancer mortality can be expected. In the model, over a 50-year period, 3,927 deaths (1,602 men and 2,329 women) were predicted to be prevented by banning the use of public tanning beds. 934 in men and 52,565 in women). By reducing the prevalence of squamous cell carcinomas and ma-lign melanomas, fewer tumors would subsequently develop to later stages, and therefore a reduction in skin cancer mortality can be expected. In the model, over a 50-year period, 3,927 deaths (1,602 men and 2,329 women) were predicted to be prevented by banning the use of public tanning beds. 934 in men and 52,565 in women). By reducing the prevalence of squamous cell carcinomas and malign melanomas, fewer tumors would subsequently develop to later stages, and therefore a reduction in skin cancer mortality can be expected. In the model, over a 50-year period, 3,927 deaths (1,602 men and 2,329 women) were predicted to be prevented by banning the use of public tanning beds.

9.1.3. Health Economic Evaluations of Population-Based Primary Prevention Interventions

Inga-Marie Hübner and Jessica Achter

- Economic evaluations of international population-based primary skin cancer prevention interventions demonstrate economic benefit/cost effectiveness.

9.2	Consensus-based Recommendation	new 2020
EC	Various measures of primary skin cancer prevention show both an economic benefit and a health-related benefit. Therefore, investments in such measures should be increased.	
	Strong Consensus (100%)	

Kyle et al. [849] provide an economic evaluation of the United States Environmental Protection Agency's so-called SunWise program. The SunWise program is a school-based teaching program for children with the goal of teaching children how to protect themselves from overexposure to the sun. The students are each given a type of test before as well as a while after the teaching sessions, regarding the students' knowledge, attitude, use as well as intended use. The purpose of the study was to assess the health benefits of the programme by means of an economic analysis in order to determine the net benefits and cost-effectiveness in a next step and to compare these data with a control group. Health outcomes were measured as number of skin cancer cases and prevention of premature mortality and QALYs saved over the 17-year course of the program. Prevented costs are measured as direct medical costs and prevented costs of lost productivity resulting from the SunWise program. Net benefits are the difference between prevented costs and program costs. The economic analysis indicates that the SunWise program should prevent more than 50 premature deaths, approximately 11,000 skin cancer cases, and 960 QALYs (undiscounted) among participants if current U.S. government financial support continues. For every dollar invested in the SunWise program, between $1.95 and $4.02, concerning medical care costs and lost productivity, are saved, according to the analysis.

Shih et al. [850] provide with their study an economic evaluation of skin cancer prevention measures in Australia. The cost-effectiveness of the SunSmart skin cancer prevention program since its inception was assessed along with its potential cost-effectiveness as an improved and ongoing national program. The primary endpoint was the reduction in melanoma incidence attributable to the SunSmart program. A utility analysis was used in which costs are expressed as dollars and outcomes are expressed as DALYs (disability-adjusted life-years). DALYs are used to ensure comparability with outcomes from a larger Australian research concerning 100 different prevention programs. This study uses data from three states, Victoria, New South Wales, and Queensland, to assess program effectiveness. These three states are representative of three latitude zones with different UV exposures. Melanoma incidence rates from the states are used to model key health outcomes. Because of the SunSmart program, more than 103,000 skin cancer cases were prevented in Victoria between 1988 and 2003, including 9,000 melanomas and 94,000 white skin cancer cases. Furthermore, more than 1,000 deaths were prevented, which equated to 28,000 DALYs and 22,000 life years. Investment in the SunSmart program in the past yielded 3.6 Australian dollars per dollar invested with an assumed reduction rate of 10% per year for white skin cancer. A retrofitted national program is estimated to prevent 120,000 DALYs over the next 20 years with associated reductions in health service resource use.

A further study by Shih et al. [851], building on the 2009 study, looked at the economic evaluation of future skin cancer prevention in Australia. The aim of the study was to update and expand the economic references for skin cancer prevention. Economic evaluations were conducted in 2015 using a range of methods applied, including a cost-effectiveness analysis and a cost-benefit analysis, as well as different study perspectives and a counterfactual analysis related to cancer incidence between the years 1982 and 2011. Modeled outcomes include "cases prevented," "deaths prevented," and "health-adjusted life-years (HALYs)." The analysis finds that implementing interventions in the form of a coordinated set of skin cancer prevention interventions over a 20-year period (2011 to 2030) would incur an additional program cost of $ 63 million Australian dollars to the government, but would also deliver a range of health, financial and economic gains for Australia. The projected health gains include 140,000 cases of skin cancer prevented at an additional per capita investment in future skin cancer prevention of 0.16 Australian dollars, the prevention of 6,200 premature deaths, and 111,000 life years gained and 92,600 health-corrected life years. The financial gains include health sector cost savings of over 200 million Australian dollars and productivity gains in the economy of 2, 269 million in the human capital approach or 221 million Australian dollars in the friction cost approach. Depending on the study perspective and methodology, the improved program (see Shih et al. 2009 study) turns out to be either dominant or highly cost-effective. Dominant in this sense refers to both the achievement of health gains and cost savings. The program is considered cost-effective if health gains are achieved at a moderate net cost. The return on investment (ROI) according to the analysis is 3.2 Australian dollars per dollar invested by the government in the program (present value, 3% discount rate), with a net societal benefit of 1.43 trillion Australian dollars. Dominant in this sense refers to both the achievement of health gains and cost savings. The program is considered cost-effective if health gains are achieved at a moderate net cost. The return on investment (ROI) according to the analysis is 3.2 Australian dollars per dollar invested by the government in the program (present value, 3% discount rate), with a net societal benefit of 1.43 trillion Australian dollars. Dominant in this sense refers to both the achievement of health gains and cost savings. The program is considered cost-effective if health gains are achieved at a moderate net cost. The return on investment

(ROI) according to the analysis is 3.2 Australian dollars per dollar invested by the government in the program (present value, 3% discount rate), with a net societal benefit of 1.43 trillion Australian dollars.

In the retrospective cost-of-illness study by Pil et al. (2016) mentioned earlier, additional analyzes were conducted related to an awareness campaign. The Markov model simulation over 50 years showed that of the 8 billion Euros, 228 million (2.8%) could be saved through an awareness campaign. Furthermore, the budget impact analysis showed that each euro invested in an awareness campaign would save the health care payer 3.6 euros in the long run. After a period of 50 years, according to the analysis, the awareness campaign would lead to a reduction in the prevalence of diagnosed malignant melanoma stage I of 11.3% (absolute number: 10,954 in men and 15,053 in women). The model predicted over a 50-year period that 3,991 deaths (1,593 men and 2,398 women) would be prevented using an annual awareness campaign.

The systematic review by Gordon and Rowell [852] includes a total of 16 studies reporting national estimates of the costs of skin cancer and 11 studies reporting the cost-effectiveness of skin cancer prevention or screening. Studies were included through August 2013 via the Medline, Cochrane Library, and National Health Service Economic Evaluation Database programs. The focus here is on skin cancer as defined by MM, BCC and SCC. Depending on the size of the population considered, the annual direct health system costs of skin cancer are highest in Australia, New Zealand, Sweden and Denmark. Skin cancer prevention initiatives were found to be highly cost-effective and could also save costs. Programmes to screen for melanoma in high-risk individuals, such as older men or individuals with a family history of melanoma, may also be cost-effective. However, further analysis is needed to confirm these observations. Furthermore, a significant cost burden of skin cancer exists in many of the countries analyzed. Health care expenditures for skin cancer will increase in the future as a result of an increase in the incidence of skin cancer. Public investment in skin cancer prevention and screening programmes shows great potential for health and economic benefits.

9.1.4. Health Economic Evaluations of Specific Primary Prevention Measures

Inga-Marie Huebner and Jessica Achter

Gordon et al. [853]

analyzed in their study the cost-effectiveness of an intervention with the aim to encourage men over 50 years of age to self-examine their skin in order to detect skin cancer at an early stage. The cost-effectiveness analysis was conducted using data from a skin awareness study and data obtained from a review of literature. A lifetime Markov model was constructed to combine these data. In the skin awareness study, a total of 929 participants were randomly assigned to either the intervention or control group. The intervention group received a DVD on skin self-examination and the importance of seeking medical attention for suspicious lesions. In addition, participants received reminders to watch the DVD, a graphic representation of the body to note possible locations of skin lesions, and a brochure on the differentiation between benign and malignant skin lesions. Participants in the control group received only the brochure. All participants completed an assessment at baseline and at six and twelve months. The primary outcomes represented self-examinations of the skin, clinical examinations of the skin by a physician, self-efficacy, and perceived social support. For

a cohort of older men over their remaining lifetime, the average cost per person of a screening intervention for skin cancer was $ 5,298 Australian compared with $ 4,684 Australian for usual care, according to the analysis. The corresponding average QALY was 7.58 for the intervention group and 7.77 for the control group. Consequently, as the intervention involved higher costs and lower health gains in terms of QALYs compared with usual care, usual care dominates the intervention in this case. When considering the gains in terms of survival, the model predicted a cost of 1,059 Australian dollars per life year saved. The probability that the intervention was cost-effective at up to 50,000 Australian dollars gained per QALY was 43.9%. In conclusion, although the intervention improved participant behavior regarding skin self-examination, which spurred men to seek medical attention for abnormal lesions, the overall costs and effects of a higher detection rate of SCC, BCC, and benign lesions outweighed the positive health gains from detecting more thin melanomas. 000 Australian dollars gained per QALY was 43.9%. In conclusion, although the intervention improved participant behavior regarding skin self-examination, which spurred men to seek medical attention for abnormal lesions, the overall costs and effects of a higher detection rate of SCC, BCC, and benign lesions outweighed the positive health gains from detecting more thin melanomas. 000 Australian dollars gained per QALY was 43.9%. In conclusion, although the intervention improved participant behavior regarding skin self-examination, which spurred men to seek medical attention for abnormal lesions, the overall costs and effects of a higher detection rate of SCC, BCC, and benign lesions outweighed the positive health gains from detecting more thin melanomas.

Hirst et al. [854] examined the lifetime cost-effectiveness of skin cancer prevention by promoting daily sunscreen use. A Markov model was used to integrate data from a community-based randomized controlled trial conducted in Australia, as well as other epidemiological and published sources. In the controlled trial, a total of 1,621 residents from Nambour in Queensland were randomly assigned to either the sunscreen intervention group or a control group. The intervention group was encouraged to apply sunscreen with SPF 15+ to their face, neck, arms, and hands every morning. Furthermore, they were given one or more bottles of sunscreen as needed. Participants in the control group, on the other hand, were instructed to use the sunscreen at their discretion. The primary outcome of the study represented the incremental cost per QALY. The discounted incremental benefit per QALY gained of the sunscreen intervention was 40,890 Australian dollars. Over the projected lifetime of the intervention cohort, this would prevent a total of 33 melanomas, 168 squamous cell carcinomas, and four melanoma deaths at an incurred cost of approximately 808,000 Australian dollars. The probability that the sunscreen intervention was cost-effective was 64% at a willingness-to-pay threshold of 50,000 Australian dollars per QALY gained.

Research Needed

The studies presented here demonstrate the high (economic) benefits of primary prevention interventions. As these are exclusively international studies, a clear need for research can be formulated for cost-benefit analyses of primary prevention measures specific to Germany. However, the challenge here is that the interventions currently implemented mostly aim to change endpoints that can be measured in the short term (such as a change in behaviour or an increase in knowledge, cf. Chapter 5) and therefore the possibilities for using relevant effect measures of economic evaluations (see above) are limited. The discussion on the integration of health economic issues in practice projects should therefore be advanced in the future.

9.2. Health Economic Evaluation of Measures of Secondary Prevention of Skin Cancer

Uwe Siebert, Igor Stojkov, Ursula Rochau

As part of the development of the S3 guideline, a systematic literature search was conducted on cost-effectiveness analyses for secondary prevention of skin cancer, including skin cancer screening.

The literature search was conducted using the PubMed search interface in the electronic databases MEDLINE and PubMed Central (PMS) up to and including October 2019. No restrictions were placed on the start date of the search period, geographic region of study, or language. The search of the electronic literature databases was supplemented by a manual search based on the references of the identified studies and by an internet search.

All publications that reported results on cost-effectiveness analyses were included. Both original studies and reviews were included. Studies that did not report a relationship between benefits and costs, pure risk factor studies, studies on primary or tertiary prevention measures, diagnostic studies, prognostic studies, therapy studies, as well as studies without reference to one of the relevant skin cancer types were excluded. The results of identified systematic reviews with comprehensive search strategies were used (a) to support the selection of further studies to include and (b) to extract results directly from these reviews.

Using an a priori extraction form, information on the following characteristics of the publications was extracted and documented:

Reference of publication, country, tumour type, target population, setting, screening strategies compared, study type of cost-effectiveness analysis, use and type of decision analytic model (with simulation method, perspective, analytic time horizon, outcomes, effectiveness, costs, incremental cost-effectiveness ratio). Incremental cost-effectiveness ratio is defined as incremental costs divided by incremental benefits.

The results were summarized in standardized form in systematic evidence tables.

9.3	Evidence-based Statement	new 2020
LoE **n.a.**	Various measures of skin cancer screening can be classified as cost-effective based on international evidence. Screening of high-risk individuals has a more favourable cost-effectiveness ratio than population-based screening.	
	[848]; [855]; [856]; [857]; [858]; [859]; [860]; [861]; [862]	
	Strong Consensus (97%)	

The systematic search identified a total of five reviews and 411 original studies. Four reviews were excluded due to lack of information on cost-effectiveness. One review by Gordon et al. [852][852], which included a systematic search up to September 2013, was included. All studies included by Gordon et al. and all original studies published after September 2013 (186 studies) were reviewed against the inclusion criteria. A total of nine original studies with cost-effectiveness analyses of secondary

prevention interventions were included, these were all studies of the cost-effectiveness of screnning programmes (see guideline report). The systematic evidence tables summarising the study characteristics and results of the cost-effectiveness analyses are presented in the guideline report. All included studies were published in English.

Five of the included studies were conducted in the USA, two in Australia, one in Belgium and one in the UK. Seven studies focused on malignant melanoma, one on BCC/SCC and one included all skin cancers. The type of screening strategies and the comparative strategies differed between the studies. Seven studies included prior risk stratification, of which five were based on family or personal history and two on a prior diagnosis of inflammatory bowel disease. The remaining studies evaluated screening in the general population.

All studies were conducted from a health system perspective. Six studies evaluated a lifetime time horizon and three studies used a shorter time horizon. Six studies used a cohort state transition model, two studies implemented a decision tree model, and one study implemented a discrete event simulation model.

Seven studies showed health-related benefits in terms of quality-adjusted life years (QALY). Six studies reported an incremental cost-effectiveness ratio below US$50,000 per QALY gained and one study of US$140,000 per QALY gained. The other two studies evaluated life years gained (GLJ), of which one study reported an incremental cost-effectiveness ratio above US$50,000 per GLJ gained.

Limitations

A limitation is the lack of studies for the context of the German health care system. The cost-effectiveness of skin cancer screening depends, among other factors, on the cost of screening, testing, and follow-up therapies, the prevalence and incidence of skin cancer, and the potential participation rate in Germany. For this reason, results from other countries are not directly transferable.

One of the most important limitations in the evidence-based assessment of the cost-effectiveness of skin cancer screening is therefore the lack of cost-effectiveness analyses specific to the context of the German health care system. In order to provide comprehensive decision support regarding the short- and long-term consequences, the development of a decision analytic model (e.g. Markov state-transition model) for the specific context is necessary, in which the relevant and currently available evidence on epidemiological and clinical parameters, patient-relevant benefits and harms, as well as resource use and costs, are combined [863], [864]; [865]. The use of systematic decision analyses to support the development of S3 guidelines in the context of the German health care system was already recommended in 2001 as a specific component of the S3 level [867]; [866]. German institutions involved in health technology assessments also recommend the use of decision analytic models for conducting cost-benefit assessments [869]; [868]. In the context of S3 guideline development, decision analytic models have been used, for example, for the S3 guideline "Prevention of Cervical Cancer" to evaluate long-term benefits, harms and cost-effectiveness of different cervical cancer screening strategies.

Research needs

In the field of skin cancer screening, future research needs include the development of a decision analytic model and the implementation of a systematic evidence-based decision analysis with a sufficiently long time horizon to assess and weigh the short-

and long-term benefit and harm outcomes, as well as the cost-effectiveness of the different screening alternatives in the context of the German health care system, so that this evidence gap can be closed.

10. Documentation of changes from version 1.2 to version 2.1

Table 31: Dokumentation der Änderungen von Version 1.2 zu Version 2.1

Version 1.2	Version 2.1	Kommentare
	3. Concepts of Prevention	
3. Status quo of skin cancer	**4. Status Quo Skin Cancer**	
3.1. The aetiology of skin cancer	**4.1. The Etiology of Skin Cancer**	
3.1. Consensus-based statement On the basis of current knowledge, ultraviolet (UV) radiation is considered to be the most significant risk factor in the aetiology of skin cancer, even if not all details of the induction, promotion and progression of skin cancer in humans have been elucidated.	4.1. Consensus-based statement On the basis of current knowledge, ultraviolet (UV) radiation is considered to be the most significant risk factor in the etiology of skin cancer, even if not all details of the induction, promotion and progression of skin cancer in humans have been elucidated.	Checked 2020
3.2. Incidence and prevalence of skin cancer	4.2. Incidence, Prevalence, and Mortality of Skin Cancer	
	4.2. Consensus-based recommendation In the clinical cancer registries, basal cell carcinomas (including multiple basal cell carcinomas occurring in one person) and squamous cell carcinomas should be included in the registration.	New 2020

Version 1.2	Version 2.1	Kommentare
3.4. Risk factors of skin cancer	**4.3. Risk Factors of Skin Cancer**	
3.2. Consensus-based statement Constitutional risk factors: Non-melanocytic skin cancer (NMSC) An important constitutional risk factor for NMSC (basal cell carcinoma and squamous cell carcinoma) is skin type. All other risk factors can be acquired during the course of life.	4.3. Consensus-based statement Constitutional risk factors: Non-melanocytic skin cancer (NMSC) An important constitutional risk factor for non-melanocytic skin cancer (basal cell carcinoma and squamous cell carcinoma) is: skin type. Other risk factors (see 4.3.2, 4.3.4) can be acquired during the course of life.	Modified 2020
3.3. Consensus-based statement Constitutional risk factors: Malignant melanoma (MM) The class of constitutional risk factors for MM includes a) skin type and b) (large) congenital naevus. All other risk factors can be acquired during the course of life.	4.4. Consensus-based statement Constitutional risk factors: Malignant melanoma (MM) The class of constitutional risk factors for MM includes a) skin type and b) large congenital naevus. Other risk factors (see sections 4.3.2, 4.3.4, and 5.1) can be acquired during the course of life.	Checked 2020

Version 1.2	Version 2.1	Kommentare
3.4. Consensus-based statement Acquired risk factors: Non-melanocytic skin cancer (NMSC) The main acquired risk factors for NMSC (basal cell carcinoma and squamous cell carcinoma) are: a) actinic keratosis, b) previous history of NMSC, c) immunosuppression, d) chronic radiation keratoses.	4.5. Consensus-based statement Acquired risk factors: Non-melanocytic skin cancer (NMSC) The main acquired risk factors for non-melanocytic skin cancer (basal cell carcinoma and squamous cell carcinoma) are: a) actinic keratosis, b) previous history of NMSC, c) immunosuppression, d) chronic radiation keratoses.	Checked 2020
3.5. Consensus-based statement Acquired risk factors: Malignant melanoma (MM) The main acquired risk factors for MM are: a) previous history of melanoma, b) family history of melanoma, c) number of acquired naevi, d) clinically atypical moles.	4.6. Consensus-based statement Acquired risk factors: Malignant melanoma (MM) The main acquired risk factors for malignant melanoma are: a) previous history of melanoma, b) family history of melanoma, c) number of acquired naevi, d) clinically atypical naevi.	Checked 2020

Version 1.2	Version 2.1	Kommentare
3.6. Consensus-based statement The probability of developing a squamous cell carcinoma is correlated with the UV dose to which a person is exposed during their life (cumulative dose). For basal cell carcinoma, the cumulative UV exposure appears to be of secondary importance. Intermittent UV exposure and sunburn are important in the case of BCC. For malignant melanoma, intermittent UV exposure and sunburn (at any age) are of major importance.	-	Deletion and inclusion in the background text
3.7. Consensus-based statement Other risk factors that are described for non-melanocytic skin cancer are exposure to arsenic or tar, particularly in the work environment. HPV infections are discussed both as a risk factor for skin cancer in their own right and as a cofactor in combination with ultraviolet (UV) radiation.	4.7. Consensus-based statement Other risk factors that are described for non-melanocytic skin cancer are exposure to arsenic or tar, particularly in the work environment. HPV infections are discussed both as a sole risk factor for skin cancer and as a cofactor in combination with ultraviolet (UV) radiation.	Checked 2020

3.8. Consensus-based statement

Values for relative risks (RR) or lifetime risks are given in the literature in various studies for the constitutional risk factors described. Examples of such values are listed below for non-melanocytic skin cancer:

Risk factor	**RR (95 % CI)**
Skin type I vs. IV (BCC)	5.1 (1.4-11.3)
Skin type II vs. IV (BCC)	5.3 (1.7-10.6)
Skin type I vs. IV (SCC)	1.4 (0.5-3.0)
Skin type II vs. IV (SCC)	2.2 (0.7-3.8)

Sources: [21, 213]

The presence of multiple actinic keratoses over a 10-year period is reported as being associated with a lifetime risk for the development of a squamous cell carcinoma (SCC) in the region of 6-10%.

With a personal history of SCC, the risk of developing another SCC within 5 years is 30% and of developing a basal cell carcinoma (BCC) about 40%.

With a personal history of BCC, the risk of developing another BCC within 3 years is 44% and of developing an SCC about 6%.

SCC occurs up to 65 times more frequently in immunosuppressed transplant patients than in controls. Immunosuppressed transplant patients develop more SCC than BCC (4:1).

-

Deletion and inclusion in the background text

3.9. Consensus-based statement

Values for relative risks (RR) or lifetime risks are given in the literature in various studies for the constitutional risk factors described. Examples of such values are listed below for malignant melanoma:

Risk factor	**RR (95 % CI)**
Number of acquired naevi (100-120 vs. < 15)	6.89 (4.63-10.25)
Skin type (I vs. IV)	2.09 (1.67-2.85)
Family history of melanoma (yes vs. no)	1.74 (1.41-2.14)
Number of atypical naevi (5 vs. 0)	6.36 (3.80-10.33)
Personal history of melanoma (yes vs. no)	8.5 (5.8-12.2)

-

Deletion and inclusion in the background text

Sources: [214, 247, 249]

Congenital naevi with a diameter of > 10 to 20 cm are known as “large congenital naevi”. They are associated with a risk of approximately 2 10% of developing a melanoma during the course of life.

Version 1.2	Version 2.1	Kommentare
3.10. Consensus-based statement The relative risks (RR) for the development of different skin cancer entities (basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and malignant melanoma (MM)) depend on the UV exposure pattern. BCC does not depend on the cumulative UV dose (RR = 0.98, 95% CI 0.68 1.41), whereas SCC is more strongly dependent on the cumulative dose (RR = 1.53, 95% CI 1.02 2.23). MM is intermediate between the two in relation to the cumulative dose (RR = 1.2, 95% CI 1.00 1.44). For MM, however, there is an increased risk from intermittent UV exposure (RR = 1.71, 95% CI 1.54 1.90) or from sunburn at any age (RR = 1.91, 95% CI 1.69 2.17) [20].	-	Deletion and inclusion in the background text
3.11. Consensus-based statement The relative life risk (RR) for a malignant melanoma is RR = 1.75 (95% CI: 1.35 2.26) if solariums are used regularly (at least once a month) before the age of 35 [290].	-	Deletion and inclusion in the background text
	4.4 Importance of Biomarkers for Primary and Secondary Prevention of Skin Cancer	
4. Primary prevention	**5. Primary Prevention**	
4.1. Individual behaviours	**5.1. Individual Behaviours**	

Version 1.2	Version 2.1	Kommentare
4.1. Consensus-based recommendation Protective measures against solar ultraviolet radiation must be applied in the following order: avoidance of exposure to strong solar radiation, wearing suitable clothing, using sunscreens.	5.1. Consensus-based recommendation Protective measures against solar ultraviolet radiation is particularly important for persons at increased risk and must be applied in the following order: avoidance of exposure to strong solar radiation, wearing suitable clothing, using sunscreens.	Modified 2020

Version 1.2	Version 2.1	Kommentare
4.2. Consensus-based recommendation The following measures must be taken to avoid exposure to strong solar radiation in the relevant weather conditions: remain outside as little as possible, avoid staying outside in the middle of the day, the length of time in the sun should not exceed the individual intrinsic protection time of the skin, seek shade, undertake outdoor activities in the morning and evening hours, accustom the skin slowly to the sun (e.g. in spring / on holiday), avoid sunburn at all events.	5.2. Consensus-based recommendation The following measures must be taken to avoid exposure to strong solar radiation (taking into account the type of skin): At medium and high UV irradiance (UVI 3-7), seek shade during midday, In the case of very high UV irradiance (UV index 8 and higher), avoid going outdoors during the midday period if possible. If this is not possible, seek shade, If necessary, postpone outdoor activities to the morning and evening hours, **Avoid sunburn.**	Modified 2020
4.3. Consensus-based recommendation When staying outside in the sun, suitable clothing, headwear and sunglasses should be worn for protection.	5.3. Consensus-based recommendation When staying outside in the sun, suitable clothing, headwear and sunglasses should be worn for protection.	Checked 2020

Version 1.2	Version 2.1	Kommentare
4.4. Consensus-based recommendation Suitable sunglasses must be worn in strong sunlight. Never look directly at the sun in the sky. This applies even when wearing sunglasses.	5.4. Consensus-based recommendation Suitable sunglasses must be worn in strong sunlight. Never look directly at the sun in the sky. This applies even when wearing sunglasses.	Checked 2020
4.5. Evidence-based recommendation Where possible, physical measures (avoidance of exposure, textiles) must be used in the first place for protection from sunlight. Sunscreens must be used for areas of the skin that cannot otherwise be protected. The use of sunscreens must not result in staying out longer in the sun.	5.5. Evidence-based recommendation Appropriate sunscreen products should be used for skin areas that cannot be protected in any other way. The use of sunscreens must not result in a prolonged stay in the sun.	Modified 2020
4.6. Consensus-based recommendation Sunscreens should be applied carefully to free areas of skin that are not covered by clothing (head, face, hands, arms, legs) and the following should be observed: use an appropriate sun protection factor, apply as thick a layer as possible (2 mg/cm²), apply evenly to all uncovered areas of skin, apply before exposure to the sun,	5.6. Consensus-based recommendation Sunscreens should be applied carefully to free areas of skin that are not covered by clothing (head, face, hands, arms, legs) and the following should be observed:	Modified 2020

Version 1.2	Version 2.1	Kommentare
repeat the application after 2 hours and after bathing (the protective time is not prolonged as a result).	use an adequate sun protection factor, apply a sufficiently thick layer (2 mg/cm²), apply evenly to all uncovered areas of skin, apply before exposure to the sun, repeat the application after 2 hours and after bathing (the protective time is not prolonged as a result).	
4.7. Evidence-based statement There are contradictory data as to whether the risk of melanoma is reduced by using sunscreen.	5.7. Evidence-based statement There is contradictory data on whether the risk of melanoma is reduced by sunscreen use.	Modified 2020
4.8. Consensus-based recommendation In accordance with international and national recommendations (WHO, ICNIRP, EUROSKIN, SSK, DKH and ADP), the use of sun studios must be avoided to reduce the risk of development of skin cancer.	-	Deletion due to evidence-based chapters 5.8 to 5.10

Version 1.2	Version 2.1	Kommentare
	5.8. Evidence-based statement The risk of malignant melanoma (MM) is increased in sunbed users compared to non-sunbed users and increases with the frequency of sunbed visits. The younger the tanning bed user was at the first visit, the higher the risk.	New 2020
	5.9. Evidence-based statement Tanning bed users have an increased risk of basal cell carcinoma compared to non-tanning bed users. The risk is even higher for people who use a tanning bed for the first time at the age of less than 20 years.	New 2020
	5.10. Evidence-based recommendation The use of sunbeds must be avoided in order to reduce the risk of developing skin cancer (especially melanoma).	New 2020
4.9. Evidence-based recommendation Food supplementation with selenium, vitamin A and beta-carotene must not be recommended as a measure for skin cancer prevention.	5.11. Evidence-based recommendation Food supplementation with selenium, vitamin A and beta-carotene must not be recommended as a measure	Checked 2020

Version 1.2	Version 2.1	Kommentare
	for skin cancer prevention.	
4.10. Consensus-based recommendation Intensive solar / ultraviolet (UV) radiation represents a risk for skin cancer to all certain groups and must be avoided.	-	Deletion and inclusion in the background text.
4.11. Consensus-based recommendation Children must not be allowed to develop sunburn.	5.12. Consensus-based recommendation Children must not get sunburned.	Checked 2020
4.12. Consensus-based recommendation Babies must not be exposed to direct sunlight.	5.13. Consensus-based recommendation Babies must not be exposed to direct sunlight.	Checked 2020
4.13. Consensus-based recommendation Children must be required to wear skin-covering clothing in strong sunlight.	5.14. Consensus-based recommendation Children must be required to wear skin-covering clothing in strong sunlight.	Checked 2020

Version 1.2	Version 2.1	Kommentare
4.14. Evidence-based recommendation Children with a light skin colour in particular must use sunscreens as well as avoid strong ultraviolet (UV) radiation exposure and additionally wear sun-protective textiles.	5.15. Consensus-based recommendation In the development of nevi, textile sunscreen is protective. The role of sunscreens is open.	Modified 2020 Conversion into Consensus-based recommendation, reformulation and further explanations in background text
4.15. Consensus-based recommendation Children's eyes must be protected by suitable children's sunglasses that meet the previously mentioned requirements (see Recommendation 4.4.).	5.16. Consensus-based recommendation Children's eyes must be protected by suitable sunglasses.	Modified 2020
4.16. Evidence-based recommendation Immunosuppressed transplant recipients must use sunscreens to protect themselves from skin cancer as part of a consistent, comprehensive ultraviolet (UV) radiation protection strategy.	5.17. Evidence-based recommendation Immunosuppressed transplant recipients must use sunscreens to protect themselves from skin cancer as part of a consistent, comprehensive ultraviolet (UV) radiation protection strategy.	Checked 2020
4.17. Consensus-based recommendation Immunosuppressed people must ensure they have a consistent, comprehensive untraviolet (UV) radiation protection strategy.	5.18. Consensus-based recommendation Immunosuppressed people must ensure they have a consistent, comprehensive untraviolet (UV) radiation protection strategy.	Checked 2020

Version 1.2	Version 2.1	Kommentare
4.18. Consensus-based recommendation In people at high risk for skin cancer (e.g.: transplant recipients, immunosuppressed patients) who practice consistent, extensive sun protection, vitamin D levels should be checked and vitamin D supplements given where necessary.	5.19. Consensus-based recommendation In people at high risk for skin cancer (e.g.: transplant recipients, immunosuppressed patients) who practice consistent, extensive sun protection, vitamin D levels should be checked and vitamin D supplements given where necessary.	Checked 2020
4.19. Evidence-based statement Moderate exposure to ultraviolet (UV) radiation and high vitamin D levels possibly have a protective effect against the occurrence and development of various types of cancer, including malignant melanoma. However, the existing evidence for a relationship between the risk of cancer and vitamin D intake is insufficient.	-	Deletion, inclusion in the background text including further explanations
4.20. Consensus-based statement The Guideline Group is currently unable to answer the question as to the optimal (reasonable) ultraviolet (UV) radiation exposure to ensure sufficient endogenous vitamin D production without incurring an increased risk of skin cancer.	5.20. Consensus-based statement For sufficient vitamin D synthesis, it is sufficient to expose the face, hands, and arms uncovered and without sunscreen two to three times a week to half of the minimum sunburn-effective UV dose (0.5 MED), i.e., half of the time in which one would otherwise get a sunburn without protection.	Modified2020

Version 1.2	Version 2.1	Kommentare
4.21. Dessenting opinion of DEGAM on section 4.1. The German Society of General Practice and Family Medicine (DEGAM) generally does not pass on recommendations with the strength of recommendation “must” to the general population. On the one hand, the data relating to a possible vitamin D deficiency and the need to spend time outdoorsdoes not suffice to issue a general recommendation to avoid sunlight. Secondly, it is not DEGAM’s policy to give- well-intentioned-generalised recommendations for behaviour in terms of cancer prevention to the population, which fail to take into account the particular aspects and preferences of the individual subjects.	-	Deletion
	5.2. Status Quo: Sun Protection and Exposure Behaviour	
	5.3 Status Quo: Skin Cancer-Related Knowledge, Perceptions and Attitudes	
4.2. Primary prevention measures for the population	**5.4. Primary Prevention Measures for the Population**	

	5.21. Consensus-based statement Measures of primary prevention of skin cancer start well before the development of a disease and aim to reduce risk factors for the occurrence of skin cancer. Therefore, the following risk factors and indicators are considered relevant as intermediate endpoints for the evaluation of primary prevention measures: Sun protection and tanning behaviour, use of sunbeds, etc. Knowledge, attitudes towards skin cancer, sun protection, and exposure Number of nevi Number of sunburns Most studies in primary prevention were only able to influence these intermediate endpoints. Because of the long time lag before skin cancer develops and multiple other influencing factors (confounders), it is extremely difficult, if not impossible, to assess the effect of preventive interventions to reduce skin cancer incidence. When evidence-based recommendations are made in the following, the corresponding evidence refers exclusively to the above-	New 2020

	mentioned intermediate endpoints, not to the skin cancer risk itself. Because the risk markers described increase the risk of skin cancer, the guideline group assumes a benefit.	

Version 1.2	Version 2.1	Kommentare
4.22. Evidence-based recommendation Knowledge about the effects of ultraviolet (UV) radiation and sun protection measures must be passed on constantly.	5.22. Evidence-based statement Educational measures on UV radiation and protective measures in kindergartens or schools can improve knowledge on UV protection.	Modified 2020
4.23. Evidence-based recommendation To improve sun protection behaviour, interventions about ultraviolet (UV) radiation protection should be conducted in schools and playschools or day care centres, with particular regard to the target group of younger children.	-	Deletion due to detailled assessment in the following recommendations
	5.23. Consensus-based recommendation UV risk communication should address aspects relevant to everyday life, the subjective perception of the benefits of UV exposure, and the beauty ideal of tanned skin. An important starting point for communication should be social ideals and behavioural routines with regard to tanned skin and sunbathing.	New 2020

Version 1.2	Version 2.1	Kommentare
	5.24. Consensus-based recommendation The media information on skin cancer prevention must be qualitatively and quantitatively expanded, since the media are the most important source of information for adults.	New 2020
	5.25. Consensus-based recommendation Digital media literacy as part of the health literacy of the population should be promoted in order to be able to find, understand, and assess the quality of targeted information on skin cancer and skin cancer prevention.	New 2020
	5.26. Consensus-based recommendation Parents with children of kindergarten age as well as educators, teachers, and directors of day-care centres must be informed about UV radiation as a risk factor for skin cancer and about the insufficient protective function of clouds against UV radiation.	New 2020

Version 1.2	Version 2.1	Kommentare
4.24. Evidence-based recommendation Interventions that target a sustained effect on behaviour should involve several components and should be implemented intensively and repeatedly.	5.27. Evidence-based recommendation Interventions that target a sustained effect on behaviour must involve several components and must be implemented intensively and repeatedly.	Modified 2020
	5.28. Evidence-based recommendation Behaviour change interventions should be based on behavioural theories and take into account the available evidence.	New 2020
	5.29. Evidence-based recommendation Measures to communicate primary prevention of skin cancer should be multimedia, interactive, and integrate multiple communication channels.	New 2020
	5.30. Evidence-based statement Personalised messages have a greater impact on sun protection behaviour than generalised messages.	New 2020
	5.31. Evidence-based recommendation Education and training programmes for the primary prevention of skin cancer should	New 2020

Version 1.2	Version 2.1	Kommentare
	address the target persons individually ("individual-level-interventions") and include individualised information and feedback elements.	
	5.32. Consensus-based recommendation Information can be provided via parents, teachers, educators, peers, and other multipliers.	New 2020
	5.33. Consensus-based recommendation Skin cancer prevention interventions can also use new media (websites, social media, SMS, apps) as a communication strategy.	New 2020
	5.34. Consensus-based statement Skin cancer prevention interventions that also address external appearance are one strategy to change sun protection behaviour.	New 2020

Version 1.2	Version 2.1	Kommentare
	5.35. Evidence-based statement The use of personalised digital methods to depict potential UV radiation-related attractiveness losses can have positive effects on sun protection and exposure behaviour in certain target groups.	New 2020
	5.36. Consensus-based recommendation Measures of primary prevention of skin cancer should be designed in a target group-oriented way and take into account the target group-specific needs.	New 2020
	5.37. Consensus-based recommendation Measures of primary prevention of skin cancer should start in the living environment (i.e., be setting-related) in order to reach people where they live their daily lives.	New 2020

Version 1.2	Version 2.1	Kommentare
	5.39. Consensus-based recommendation To improve sun protection behaviour, UV protection interventions should be implemented in schools and preschools or day care centres.	New 2020
	5.40. Consensus-based recommendation Measures of primary prevention of skin cancer must specifically address the target group of sunbed users, inform them about the risks of use, and aim to change their behaviour. The interventions must take into account the heterogeneity of the target group (e.g. migration background, level of education) and address this in their approach. Special attention must be paid to underage sunbed users.	New 2020
	5.41. Consensus-based recommendation The knowledge about an increased risk of skin cancer and the implementation of protective behaviours among organ transplant patients and skin cancer patients should be further improved.	New 2020

Version 1.2	Version 2.1	Kommentare
4.25. Evidence-based recommendation Doctor-patient communication (e.g. in connection also with skin cancer screening) should be used for primary preventive measures. (see also section 5.4 Doctor-patient communication)	5.42. Evidence-based recommendation The medical consultation (e.g. in connection also with skin cancer screening) must be used for indications of primary prevention measures on an ad hoc basis.	Modified 2020

4.26. Consensus-based recommendation

The following recommendations must be given in the doctor-patient discussion on cancer prevention:

Content	Done?
Information about the risks of ultraviolet (UV) radiation	
Motivation to change behaviour	
Avoid exposure to strong solar radiation	
Avoid the midday sun	
Stay out in the sun for as little as possible	
Seek shade	
Avoid sunburn	
Be aware of the ultraviolet (UV) radiation index	
Accustom the skin slowly to the sun	
Wear protective clothing	
Use sunscreens without prolonging exposure time	
Be aware of individual skin sensitivity	
Give information about the different skin types	
Advice on individual protective measures according to the patient's skin type	

5.43. Consensus-based recommendation

The following recommendations must be given in the doctor-patient discussion on cancer prevention:

Content

Information about the risks of excessive ultraviolet (UV) radiation

Motivation to change behaviour

Avoid exposure to strong solar radiation

In the case of medium and high UV exposure (UVI 3-7), seek shade during the midday periode

In the case of very high UV exposure (UV index 8 and higher), avoid being outdoors during the midday period if possible. If this is not possible, seek shade

If necessary, postpone outdoor activities to the morning and evening hours

Avoid sunburn at all costs

Wear protective clothing

Use sunscreens without prolonging exposure time

Be aware of individual skin sensitivity

Give information about the different skin types

Modified 2020

Pay attention to possible side effects of medicines in the sun	
Protect children in particular	
Avoid sun studios (refer to NiSG)	
Wear sunglasses	

Advice on individual protective measures according to the patient's skin type

Pay attention to possible side effects of medicines in the sun

Protect children and infants in particular

Avoid sun studios (refer to NiSG)

Wear sunglasses

Version 1.2	Version 2.1	Kommentare
	5.44. Consensus-based recommendation The knowledge about and the importance of the UV index for the sun protection behaviour of the population is currently low and dependent on age and socio-economic status.	New 2020
4.27. Consensus-based recommendation The ultraviolet (UV) radiation index should be more intensively publicised, firmly anchored in the media and used as an aid in UV protection campaigns. At the same time, the limits of its value should be observed. abei sollten die Grenzen seiner Aussagekraft beachtet werden.	5.45. Consensus-based recommendation The ultraviolet (UV) radiation index should be more intensively publicised as part of sun protection recommendations, firmly anchored in the media and used as an aid in UV protection campaigns. Attention must be paid to a comprehensible explanation of the UVI so that it is correctly understood and used in the sense of UV protection.	Modified 2020

Version 1.2	Version 2.1	Kommentare
4.28. Evidence-based recommendation Parents of babies and young children must be informed about appropriate sun protection for their children. (see also Recommendation 4.7.)	5.38. Evidence-based recommendation Parents of babies and young children must be informed about appropriate sun protection for their children. Regular early detection examinations must also be used for this purpose.	Modified 2020
	5.46. Consensus-based recommendation Proportional prevention measures for skin cancer prevention must be guided by the policy paper "Preventing Health Damage from the Sun – Proportional Prevention in Urban and Rural Areas" (2017) of the UV Protection Alliance.	New 2020
	5.47. Consensus-based recommendation In order to ensure compliance with the NiSG and the UVSV, in particular with regard to the prohibition of the use of sunbeds by minors and the presence of qualified personnel in sunbed establishments, controls and enforcement of the law and the ordinance must be improved.	New 2020

Version 1.2	Version 2.1	Kommentare
4.29. Evidence-based recommendation Schoolchildren and adolescents must be intensively informed about skin cancer risks, instructed in the practical use of protective measures and receive appropriate support from teachers.	-	Deletion due to inclusion in other recommendations
4.30. Evidence-based recommendation The tendency to acquire risk factors for skin cancer (e.g. naevi) must be reduced by interventions at school age with a long-term and repetitive approach.	-	Deletion due to inclusion in other recommendations
4.31. Evidence-based recommendation Sufficient shaded areas must be established in day-care centres, kindergartens and schools.	5.48. Evidence-based recommendation Sufficient shaded areas must be established in day-care centres, kindergartens and schools.	Checked 2020
4.32. Evidence-based recommendation Technical and organisational measures to minimise ultraviolet (UV) radiation exposure, particularly during the midday hours (e.g. provision of shaded areas, structuring of the timetable, consideration of UV radiation protection in the timetabling of sports events), should be an essential part of primary prevention.	5.49. Evidence-based recommendation Technical and organisational measures to avoid excessive UV exposure, particularly during the midday hours (e.g. provision of shaded areas, structuring of the timetable, consideration of UV radiation protection in the timetabling of sports events), must be an essential part of primary prevention.	Modified 2020

Version 1.2	Version 2.1	Kommentare
	5.50. Consensus-based recommendation Intervention projects and programmes in the context of primary skin cancer prevention should be evaluated formatively and summatively. The evaluation parameters used should be derived from a theoretically proven model.	New 2020
	5.51. Consensus-based recommendation Evaluations of interventions in the context of primary skin cancer prevention must use empirically proven measurement methods that are specific to the endpoints in question.	New 2020
	5.52. Evidence-based recommendation To evaluate the effectiveness of interventions for the primary prevention of skin cancer, skin cancer prevention-specific attitudinal and behavioural parameters as well as indicators on contact frequency/intensity, assessment of communication tools and their mediation quality, and performance should be used.	New 2020

Version 1.2	Version 2.1	Kommentare
4.33. Consensus-based recommendation For outdoor workers, suitable technical and organisational ultraviolet (UV) radiation protection measures (shaded areas, work organisation, rules governing breaks) should be promoted and take precedence over personal protective measures.		Deletion due to specific new chapter 7. Occupational Skin Cancer
4.34. Evidence-based recommendation Outdoor workers must be informed of the ultraviolet (UV) radiation risks and UV radiation protection measures by means of training measures.		Deletion due to specific new chapter 7. Occupational Skin Cancer
4.35. Consensus-based recommendation Outdoor workers must be protected by detailed legal regulations as they are at particular risk from intensive ultraviolet (UV) radiation.		Deletion due to specific new chapter 7. Occupational Skin Cancer
	6. Climate Change and UV Radiation	
	6.1. Climate Change and UV Radiation	

Version 1.2	Version 2.1	Kommentare
	6.1. Consensus-based statement Climate change has an influence on global and regional air temperature. Climate change has an indirect influence on UV radiation exposure. So far, however, no quantitative statements can be made on the associated region-specific impacts.	New 2020

Version 1.2	Version 2.1	Kommentare
	6.2. Consensus-based recommendation Rising air temperatures and changes in UV radiation exposure due to climate change have an influence on the morbidity of society. An influence on mortality can currently only be seen in relation to rising air temperatures. The extent to which climate change, in interaction with processes in the stratospheric ozone layer, has or will have an impact on the incidence and prevalence of skin cancer, can currently only be quantified under simplified assumptions. Adaptation strategies to the health consequences of climate change must accordingly focus on preventive measures for the prevention of UV- and heat-related diseases, especially skin cancer.	New 2020

Version 1.2	Version 2.1	Kommentare
	6.3. Consensus-based recommendation There is an influence of climate change (global warming) on the processes in the stratospheric ozone layer with the consequence of temporarily and locally increased UV radiation exposure in the northern hemisphere with great significance for the health of the population. Efforts should therefore be made to identify these short-term and temporary events at an early stage and to communicate them effectively so that protective measures can be taken to prevent skin cancer at the moment of the event.	New 2020
	6.2. Status Quo: Perception of Heat and UV Radiation	

Version 1.2	Version 2.1	Kommentare
	6.4. Consensus-based recommendation Findings on temperature-dependent behaviour are not yet available independent of the season, and thus daylight duration. The frequency and duration of outdoor activities increase with longer daylight hours and higher temperatures in the range of thermal comfort to mild heat stress. With free choice, temperature-dependent behaviour depends on thermal sensation and internal attitudes toward the prevailing temperature. In hot conditions (severe or extreme thermal discomfort), outdoor activities tend to be avoided. The temperature-dependent behaviour can be influenced by and dependent on specifications and organisational boundary conditions in the various living environments. Temperature-dependent behaviour should therefore be taken into account when designing prevention measures.	New 2020
	6.3. Status Quo: Climate Change and Urban Development	

Version 1.2	Version 2.1	Kommentare
	6.5. Consensus-based recommendation The primary objective of urban development and planning measures relating to protection from excessive UV radiation and heat must be to protect people in their living environments from unhealthy and unwanted exposure. This requires that the protection offered must be increased.	New 2020

Version 1.2	Version 2.1	Kommentare
	6.6. Consensus-based recommendation Development, structural engineering measures, and, above all, planting (trees, greening of buildings and lawns), which individually and in combination enable an effective reduction of high solar radiation loads, must be increasingly integrated into climate adaptation strategies of the federal government and local authorities. Particularly for areas with high solar radiation, development must ensure good shading and, where appropriate, canopies with shading elements. Sunlight loads must be reduced through informed planning of daily routines in kindergartens and schools as well as work scheduling.	New 2020

Version 1.2	Version 2.1	Kommentare
	6.7. Consensus-based recommendation In view of the advancing climate change, surfaces with the lowest possible albedo should be used when creating or redesigning squares (including schoolyards and kindergartens) or streets. In order to reduce the albedo and for the purpose of shading, the majority of all surfaces in residential areas that are not built over must be planted with vegetation.	New 2020
	6.8. Consensus-based recommendation UV protection must be consistently introduced in cities and municipalities as a further line of argument and guiding objective for the implementation of climate protection and adaptation measures. Laws and regulations to implement measures as comprehensively as possible must be enacted or expanded, and funding programmes to optimise UV protection must be launched by municipalities.	New 2020
	7. Occupational Skin Cancer	
	7.1. Status Quo Outdoor Worker	

Version 1.2	Version 2.1	Kommentare
	7.1. Consensus-based recommendation If employees are exposed to intensive UV radiation outdoors due to their work, targeted technical, organisational, and personal protection and prevention measures must be integrated into everyday working life.	New 2020
	7.2. Measures of Behavioural and Situational Prevention for Outdoor Workers	
	7.2. Evidence-based recommendation <u>Technical measure:</u> Workplaces and break areas must offer shading.	New 2020
	7.3. Evidence-based recommendation <u>Organisational measure:</u> Employees working outdoors must be informed about UV radiation and the associated health risks as well as the protective measures to be taken.	New 2020

Version 1.2	Version 2.1	Kommentare
	7.4. Consensus-based recommendation Organisational measure: Necessary means (e.g. sun hat with brim and neck protection, sunglasses, covering clothing, sunscreen) to protect against UV radiation must be provided at the workplace.	New 2020
	7.5. Consensus-based recommendation Organisational measure: In order to reduce UV exposure, working hours including breaks (e.g. avoiding outdoor work at lunchtime) must be organised.	New 2020
	7.6. Evidence-based recommendation Personal measure: The skin and eyes of outdoor workers must be protected from solar radiation. The body must be covered to the maximum with suitable clothing, i.e., in the form of long-sleeved clothing and headgear with neck protection.	New 2020

Version 1.2	Version 2.1	Kommentare
	7.7. Evidence-based recommendation <u>Personal measure:</u> Body parts that cannot be covered or shaded by textiles must be covered with suitable sunscreens.	New 2020
	7.3. Providing Information and Motivating Employees to Take Protective Measures	
	7.8. Evidence-based recommendation Protection and prevention measures must be taught in person. Visual support or reminders of the desired target behaviour can be provided, e.g. in the form of posters, pictures, or videos.	New 2020
	7.4. Occupational Health Screening for Outdoor Workers	
	7.9. Evidence-based recommendation The fact that UV radiation exposure represents the highest occupational cancer risk for outdoor workers in Germany must be the reason for the legislator to prescribe mandatory screening for all highly exposed persons.	New 2020

Version 1.2	Version 2.1	Kommentare
5. Secondary prevention	**8. Secondary Prevention**	
5.1. Early detection of skin cancer	**8.1. General Information on the Early Detection of Skin Cancer**	
5.1. Evidence-based statement Population-based screening with the target diseases of malignant melanoma, basal cell carcinoma and squamous cell carcinoma, in which a standardised examination of the skin over the whole body is performed by trained physicians, has been shown to result in an increase in the detection rate of tumours at an early stage.	-	Deletion
5.2. Evidence-based statement Skin cancer screening of the general adult population results in an initial increase in the incidence of skin cancer (prevalence phase of screening) and an increase in the detection rate of skin cancer at an early stage. This result could impact on the morbidity of malignant melanoma, basal cell carcinoma and squamous cell carcinoma.	-	Deletion
5.3. Evidence-based statement A single study indicates that population-based skin cancer screening could reduce mortality from melanoma.	-	Deletion

Version 1.2	Version 2.1	Kommentare
5.4. Evidence-based recommendation Skin cancer screening should be offered as part of the prevention of skin cancer.	8.20. Evidenzbasierte Empfehlung Skin cancer screening should be offered as part of the prevention of skin cancer.	Checked 2020
5.5. Dessenting opinion of DEGAM The German Society of General Practice and Family Medicine (DEGAM) regards the evidence for the benefit of a general skin cancer screening programme as insufficient. In individual cases, early detection of skin cancer can be performed following balanced information about the pros and cons.	8.21. Dessenting opinion of DEGAM The German Society of General Practice and Family Medicine (DEGAM) and the German Society of HNO (DGHNO), Head and Neck Surgery e.V. regard the evidence for the benefit of a general skin cancer screening programme as insufficient compared to opportunistic screening, in agreement with international institutions. Since the introduction of skin cancer screening, the mortality from skin cancer in Germany has not decreased. Therefore, no opportunistic skin cancer screening must be offered. In individual cases, early detection of skin cancer can be performed following balanced information about the pros and cons, especially in people at increased risk.	Modified 2020

Version 1.2	Version 2.1	Kommentare
5.6. Evidence-based recommendation The standardised whole-body skin examination to screen for malignant skin tumours must be performed by physicians. The precondition for this is participation in special advanced education courses on the early detection of skin cancer.	8.10 Consensus-based recommendation For skin cancer screening, a standardized whole-body skin examination of the skin must be performed by physicians who have participated in a special training course on the early detection of skin cancer as defined in the guideline for early detection of cancer.	Modified 2020
5.7. Consensus-based recommendation On the basis of the current evidence, it is not possible to make any statement about examination intervals for people not at increased risk.	8.13. Consensus-based statement On the basis of the current evidence, it is not possible to make any statement about the intervals between screening examinations for skin cancer for people not at increased risk.	Modified 2020
5.8. Consensus-based recommendation In the context of skin cancer screening, the time to presentation for further confirmation of the findings following the suspicion of a malignant melanoma, basal cell carcinoma or squamous cell carcinoma should not exceed ten working days.	8.11. Consensus-based recommendation In the context of skin cancer screening, the period of time until the next appointment for further confirmation of findings following the suspicion of a malignant melanoma or squamous cell carcinoma should not exceed ten days.	Modified 2020

Version 1.2	Version 2.1	Kommentare
	8.12. Consensus-based recommendation Within the scope of a skin cancer screening, the period of time until the next appointment for further confirmation of findings after a suspected basal cell carcinoma can be individually adjusted.	New 2020
5.9. Dessenting opinion of DEGAM In the context of skin cancer screening, people with a suspected malignant melanoma must be given the opportunity to attend for further, where necessary surgical, investigations within ten working days.		Deletion
5.10. Consensus-based recommendation At-risk persons (see section 3.4) must be taught to carry out skin self-examination so as to be able to identify abnormal skin lesions. At-risk persons must be informed about their individual risk and be regularly examined (at intervals to be defined individually) by a trained physician by means of a whole-body skin examination.	8.7. Consensus-based recommendation At-risk persons must be taught to carry out skin self-examination so as to be able to identify abnormal skin lesions. At-risk persons must be informed about their individual risk and be regularly examined (at intervals to be defined individually) by a trained physician by means of a whole-body skin examination.	Checked 2020

Version 1.2	Version 2.1	Kommentare
5.11. Consensus-based recommendation For people at increased risk for skin cancer, the physician, together with the person to be screened, should define an appropriate interval, based on an assessment of the individual risk profile.	8.14. Consensus-based recommendation For people at increased risk for skin cancer, the physician, together with the person to be screened, should define an appropriate interval until the next presentation, based on an assessment of the individual risk profile.	Modified 2020
5.12. Evidence-based statement Negative consequences of skin cancer screening involve excisions with a benign histology (false-positive tests). The number-needed-to-excise described in studies ranges from 3.25 to 179, i.e. between 3.25 and 179 excisions are needed to confirm one malignant skin tumour histologically.	8.1. Evidence-based statement Negative consequences of skin cancer screening involve excisions with a benign histology (false-positive tests). The number-needed-to-excise described in studies ranges from 3.25 to 179, i.e. between 3.25 and 179 excisions are needed to confirm one malignant skin tumour histologically.	Checked 2020

Version 1.2	Version 2.1	Kommentare
5.13. Consensus-based recommendation With the exception of false-positive tests, there is little evidence to date about potential risks and negative consequences of skin cancer screening. Possible negative consequences are overdiagnosis, overtreatment, negative psychological consequences and possible delays in diagnosis as a result of false-negative tests. These potential risks and negative consequences of skin cancer screening should be reduced as far as possible by appropriate physician training and teaching measures. Physicians should discuss potential risks and negative consequences with their patients before the screening.	8.2. Consensus-based recommendation With the exception of false-positive tests, there is little evidence to date about potential risks and negative consequences of skin cancer screening. Possible negative consequences are overdiagnosis, overtreatment, negative psychological consequences and possible delays in diagnosis as a result of false-negative tests. These potential risks and negative consequences of skin cancer screening should be reduced as far as possible by appropriate physician training and teaching measures. Physicians should discuss potential risks and negative consequences with their patients before the screening.	Checked 2020
	8.3. Consensus-based recommendation Skin self-examination must be recommended.	New 2020
5.2. Screening test / presumptive diagnostic procedures		

Version 1.2	Version 2.1	Kommentare
5.14. Evidence-based recommendation A whole-body examination must be performed for skin cancer screening.	8.4. Evidence-based recommendation To screen for skin cancer, a whole-body examination must be performed.	Modified 2020
5.15. Consensus-based recommendation For a whole-body examiantion, the examination room must be well-lit and the examiner must approach the person to be screened close enough to be able to detect skin changes with the naked eye.	8.5. Consensus-based recommendation For a whole-body examiantion, the examination room must be sufficiently bright and the examiner must approach the person to be screened close enough to be able to detect skin changes with the naked eye.	Modified 2020
5.16. Evidence-based statement The diagnosis of non-melanocytic skin cancer by whole-body examination has a sensitivity of 56 90% and a specificity of 75 90%.		Deletion and inclusion in the background text
5.17. Evidence-based statement In a cross-sectional study with Australian family physicians, sensitivity in the diagnosis of skin cancer types by whole-body examination was 100% for melanomas (n=1), 89% for basal cell carcinomas (n=62), 80% for dysplastic naevi (n=30), 58% for benign naevi (n=69), 42% for squamous cell carcinomas (n=18) and 10% for actinic keratoses (n=31), while specificity for these entities was 76 99%.		Deletion and inclusion in the background text

Version 1.2	Version 2.1	Kommentare
5.18. Evidence-based statement In the diagnosis of melanoma by clinical examination, the sensitivity of non-dermatologically trained practitioners was 86 95% and the specificity 49 77%. Training in the diagnosis of melanoma did not produce any substantial increase in sensitivity and specificity in general practitioners.		Deletion and inclusion in the background text
5.19. Evidence-based statement According to a systematic review, the available study data are insufficient to draw conclusions about statistically significant differences between dermatologists and primary care physicians in terms of accuracy in classifying suspected melanoma lesions. In terms of diagnostic accuracy, the sensitivity of dermatologists was 0.81-1.0 and of primary care physicians 0.42-1.00. In terms of biopsy or referral accuracy, the sensitivity was 0.82-1.0 (dermatologists) and 0.70-0.88 (primary care physicians).	8.6. Evidence-based statement According to a systematic review, the available study data are insufficient to draw conclusions about statistically significant differences between dermatologists and primary care physicians in terms of accuracy in classifying suspected melanoma lesions.	Modified 2020
	8.2. Population-Based Skin Cancer Screening in Germany	

Version 1.2	Version 2.1	Kommentare
5.20. Consensus-based recommendation The person to be screened must be asked about skin changes at the beginning of the screening / presumptive diagnostic procedures.	8.8. Consensus-based recommendation The person to be screened must be asked about skin changes at the beginning of the screening / presumptive diagnostic procedures.	Checked 2020
5.21. Evidence-based recommendation The results of the self-examination of the person to be screened should be included at the beginning of the screening / presumptive diagnostic procedures to identify and differentiate between malignant and benign skin changes.	8.9. Evidence-based recommendation The results of the self-examination of the person to be screened must be included at the beginning of the screening / presumptive diagnostic procedures to identify malignant and benign skin changes.	Modified 2020
	8.15. Evidence-based statement Data on skin cancer screening in Germany show that the population-wide offer of a standardized examination of the skin on the entire body by trained physicians leads to an initially emphasized increase in the incidence of detected cases of melanocytic and non-melanocytic skin cancer.	New 2020

Version 1.2	Version 2.1	Kommentare
	8.16. Evidence-based statement As a result of skin cancer screening, there is a more marked increase in the incidence of in situ carcinomas compared to invasive tumours. In the case of invasive melanomas, there is a shift in stage with a lower proportion of advanced tumours (stage T2-T4).	New 2020
	8.17. Evidence-based statement The incidence of advanced melanoma is declining after the introduction of population-based skin cancer screening.	New 2020
	8.18. Evidence-based statement Screening participants with unremarkable results are diagnosed with fewer invasive melanomas (in the sense of interval carcinomas) within two years of screening than would be expected without the intervention.	New 2020

Version 1.2	Version 2.1	Kommentare
	8.19. Evidence-based statement In the temporal context of a feasibility study on population-based screening, there was a significant decrease in documented melanoma mortality. For nationwide skin cancer screening, no decrease in melanoma mortality could be observed in studies covering a maximum period of seven years after introduction.	New 2020
Presumptive diagnostic procedures		
5.22. Evidence-based recommendation Dermatoscopy should be performed in the presumptive diagnostic procedure. It should be used to improve the clinical diagnosis of melanocytic lesions.	8.48. Evidence-based recommendation Dermatologists must offer dermoscopy in the presumptive diagnostic procedure of pigmented and non-pigmented skin and nail lesions.	Modified 2020
5.23. Evidence-based recommendation Dermatoscopy must be performed only after appropriate practical training.	8.49. Consensus-based recommendation Dermatologists must be trained in dermoscopy for the presumptive diagnostic procedure.	Modified 2020

Version 1.2	Version 2.1	Kommentare
5.24. Evidence-based recommendation Dermatoscopy can be performed in people at increased risk undergoing an individualised check-up.	8.50. Evidence-based recommendation Dermatoscopy can be performed in people at increased risk undergoing an individualised check-up.	Checked 2020
5.25. Consensus-based recommendation For all lesions of the skin and the adjacent mucosae in the facial, genital or anal region that would be insufficiently investigated by diagnostic procedures involving the use of dermatoscopy, the patient must have a consultation with further specialist diagnostic procedures.	8.51. Consensus-based recommendation For all lesions of the skin and the adjacent mucosae in the facial, genital or anal region that would be insufficiently investigated by diagnostic procedures involving the use of dermatoscopy, the patient must have a consultation with further specialist diagnostic procedures.	Checked 2020
5.26. Evidence-based recommendation Algorithms for describing pigmented lesions and instant cameras for observing the disease course with the aim of reducing the proportion of excised benign lesions relative to melanomas should not be used.	8.52. Consensus-based statement Computer-based algorithms for the classification of (pigmented) skin lesions are currently being developed and investigated in many cases, but the guideline group is not yet in a position to make any statements in this respect.	Modified 2020

Version 1.2	Version 2.1	Kommentare
5.27. Evidence-based statement The value of whole-body photography in melanoma risk patients remains unproven.	8.53. Evidence-based statement The value of whole-body photography in melanoma risk patients remains unproven.	Checked 2020
5.28. Evidence-based statement Special image processing programmes for the detection of melanomas have been developed, but their value remains unproven.		Deletion and inclusion in the background text
5.22 Evidence-based recommendation Dermatoscopy should be performed in the presumptive diagnostic procedure. It should be used to improve the clinical diagnosis of melanocytic lesions.	8.54. Evidence-based statement Sequential digital dermoscopy can improve the early detection of malignant melanomas in follow-up control that do not have specific dermoscopic malignancy criteria.	Modified 2020
5.29. Evidence-based recommendation Teledermatology can be used to assess benign and malignant skin tumours.	8.55. Consensus-based recommendation Teledermatology can be used to assess benign and malignant skin tumours.	Modified 2020
5.30. Evidence-based statement Spectrophotometric analysis of pigmented lesions has shown no improvement in sensitivity and specificity in the diagnosis of melanoma.		Deletion and inclusion in the background text (in alignment with the guideline Malignant Melanoma)

Version 1.2	Version 2.1	Kommentare
5.31. Evidence-based statement The value of near-infrared spectroscopy in distinguishing melanocytic and non-melanocytic skin changes from one another and from normal skin remains unproven.		Deletion and inclusion in the background text (in alignment with the guideline Malignant Melanoma)
5.32. Evidence-based statement Confocal laser scanning microscopy (CLSM) has a high resolution in assessing pigmented and non-pigmented skin lesions. Following suitable training, CLSM can improve the diagnostic accuracy of individual lesions		Deletion and inclusion in the background text (in alignment with the guideline Malignant Melanoma)
5.33. Consensus-based statement The value of multiphoton laser tomography in the diagnosis of melanoma remains unproven.		Deletion and inclusion in the background text (in alignment with the guideline Malignant Melanoma)
5.34. Consensus-based statement The value of optical coherence tomography (OCT) in distinguishing melanocytic and non-melanocytic skin changes from one another and from normal skin remains unproven.		Deletion and inclusion in the background text (in alignment with the guideline Malignant Melanoma)

Version 1.2	Version 2.1	Kommentare
5.35. Consensus-based statement The value of multifrequency electrical impedance spectroscopy (EIS) in distinguishing melanocytic and non-melanocytic skin changes from one another and from normal skin remains unproven.		Deletion and inclusion in the background text (in alignment with the guideline Malignant Melanoma)
5.36. Consensus-based statement The value of high-resolution ultrasonography in distinguishing melanocytic and non-melanocytic skin changes from one another and from normal skin remains unproven.		Deletion and inclusion in the background text (in alignment with the guideline Malignant Melanoma)
5.3. Confirmatory diagnostic procedures		
5.37. Consensus-based recommendation The histopathological examination of a suitable tissue sample is the standard confirmatory diagnostic method. The histopathological diagnosis must be used to confirm a suspicious lesion.	8.56. Consensus-based recommendation The histopathological examination of a suitable tissue sample is the standard confirmatory diagnostic method. The histopathological diagnosis must be used to confirm a suspicious lesion.	Checked 2020

Version 1.2	Version 2.1	Kommentare
5.38. Consensus-based recommendation At the time of tissue sampling, consideration must be given to the relevant specific functional features in each case (e.g. in the facial and genital region) to prevent a functional disorder (e.g. ectropion, facial nerve paralysis) simply as a result of the tissue sampling.	8.57. Consensus-based recommendation At the time of tissue sampling, consideration must be given to the relevant specific functional features in each case (e.g. in the facial and genital region) to prevent a functional disorder (e.g. ectropion, facial nerve paralysis) simply as a result of the tissue sampling.	Checked 2020
5.39. Consensus-based recommendation On clinical suspicion of a malignant melanoma, this lesion must first of all be completely excised with a small safety margin.	8.58. Consensus-based recommendation On clinical suspicion of a malignant melanoma, this lesion must first of all be completely excised with a small safety margin.	Checked 2020
5.40. Evidence-based statement The optimal tissue sample for histopathological assessment of a skin lesion suspected of being malignant melanoma is the complete excision (excision biopsy) with a safety margin of 2 mm, including the removal of fatty tissue.	8.59. Evidence-based statement The optimal tissue sample for histopathological assessment of a skin lesion suspected of being malignant melanoma is the complete excision (excision biopsy) with a safety margin of 2 mm, including the removal of fatty tissue.	Checked 2020

Version 1.2	Version 2.1	Kommentare
5.41. Consensus-based recommendation In the case of large, extensive tumours on the face or acral skin that are suspicious for melanoma and for which a primary diagnostic excision is difficult, a sample biopsy or partial excision can be performed.	8.60. Consensus-based recommendation In the case of large, extensive tumours on the face or acral skin that are suspicious for melanoma and for which a primary diagnostic excision is difficult, a sample biopsy or partial excision can be performed.	Checked 2020
5.42. Evidence-based recommendation On clinical suspicion of a basal cell carcinoma or a squamous cell carcinoma, the tumour can undergo complete primary excision with a small safety margin or a sample biopsy can be taken beforehand.	8.61. Evidence-based recommendation On clinical suspicion of a basal cell carcinoma or a squamous cell carcinoma, the tumour can undergo complete primary excision or a sample biopsy can be taken beforehand.	Modified 2020
5.43. Consensus-based recommendation Each histopathological report (cf. quality assurance agreement) must contain a description of the microscopic findings and the formulation of a diagnosis. The type of tumour must be stated in accordance with the WHO classification and the histological staging in accordance with the currently valid TNM classification (UICC).	8.62. Consensus-based recommendation Each histopathological report (cf. quality assurance agreement) must contain a description of the microscopic findings and the formulation of a diagnosis. The type of tumour must be stated in accordance with the WHO classification and the histological staging in accordance with the currently valid TNM classification (UICC).	Checked 2020

Version 1.2	Version 2.1	Kommentare
5.44. Consensus-based statement [In Germany,] the aspects of quality assurance are defined in accordance with the agreement on quality assurance measures laid down in section 135(2) SGB V[1] on the histopathological examination in association with skin cancer screening [432] of 12 August 2009.		Deletion
5.4. Doctor-patient communication		

5.45. Consensus-based recommendation Prior to the doctor-patient conversation, the patient should be issued with an information sheet on the early detection of skin cancer (skin cancer screening) that provides information about the pros and cons of early detection in simple language without engendering any anxiety. The subject matter should be kept to the checklist agreed in connection with the German National Cancer Control Plan Recommended content of information about early detection measures [439]. In addition, reference should be made to the possibility that outstanding queries can be clarified in the subsequent doctor-patient conversation. During the doctor-patient conversation, which should take place in a quiet and undisturbed atmosphere, the checklist should also serve as a guide. Emphasisie should be placed on the following aspects: Procedure of the skin cancer screening, Pros and cons of skin cancer screening, Primary prevention information, Personal risk profile and resultant consequences (risk communication). A period of time commensurate with the patient's personal preferences should be allowed to elapse between the provision of information and the decision. Associated professional groups and, where applicable, relatives should be included in the communication process.	8.44. Consensus-based recommendation (Chapter 8.4.) Prior to the doctor-patient conversation, the patient must be issued with evidence-based information on the early detection of skin cancer (skin cancer screening) that provide information about the pros and cons of early detection in comprehensible language without engendering any anxiety. The subject matter must be kept to the checklist agreed in connection with the German National Cancer Control Plan Recommended content of information about early detection measures (Federal Ministry of Health, 2010). In addition, reference must be made to the possibility that outstanding queries can be clarified in the subsequent doctor-patient conversation. During the doctor-patient conversation, which must take place in a quiet and undisturbed atmosphere, the checklist must also serve as a guide. Emphasisie must be placed on the following aspects: Procedure of the skin cancer screening,	Modified 2020

	Pros and cons of skin cancer screening, Primary prevention information, Personal risk profile and resultant consequences (risk communication). A period of time commensurate with the patient's personal preferences must be allowed to elapse between the provision of information and the decision. Associated professional groups and, where applicable, relatives must be included in the communication process.	

Version 1.2	Version 2.1	Kommentare
5.46. Consensus-based recommendation A negative examination result must be communicated to the patient personally by the doctor carrying out the early detection in a counselling immediately after the examination. It must be pointed out that the result of the examination reflects the current status. In addition, the patient's individual risk factors must be explained to him and he must be motivated to practise primary preventive behaviour and skin self-examination. The patient must also be informed that he can visit the doctor again at any time in the event of any uncertainties about self-recorded skin findings.	8.45. Consensus-based recommendation (Chapter 8.4.) If the screening does **not** reveal any suspicion of skin cancer, this must be communicated to the patient personally by the doctor carrying out the early detection in a counselling immediately after the examination. It must be pointed out that the result of the examination reflects the current status. In addition, the patient's individual risk factors must be explained to him and he must be motivated to practise primary preventive behaviour and skin self-examination. The patient must also be informed that he can visit the doctor again at any time in the event of any uncertainties about self-recorded skin findings.	Modified 2020

5.47. Consensus-based recommendation The suspicion of skin cancer must be communicated to the patient personally by the doctor carrying out the early detection in a counselling immediately after the examination. Family physicians (specialists in general medicine working in family practice, internal specialists, medical practitioners and non-specialist practitioners): following the communication of a suspicion, the subsequent procedure must be explained, including a referral to the dermatologist for further investigations. Dermatologist: the subsequent diagnostic investigations of the clinical suspicion must be communicated and explained. The patient must be informed that the findings will be communicated in a personal conversation and that he has the possibility of including a person of trust in this conversation. The patient must be asked about resources for psychological support during the waiting period and encouraged to practise self-care. The detailed interview must take place following receipt of the histological report. Information about the exclusion or demonstration of skin cancer (following histological confirmation of the findings) must not be given over the telephone.	8.46. Consensus-based recommendation (Chapter 8.4.) If the screening results in a suspicion of skin cancer, this must be communicated to the patient personally by the doctor carrying out the early detection in a counselling immediately after the examination. Family physicians (specialists in general medicine working in family practice, internal specialists, medical practitioners and non-specialist practitioners): following the communication of a suspicion, the subsequent procedure must be explained. Dermatologist: the subsequent diagnostic investigations of the clinical suspicion must be communicated and explained. The patient must be informed that the findings will be communicated in a personal conversation and that he has the possibility of including a person of trust in this conversation. The patient must be asked about resources for psychological support during the waiting period and encouraged to practise self-care. The detailed interview must take place	Modified 2020

	following receipt of the histological report.	

5.48. Consensus-based recommendation The period between the measures to confirm the diagnosis and the communication of the diagnosis must be kept as short as possible. Exclusion of skin cancer: the patient must be told of the histological exclusion of skin cancer. In addition, the patient must be given an explanation about his individual risk factors and he must be encouraged to practise primary preventive behaviour and skin self-examination. The patient must also be informed that he can visit the doctor again at any time in the event of any uncertainties about self-recorded skin findings. Confirmation of skin cancer: the finding of skin cancer must be communicated to the patient in detail with the diagnosis and grading in a personal (face-to-face) conversation. The existing diagnostic and therapeutic steps consistent with the current state of scientific knowledge must be conveyed comprehensibly to the patient over several sessions.	8.47. Consensus-based recommendation (Chapter 8.4.) The period between the measures to confirm the diagnosis and the communication of the diagnosis must be kept as short as possible. Exclusion of skin cancer: The patient must be told of the histological exclusion of skin cancer. In addition, the patient must be given an explanation about his individual risk factors and he must be encouraged to practise primary preventive behaviour and skin self-examination. The patient must also be informed that he can visit the doctor again at any time in the event of any uncertainties about self-recorded skin findings. Confirmation of skin cancer: The finding of skin cancer must be communicated to the patient in detail with the diagnosis and grading in a personal (face-to-face) conversation. The existing diagnostic and therapeutic steps (including benefits and harms) consistent with the current state of scientific knowledge must be conveyed comprehensibly to the patient.	Modified2020

Version 1.2	Version 2.1	Kommentare
5.5. Implementation and quality assurance of skin cancer screening		
5.49. Consensus-based recommendation Skin cancer screening must be conducted only by qualified physicians who have successfully completed a recognised advanced education course lasting several hours on the conduct of skin cancer screening.	8.22. Consensus-based recommendation Skin cancer screening must be conducted only by qualified physicians who have successfully completed a quality-assured, accredited education course on the conduct of skin cancer screening.	Modified 2020
5.50. Consensus-based recommendation A counselling approach and/or further advice on skin cancer screening can be offered and carried out by health professionals who are not medical practitioners (health assistants, practice nurses, nursing professions, other specialist professions within the healthcare system). The precondition for this is: completion of appropriate professional training and successful completion of a recognised advanced education course lasting several hours on counselling in connection with skin cancer screening.	8.23. Consensus-based recommendation A counselling approach and/or further advice on skin cancer screening cannot be offered and carried out by health professionals who are not medical practitioners (health assistants, practice nurses, nursing professions, other specialist professions within the healthcare system). The precondition for this is: completion of appropriate professional training and successful completion of a recognised quality-assured education course on counselling in connection with skin cancer screening.	Checked 2020

Version 1.2	Version 2.1	Kommentare
5.51. Consensus-based recommendation Advanced education/advanced education programmes in skin cancer screening for physicians and other health professionals (health assistants, practice nurses, nursing professions, other specialist professions in the healthcare system) must be extensively offered and carried out by certified trainers.	8.24. Consensus-based recommendation Advanced education/advanced education programmes in skin cancer screening for physicians and other health professionals (health assistants, practice nurses, nursing professions, other specialist professions in the healthcare system) must be extensively offered and carried out by certified trainers.	Checked 2020

5.52. Consensus-based recommendation Advanced education provision in skin cancer screening for physicians or other health professionals (health assitants, practice nurses, nursing professions, other specialist professions in the healthcare system) must impart practical and theoretical knowledge and methods. To this end, the following content matter must be included in a curriculum: Epidemiology of skin cancer (MM, NMSC), Aetiology, risk factors and groups, Clinical pictures (MM, NMSC), Definition of prevention (primary, secondary and tertiary prevention), Early detection of cancer as a screening measure, Legal framework conditions, Benefit and harms of early detection measures/screening programmes, Criteria for assessing early detection measures, Key performance indicators of a screening test, Skin cancer screening, Measures for targeting potential participants, Requirements for advice about an informed decision in the context of skin cancer screening, Screening test: visual standardised whole-body examination, Targeted case history-taking, Reporting of findings and advice, Quality assurance of pathology (histopathological differential diagnoses), Quality requirement of histopathology, Histopathological diagrams, The histopathological report (completeness, significance of contents), Referral, Documentation, Invoicing, Notification to cancer registries,		Deletion and inclusion in the background text

Interdisciplinary co-operation, Principles of communication, Communication between family physician and dermatologist, dermatologist and pathologist, physician and patient, Communication tools for conversation techniques.		

Version 1.2	Version 2.1	Kommentare
5.53. Evidence-based recommendation Curricula for the training, advanced education and continuing professional development of physicians or other health professionals (health assistants, practice nurses, nursing professions, other specialist professions in the healthcare system) in primary care provision can include the following subject areas in relation to the primary and secondary prevention of skin cancer: Epidemiology, Diagnostic procedures including dermatoscopy and clinical algorithms, aided by photographic images of skin lesions, Advice (primary and secondary prevention), Communication, Treatment. Curricula can be divided into one of more intervention units and incorporate the following educational means and conditions: course attendance, web-based, interactive, multimedia, role play, conveyed theoretically and/or practically.	8.25. Evidence-based statement Curricula for the training, advanced education and continuing professional development of physicians or other health professionals (health assistants, practice nurses, nursing professions, other specialist professions in the healthcare system) in primary care provision should include the following subject areas in relation to the primary and secondary prevention of skin cancer: Epidemiology, Diagnostic procedures including dermatoscopy and clinical algorithms, aided by photographic images of skin lesions, Advice (primary and secondary prevention), Communication, Treatment. Curricula can be divided into one of more intervention units and incorporate the following educational means and conditions: course attendance, web-based, interactive, multimedia, role play, conveyed theoretically and/or practically.	Modified 2020

Version 1.2	Version 2.1	Kommentare
5.54. Evidence-based recommendation Pharmacy staff can be trained in primary skin cancer prevention.		Deletion and inclusion in the need for research in chapter 5.4

5.55. Consensus-based recommendation In skin cancer screening, participating physicians must collect the following data for each patient examined for skin cancer: Family physician (specialists in general medicine working in family practice, internal specialists, medical practitioners, non-specialist physicians): Clear personal identification of the examinee (screening ID or pseudonym in the cancer registry), Identification of the physician, Age and sex of examinee, Date of examination, Presumptive diagnosis, differentiated by type of skin cancer (malingnant melanoma, squamous cell carcinoma, basal cell carcinoma). Dermatologists (specialists in skin and venereological diseases) must record the following data in addition to those mentioned above: On referral: presumptive diagnosis of the referring physician and date of first examination, Date of examination (dermatologist), Presumptive diagnosis (dermatologist), differentiated by type of skin cancer (malingnant melanoma, squamous cell carcinoma, basal cell carcinoma), Following excision: excision date, histopathological findings and where applicable tumour stage (tumour thickness or spread, where applicable TNM stage, grading).		

Version 1.2	Version 2.1	Kommentare
5.56. Consensus-based recommendation If an invitation system is introduced for skin cancer screening, the following data on the invitation of the general population must be recorded: Agency issuing the invitation (central agency or health insurance company): Clear personal identification of the invitee (screening ID or pseudonym in the cancer registry), Date of invitation Age and sex of invitee, Rejection / exclusion (active rejection of skin cancer screening or skin cancer screening not applicable, e.g. with prevalent skin cancer).		Deletion and inclusion in the background text
5.57. Dessenting opinion of DEGAM In view of the unconfirmed evidence for skin cancer screening and the in any case already high level of doctor-patient contacts in general practices compared to international standard, the German College of General Practitioners and Family Physicians (DEGAM) does not recommend an invitation system.	-	Deletion

Version 1.2	Version 2.1	Kommentare
5.58. Consensus-based recommendation Data recorded about skin cancer screening must be forwarded by family physicians and dermatologists to an evaluation centre where, together with the invitation data where applicable, they must be collated and evaluated for the quality management of skin cancer screening. In order to determine interval carcinomas and to evaluate mortality, a comparison must be undertaken with the cancer registry. The comparative data must be provided for the purposes of scientific evaluation. When a malignant finding is obtained, the responsible cancer registry must be notified by the examining physicians (including pathologists).	8.26. Consensus-based recommendation Data recorded about skin cancer screening must be forwarded by family physicians and dermatologists to an evaluation centre where, together with the invitation data where applicable, they must be collated and evaluated for the quality management of skin cancer screening. In order to determine interval carcinomas and to evaluate mortality, a comparison must be undertaken with the cancer registry. The comparative data must be provided for the purposes of scientific evaluation. When a malignant finding is obtained, the responsible cancer registry must be notified by the examining physicians (including pathologists).	Checked 2020
5.59. Consensus-based recommendation Skin cancer screening data must be recorded electronically by all those involved and transmitted electronically.	-	Deletion and inclusion in the background text

Version 1.2	Version 2.1	Kommentare
5.60. Consensus-based recommendation Documentation of the examination results for participants in skin cancer screening must be done under pseudonymised conditions taking due accounts of suitable methods and data protection concepts. The additional collection of a declaration of consent must be omitted. For non-participants, time-limited pseudonymised data storage of the invitation data is recommended for the purpose of evaluating outcomes (particularly skin cancer-related mortality). All data recording, data storage and transmission processes must be closely agreed with the data protection authorities.	-	Deletion and inclusion in the background text
5.61. Consensus-based recommendation Quality assurance measures for skin cancer screening must include structure, process and outcome quality. Because of the absence of scientifically-based quality assurance measures, quality indicators must be confirmed by evidence-based methods and where necessary new indicators developed.	8.27. Consensus-based recommendation Quality assurance measures for skin cancer screening must include structure, process and outcome quality. Because of the absence of scientifically-based quality assurance measures, quality indicators must be confirmed by evidence-based methods and where necessary new indicators developed.	Checked 2020

Version 1.2	Version 2.1	Kommentare
	8.28. Consensus-based recommendation Awareness of statutory skin cancer screening should be increased among the population through targeted measures. Different communication channels should be used to reach different target groups.	New 2020
	8.29. Consensus-based recommendation Information about and motivation to take up skin cancer screening should be addressed in a gender-specific way.	New 2020
6. Informing the general population / public		
6.1. Informing the general population / public	**8.3. Communicative Strategies and Communication Channels of Secondary Prevention**	

Version 1.2	Version 2.1	Kommentare
6.1. Consensus-based recommendation Information about the early detection of skin cancer must be guided by the recommendations of the [German] National Cancer Control Plan on an „informed decision“ to enable the potential screenee deciding for or against participation in skin cancer screening examination.	8.30. Consensus-based recommendation Information about the early detection of skin cancer must be guided by the recommendations of the [German] National Cancer Control Plan on an „informed and participatory decision“ to enable the person seeking advice deciding for or against participation in skin cancer screening examination.	Modified 2020
6.2. Consensus-based recommendation Strategies and measures whose aim is to reach the population with prevention messages and to allow an “informed decision“ for or against participation in skin cancer screening must be tailored to the different target groups.	8.31. Consensus-based recommendation Strategies and measures aimed at enabling the population to make an “informed and participatory decision" for or against participation in skin cancer screening must be tailored to the different target groups. Different characteristics of the target groups (such as their risk perception and self-efficacy) are to be taken into account.	Modified 2020

Version 1.2	Version 2.1	Kommentare
	8.32. Consensus-based recommendation The communication strategy for secondary prevention measures must be oriented towards the information and communication needs and routines as well as the living environments of the respective target group.	New 2020
6.3. Evidence-based statement Informing the adult population in a social setting can help promote cancer awareness.	8.33. Evidence-based statement Informing the adult population in their immediate environment can help to promote skin cancer awareness.	Modified 2020
	8.34. Consensus-based recommendation Family members or multipliers can be involved in measures, for example, to carry out self-examination and to promote informed participation in skin cancer screening.	New 2020

Version 1.2	Version 2.1	Kommentare
	8.35. Evidence-based recommendation Interventions to promote skin self-examination and inform about skin cancer screening should be multimedia, interactive, integrate multiple communication channels, and be repetitive.	New 2020
6.4. Evidence-based recommendation Children, adolescents and young adults with computer or online skills can be informed via computer or online.	.	Deletion due to inclusion in other recommendations
6.5. Consensus-based recommendation Information can also be given via agents of socialisation, peers and other multiplicators.	5.32. Consensus-based recommendation (chapter 5.4.) Information can be provided via parents, teachers, educators, peers and other multipliers.	Modified 2020
6.6. Evidence-based recommendation Adults should be informed repeatedly.	-	Deletion due to inclusion in other recommendations
6.7. Evidence-based recommendation Adults should be informed by means of multimedia.	-	Deletion due to inclusion in other recommendations

Version 1.2	Version 2.1	Kommentare
6.8. Evidence-based recommendation People at increased risk should be informed by means of tailored communication.	-	Deletion due to inclusion in other recommendations
6.9. Evidence-based recommendation Schoolchildren should be offered information via multiple media, along with information for their teachers.	-	Deletion due to inclusion in other recommendations
6.10. Evidence-based recommendation Educational and training programmes on primary and secondary prevention of skin cancer should be structured multimedially and interactively and incorporate several channels of communication.	-	Deletion due to inclusion in other recommendations
6.11. Evidence-based recommendation Educational and training programmes on primary and secondary prevention of skin cancer should use the simplest, most realistic and vivid forms of visualisation possible in structuring materials and take account of the limits to the acquisition of new skills by individual target groups beyond the transmission of knowledge.	8.36. Evidence-based recommendation Educational and training programmes on secondary prevention of skin cancer should use the simplest, most realistic and vivid forms of visualisation possible in structuring materials and take into account the competence of individual target groups.	Modified2020

Version 1.2	Version 2.1	Kommentare
6.12. Evidence-based recommendation Educational and training programmes on primary and secondary prevention of skin cancer should address the target persons individually (individual-level interventions) and at the same time include individualised information and feedback elements.	5.32. Evidence-based recommendation (Chapter 5.4.) Educational and training programmes on primary prevention of skin cancer should address the target persons individually (individual-level interventions) and at the same time include individualised information and feedback elements. 8.37. Evidence-based recommendation Measures to promote skin self-examination and to inform about the opportunities and risks of skin cancer screening must address the target persons individually (“individual-level-interventions") and include individualized/personalized information and feedback elements.	Modified 2020
6.13. Consensus-based recommendation Communication interventions in connection with primary and secondary skin cancer prevention should be evaluated formatively and summatively The evaluation parameters used should be derived from a theoretically established model.	8.38. Consensus-based recommendation Intervention projects and programmes in the context of secondary skin cancer prevention should be evaluated formatively and summatively. The evaluation parameters used should be derived from a theoretically based model.	Modified 2020

Version 1.2	Version 2.1	Kommentare
6.14. Consensus-based recommendation Evaluations of interventions in connection with primary and secondary skin cancer prevention must work with empirically established measurement procedures geared specifically to the particular outcomes.	8.39. Consensus-based recommendation Evaluations of interventions in connection with secondary skin cancer prevention must work with empirically established measurement procedures geared specifically to the particular outcomes.	Modified 2020
6.15. Evidence-based recommendation In evaluating the efficacy of interventions for the primary prevention of skin cancer, skin cancer prevention-specific attitude and behaviour parameters should be used, as well as indicators of contact frequency/intensity, to assess methods of communication and their quality and effectiveness.	8.40. Evidence-based recommendation In evaluating the efficacy of interventions for the secondary prevention of skin cancer, skin cancer prevention-specific attitudinal and behavioural parameters should be used, as well as indicators of contact frequency/intensity, to assess methods of communication and their quality and effectiveness.	Modified 2020

Version 1.2	Version 2.1	Kommentare
6.16. Consensus-based recommendation To evaluate the effectiveness of a communication-based intervention in terms of informed decision-making in connection with primary and secondary skin cancer prevention, at least the following parameters must be determined: relevant knowledge, attitude towards the measure, action or behaviour, participation or behaviour.	8.41. Consensus-based recommendation To evaluate the effectiveness of a communication-based intervention in terms of informed decision-making in connection with secondary skin cancer prevention, at least the following parameters must be determined: relevant knowledge about opportunities and risks of the measure, attitude towards the measure, action or behaviour, participation or non-participation.	Modified 2020
	8.4. Doctor-Patient Communication	
	8.42. Consensus-based recommendation A patient-centered form of communication must take place in doctor-patient conversations.	New 2020

Version 1.2	Version 2.1	Kommentare
	8.43. Consensus-based recommendation The doctor-patient conversation should be divided into two phases. The first phase should serve to clarify the patient's concerns (patient agenda). The second phase of the discussion is the doctor's agenda and should contain precise information for decision-making on examinations, therapies (including the benefits and harms of the various options), and the further course of action.	New 2020
	9. Health Economic Evaluation	
	9.1. Health Economic Evaluations of Measures for the Primary Prevention of Skin Cancer	
	8.62. Consensus-based recommendation The less sunbeds are used, the fewer sunbed-induced illness costs arise; therefore, the use of sunbeds must be avoided.	New 2020

Version 1.2	Version 2.1	Kommentare
	8.63. Consensus-based recommendation Various measures of primary skin cancer prevention show both an economic benefit and a health-related benefit. Therefore, investments in such measures should be increased.	New 2020
	9.2. Health Economic Evaluation of Measures of Secondary Prevention of Skin Cancer	
	8.64. Evidence-based statement Various measures of skin cancer screening can be classified as cost-effective based on international evidence. Screening of high-risk individuals has a more favourable cost-effectiveness ratio than population-based screening.	New 2020

11. Quality Indicators

Editorial note: The following is the result of the derivation of quality indicators from version 1.2. The quality indicators for version 2.0 were not edited for the reasons outlined below.

The derivation of quality indicators (QI) based on the strong recommendations within the S3 guideline Prevention of skin cancer went through the standardized process established within the guideline program oncology (see guideline report). This process has so far been used exclusively for guidelines on the diagnosis, therapy and follow-up of tumor diseases. The guideline presented here is the first to deal exclusively with the topic of prevention. This fundamentally different situation was discussed extensively in the QI working group. In the following, the special features and the consequences for the QI derivation are presented.

A core problem is the lack of translatability of guideline recommendations into clearly and unambiguously defined QIs, as well as the availability of corresponding data on possible indicators. In the field of primary prevention, behavioural indicators are the most important component of evaluation, with the aim of detecting changes in behaviour through appropriate interventions. However, such behavioural indicators would often have to be collected in the form of retrospective self-reporting, particularly in the context of primary prevention; as a result, the data are subject to subjective bias to a greater extent than behavioural measurements or routine medical data and must therefore be assessed as comparatively limited in terms of their objectivity and validity. This also applies in part to secondary prevention measures, where epidemiological data and data from health services research play a role in addition to behavioral indicators. Furthermore, if individual recommendations refer, for example, to the behaviour of large subpopulations or the general population, a complete survey based on routine data is hardly possible, if at all.

To compensate for the difficulties described, the guideline provides comprehensive recommendations for the formative and summative evaluation of information and education programmes in the field of primary and secondary prevention of skin cancer. Two areas can be distinguished in which the effectiveness of an intervention should be comprehensively evaluated in terms of both process and outcome: Behavioural prevention and relationship prevention.

In the area of behavioural prevention, questions need to be answered such as *What information has the citizen or certain target groups (e.g. parents) received and from what source*? *How are these perceived and processed?* This involves the survey of knowledge, but also the mapping of risk perception or attitudes as well as subjective informedness. Therefore, in addition to the behaviourally relevant endpoints, it is necessary to include intermediary factors that reflect the process of information dissemination and processing.

In relation prevention, the focus is on environmental factors and structures in the public sphere, such as in schools, kindergartens and the workplace, or in the area of urban development and urban planning. In this context, political or administrative framework conditions and processes play a formative role, which should be included in the evaluation. Evaluation can take place both within the framework of field experiments and with the help of process-accompanying non-experimental evaluation studies. Possible questions may include: *(How) have the legal, political and financial*

framework conditions required for the implementation of the measure been created? How were the relevant decision-makers involved and informed in the planning process? Which measures have been implemented in which areas and how? How are the measures received by the experts and multipliers and what effects do they have in the target groups, e.g. pupils, employees? Furthermore, individual recommendations of the guideline refer to the education, further education and training of multipliers such as physicians, medical assistants or other professional groups. Possible questions for the corresponding evaluation could be: *How well are the training contents tailored to the specifics of professional practice and everyday work of the respective professional group? How are the programmes structured in terms of content and how are the training materials prepared? Have prerequisites for participation in such training been created by the respective occupational groups? How are the programmes accepted by the respective occupational group, how are the imparted competences integrated into professional practice and what effects can be demonstrated, e.g. in patient counselling?* In addition, changes or additions in the further training regulations, licensing regulations, in nursing training, but also in the training of educators, child care workers or teachers also play a role. There is also the question of the *extent to which framework conditions for the implementation of prevention measures are taken into account in administrative systems, such as the medical billing system, e.g. in the form of a "consultation number*" .

In the evaluation of the HKS, hurdles due to the documentation requirements must also be presented. For the purpose of billing, each HKS examination must be fully documented electronically (according to §34 of the Cancer Screening Guideline) using software certified by the National Association of Statutory Health Insurance Physicians. This electronic documentation is also used for the evaluation, which is stipulated in §35 of the Cancer Screening Guideline. Target parameters of the evaluation include participation rates, suspected diagnoses and false-positive findings. However, a comprehensive evaluation of HKS also includes epidemiological endpoints such as mortality and morbidity (stage shift to earlier detected tumors), as well as interval cancers. These endpoints are of great importance for the evaluation of the effectiveness of a cancer screening programme and are also required internationally. However, due to the current data collection, a robust evaluation of the HKS is not possible, as the documentation is done without the necessary personal identification. A personal reference would allow a comparison with the epidemiological cancer registers, and the target tumours of the HKS can be divided into 'detected in screening' and 'not detected in screening'. This allows screening to be performed, for example, for possible mortality reduction in participants and non-participants.

In addition, due to the two-tier nature of skin cancer screening, it is possible that diagnoses are documented twice and therefore bias occurs when comparing suspected and confirmed diagnoses. Personal identification would also eliminate these biases. In order to provide comprehensive and scientific evidence of the effects of the HKS, it is recommended that the current electronic documentation be expanded and adapted with the relevant stakeholders to include the above-mentioned items.

For the reasons outlined above, no quality indicators could be derived based on this guideline.

12. List of Figures

13. List of Tables

14. Bibliography

1. Hurrelmann, K., Klotz, T., Haisch, J., Krankheitsprävention und GesundheitsförderungHans Huber Verlag, 2010.
2. Faltermaier, Toni, GesundheitspsychologieKohlhammer, 2017. 2, überarbeitete und erweiterte Auflage:
3. Hurrelmann, K., Klotz, T., Haisch, J., Lehrbuch Prävention und GesundheitsförderungHans Huber Verlag, 2009.
4. Hurrelmann, K., Richter, M., Gesundheits¬ und MedizinsoziologieBetlz Juventa, 2013.
5. Graf, C., Starke, D., Nellen, M., Anwendungsorientierung und Qualitätssicherung in der Krankheitsprävention und Gesundheitsförderung. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, 2008. 51:1321-1328:
6. Franzkowiak, P., Prävention und Krankheitsprävention, 2018.
7. Deutsche Gesellschaft für Nährstoffmedizin und Prävention e.V., Definition der Präventivmedizin, 2015., http://www.dgnp.de/wir-ueber-uns/definition-der-praeventionsmedizin.html
8. Starfield, B., Hyde, J., Gervas, J., Heath, I., The concept of prevention: a good idea gone astray?. J Epidemiol Community Health, 2008. 62(7): p. 580-3., https://www.ncbi.nlm.nih.gov/pubmed/18559439
9. Kühnlein, T., Sghedoni, D., Visentin, G., Gérvas, J., Jamoulle, M.,, Quartäre Prävention, eine Aufgabe für Hausärzte. Primary Care, 2010. 10(18): p. 350-354.
10. Widmer, D., Care and Do Not Harm: Possible Misunderstandings With Quaternary Prevention (P4) Comment on „Quaternary Prevention, an Answer of Family Doctors to Over Medicalization". Int J Health Policy Manag, 2015. 4(8): p. 561-3., https://www.ncbi.nlm.nih.gov/pubmed/26340401
11. Rosenbrock, R., Michel, C., Primäre Prävention - Bausteine für eine systematische GesundheitssicherungMedizinisch Wissenschaftliche Verlagsgesellschaft, 2007.
12. Kolenda, K.D., Ratje, U., Mehr Prävention!Hans Marseille Verlag GmbH, 2013.
13. Rosenbrock, R., Gerlinger, T., Gesundheitspolitik - Eine systematische Einführung, 2014.
14. Haisch, J., Hurrelmann, K., Klotz, T., Medizinische Prävention und GesundheitsförderungHans Huber Verlag, 2006.
15. Strech, D., Follmann, M., Klemperer, D., Lelgemann, M., Ollenschlager, G., Raspe, H., et.al. When Choosing Wisely meets clinical practice guidelines. Z Evid Fortbild Qual Gesundhwes, 2014. 108(10): p. 601-3., https://www.ncbi.nlm.nih.gov/pubmed/25499114
16. Kielbassa, C., Roza, L., Epe, B., Wavelength dependence of oxidative DNA damage induced by UV and visible light. Carcinogenesis, 1997. 18(4): p. 811-6., https://www.ncbi.nlm.nih.gov/pubmed/9111219
17. Perdiz, D., Grof, P., Mezzina, M., Nikaido, O., Moustacchi, E., Sage, E., Distribution and repair of bipyrimidine photoproducts in solar UV-irradiated mammalian cells. Possible role of Dewar photoproducts in solar mutagenesis. J Biol Chem, 2000. 275(35): p. 26732-42., https://www.ncbi.nlm.nih.gov/pubmed/10827179
18. Rochette, P. J., Therrien, J. P., Drouin, R., Perdiz, D., Bastien, N., Drobetsky, E. A., et.al. UVA-induced cyclobutane pyrimidine dimers form predominantly at thymine-thymine dipyrimidines and correlate with the mutation spectrum in rodent cells. Nucleic Acids Res, 2003. 31(11): p. 2786-94., https://www.ncbi.nlm.nih.gov/pubmed/12771205
19. Tornaletti, S., Rozek, D., Pfeifer, G. P., The distribution of UV photoproducts along the human p53 gene and its relation to mutations in skin cancer. Oncogene, 1993. 8(8): p. 2051-7., https://www.ncbi.nlm.nih.gov/pubmed/8336934
20. Tornaletti, S., Pfeifer, G. P., Slow repair of pyrimidine dimers at p53 mutation hotspots in skin cancer. Science, 1994. 263(5152): p. 1436-8., https://www.ncbi.nlm.nih.gov/pubmed/8128225
21. Berg, R. J., van Kranen, H. J., Rebel, H. G., de Vries, A., van Vloten, W. A., Van Kreijl, C. F., et.al. Early p53 alterations in mouse skin carcinogenesis by UVB radiation: immunohistochemical

detection of mutant p53 protein in clusters of preneoplastic epidermal cells. Proc Natl Acad Sci U S A, 1996. 93(1): p. 274-8., https://www.ncbi.nlm.nih.gov/pubmed/8552621
22. Luo, J. L., Tong, W. M., Yoon, J. H., Hergenhahn, M., Koomagi, R., Yang, Q., et.al. UV-induced DNA damage and mutations in Hupki (human p53 knock-in) mice recapitulate p53 hotspot alterations in sun-exposed human skin. Cancer Res, 2001. 61(22): p. 8158-63., https://www.ncbi.nlm.nih.gov/pubmed/11719445
23. Mitchell, D. L., Volkmer, B., Breitbart, E. W., Byrom, M., Lowery, M. G., Greinert, R., Identification of a non-dividing subpopulation of mouse and human epidermal cells exhibiting high levels of persistent ultraviolet photodamage. J Invest Dermatol, 2001. 117(3): p. 590-5., https://www.ncbi.nlm.nih.gov/pubmed/11564164
24. Mitchell, D. L., Byrom, M., Chiarello, S., Lowery, M. G., Effects of chronic exposure to ultraviolet B radiation on DNA repair in the dermis and epidermis of the hairless mouse. J Invest Dermatol, 2001. 116(2): p. 209-15., https://www.ncbi.nlm.nih.gov/pubmed/11179995
25. Gambardella, L., Barrandon, Y., The multifaceted adult epidermal stem cell. Curr Opin Cell Biol, 2003. 15(6): p. 771-7., https://www.ncbi.nlm.nih.gov/pubmed/14644204
26. Bickenbach, J. R., Holbrook, K. A., Label-retaining cells in human embryonic and fetal epidermis. J Invest Dermatol, 1987. 88(1): p. 42-6., https://www.ncbi.nlm.nih.gov/pubmed/3794386
27. Braun, K. M., Watt, F. M., Epidermal label-retaining cells: background and recent applications. J Investig Dermatol Symp Proc, 2004. 9(3): p. 196-201., https://www.ncbi.nlm.nih.gov/pubmed/15369213
28. Cairns, J., Mutation selection and the natural history of cancer. Nature, 1975. 255(5505): p. 197-200., https://www.ncbi.nlm.nih.gov/pubmed/1143315
29. Cairns, J., Somatic stem cells and the kinetics of mutagenesis and carcinogenesis. Proc Natl Acad Sci U S A, 2002. 99(16): p. 10567-70., https://www.ncbi.nlm.nih.gov/pubmed/12149477
30. Potten, C. S., Owen, G., Booth, D., Intestinal stem cells protect their genome by selective segregation of template DNA strands. J Cell Sci, 2002. 115(Pt 11): p. 2381-8., https://www.ncbi.nlm.nih.gov/pubmed/12006622
31. Quinn, A. G., Sikkink, S., Rees, J. L., Delineation of two distinct deleted regions on chromosome 9 in human non-melanoma skin cancers. Genes Chromosomes Cancer, 1994. 11(4): p. 222-5., https://www.ncbi.nlm.nih.gov/pubmed/7533525
32. Boukamp, P., Non-melanoma skin cancer: what drives tumor development and progression?. Carcinogenesis, 2005. 26(10): p. 1657-67., https://www.ncbi.nlm.nih.gov/pubmed/15905207
33. Rehman, I., Takata, M., Wu, Y. Y., Rees, J. L., Genetic change in actinic keratoses. Oncogene, 1996. 12(12): p. 2483-90., https://www.ncbi.nlm.nih.gov/pubmed/8700506
34. Popp, S., Waltering, S., Herbst, C., Moll, I., Boukamp, P., UV-B-type mutations and chromosomal imbalances indicate common pathways for the development of Merkel and skin squamous cell carcinomas. Int J Cancer, 2002. 99(3): p. 352-60., https://www.ncbi.nlm.nih.gov/pubmed/11992403
35. Rapp, A., Greulich, K. O., After double-strand break induction by UV-A, homologous recombination and nonhomologous end joining cooperate at the same DSB if both systems are available. J Cell Sci, 2004. 117(Pt 21): p. 4935-45., https://www.ncbi.nlm.nih.gov/pubmed/15367581
36. Greinert, R., Volkmer, B., Henning, S., Breitbart, E. W., Greulich, K. O., Cardoso, M. C., et.al. UVA-induced DNA double-strand breaks result from the repair of clustered oxidative DNA damages. Nucleic Acids Res, 2012. 40(20): p. 10263-73., https://www.ncbi.nlm.nih.gov/pubmed/22941639
37. Dulon, M., Weichenthal, M., Blettner, M., Breitbart, M., Hetzer, M., Greinert, R., et.al. Sun exposure and number of nevi in 5- to 6-year-old European children. J Clin Epidemiol, 2002. 55(11): p. 1075-81., https://www.ncbi.nlm.nih.gov/pubmed/12507670
38. Schaffer, J. V., Bolognia, J. L., The melanocortin-1 receptor: red hair and beyond. Arch Dermatol, 2001. 137(11): p. 1477-85., https://www.ncbi.nlm.nih.gov/pubmed/11708951

39. Gruis, N. A., van Doorn, R., Melanocortin 1 receptor function: shifting gears from determining skin and nevus phenotype to fetal growth. J Invest Dermatol, 2012. 132(8): p. 1953-5., https://www.ncbi.nlm.nih.gov/pubmed/22797298
40. Robinson, S., Dixon, S., August, S., Diffey, B., Wakamatsu, K., Ito, S., et.al. Protection against UVR involves MC1R-mediated non-pigmentary and pigmentary mechanisms in vivo. J Invest Dermatol, 2010. 130(7): p. 1904-13., https://www.ncbi.nlm.nih.gov/pubmed/20237490
41. Barnhill, R. L., Roush, G. C., Titus-Ernstoff, L., Ernstoff, M. S., Duray, P. H., Kirkwood, J. M., Comparison of nonfamilial and familial melanoma. Dermatology, 1992. 184(1): p. 2-7., https://www.ncbi.nlm.nih.gov/pubmed/1558990
42. Fountain, J. W., Bale, S. J., Housman, D. E., Dracopoli, N. C., Genetics of melanoma. Cancer Surv, 1990. 9(4): p. 645-71., https://www.ncbi.nlm.nih.gov/pubmed/2101727
43. Psaty, E. L., Scope, A., Halpern, A. C., Marghoob, A. A., Defining the patient at high risk for melanoma. Int J Dermatol, 2010. 49(4): p. 362-76., https://www.ncbi.nlm.nih.gov/pubmed/20465687
44. Mann, G. J., Pupo, G. M., Campain, A. E., Carter, C. D., Schramm, S. J., Pianova, S., et.al. BRAF Mutation, NRAS Mutation, and the Absence of an Immune-Related Expressed Gene Profile Predict Poor Outcome in Patients with Stage III Melanoma. J Invest Dermatol, 2012., https://www.ncbi.nlm.nih.gov/pubmed/22931913
45. Markovic, S. N., Erickson, L. A., Rao, R. D., Weenig, R. H., Pockaj, B. A., Bardia, A., et.al. Malignant melanoma in the 21st century, part 1: epidemiology, risk factors, screening, prevention, and diagnosis. Mayo Clin Proc, 2007. 82(3): p. 364-80., https://www.ncbi.nlm.nih.gov/pubmed/17352373
46. Hansson, J., Familial cutaneous melanoma. Adv Exp Med Biol, 2010. 685(Department of Oncology-Pathology, Karolinska Institutet, Karolinska University Hospital Solna S-171 76, Stockholm, Sweden. johan.hansson@ki.se): p. 134-45., https://www.ncbi.nlm.nih.gov/pubmed/20687502
47. Hussussian, C. J., Struewing, J. P., Goldstein, A. M., Higgins, P. A., Ally, D. S., Sheahan, M. D., et.al. Germline p16 mutations in familial melanoma. Nat Genet, 1994. 8(1): p. 15-21., https://www.ncbi.nlm.nih.gov/pubmed/7987387
48. Kamb, A., Shattuck-Eidens, D., Eeles, R., Liu, Q., Gruis, N. A., Ding, W., et.al. Analysis of the p16 gene (CDKN2) as a candidate for the chromosome 9p melanoma susceptibility locus. Nat Genet, 1994. 8(1): p. 23-6., https://www.ncbi.nlm.nih.gov/pubmed/7987388
49. Udayakumar, D., Mahato, B., Gabree, M., Tsao, H., Genetic determinants of cutaneous melanoma predisposition. Semin Cutan Med Surg, 2010. 29(3): p. 190-5., https://www.ncbi.nlm.nih.gov/pubmed/21051013
50. Chin, L., The genetics of malignant melanoma: lessons from mouse and man. Nat Rev Cancer, 2003. 3(8): p. 559-70., https://www.ncbi.nlm.nih.gov/pubmed/12894244
51. Sherr, C. J., The INK4a/ARF network in tumour suppression. Nat Rev Mol Cell Biol, 2001. 2(10): p. 731-7., https://www.ncbi.nlm.nih.gov/pubmed/11584300
52. Piccinin, S., Doglioni, C., Maestro, R., Vukosavljevic, T., Gasparotto, D., D'Orazi, C., et.al. p16/CDKN2 and CDK4 gene mutations in sporadic melanoma development and progression. Int J Cancer, 1997. 74(1): p. 26-30., https://www.ncbi.nlm.nih.gov/pubmed/9036865
53. Ha, L., Ichikawa, T., Anver, M., Dickins, R., Lowe, S., Sharpless, N. E., et.al. ARF functions as a melanoma tumor suppressor by inducing p53-independent senescence. Proc Natl Acad Sci U S A, 2007. 104(26): p. 10968-73., https://www.ncbi.nlm.nih.gov/pubmed/17576930
54. Garcia-Casado, Z., Nagore, E., Fernandez-Serra, A., Botella-Estrada, R., Lopez-Guerrero, J. A., A germline mutation of p14/ARF in a melanoma kindred. Melanoma Res, 2009. 19(5): p. 335-7., https://www.ncbi.nlm.nih.gov/pubmed/19741424
55. Randerson-Moor, J. A., Harland, M., Williams, S., Cuthbert-Heavens, D., Sheridan, E., Aveyard, J., et.al. A germline deletion of p14(ARF) but not CDKN2A in a melanoma-neural system tumour syndrome family. Hum Mol Genet, 2001. 10(1): p. 55-62., https://www.ncbi.nlm.nih.gov/pubmed/11136714

56. Daniotti, M., Oggionni, M., Ranzani, T., Vallacchi, V., Campi, V., Di Stasi, D., et.al. BRAF alterations are associated with complex mutational profiles in malignant melanoma. Oncogene, 2004. 23(35): p. 5968-77., https://www.ncbi.nlm.nih.gov/pubmed/15195137
57. Daniotti, M., Vallacchi, V., Rivoltini, L., Patuzzo, R., Santinami, M., Arienti, F., et.al. Detection of mutated BRAFV600E variant in circulating DNA of stage III-IV melanoma patients. Int J Cancer, 2007. 120(11): p. 2439-44., https://www.ncbi.nlm.nih.gov/pubmed/17315191
58. Sasaki, Y., Niu, C., Makino, R., Kudo, C., Sun, C., Watanabe, H., et.al. BRAF point mutations in primary melanoma show different prevalences by subtype. J Invest Dermatol, 2004. 123(1): p. 177-83., https://www.ncbi.nlm.nih.gov/pubmed/15191558
59. Sosman, J. A., Kim, K. B., Schuchter, L., Gonzalez, R., Pavlick, A. C., Weber, J. S., et.al. Survival in BRAF V600-mutant advanced melanoma treated with vemurafenib. N Engl J Med, 2012. 366(8): p. 707-14., https://www.ncbi.nlm.nih.gov/pubmed/22356324
60. Hodis, E., Watson, I. R., Kryukov, G. V., Arold, S. T., Imielinski, M., Theurillat, J. P., et.al. A landscape of driver mutations in melanoma. Cell, 2012. 150(2): p. 251-63., https://www.ncbi.nlm.nih.gov/pubmed/22817889
61. Kvaskoff, M., Whiteman, D. C., Zhao, Z. Z., Montgomery, G. W., Martin, N. G., Hayward, N. K., et.al. Polymorphisms in nevus-associated genes MTAP, PLA2G6, and IRF4 and the risk of invasive cutaneous melanoma. Twin Res Hum Genet, 2011. 14(5): p. 422-32., https://www.ncbi.nlm.nih.gov/pubmed/21962134
62. Whiteman, D. C., Watt, P., Purdie, D. M., Hughes, M. C., Hayward, N. K., Green, A. C., Melanocytic nevi, solar keratoses, and divergent pathways to cutaneous melanoma. J Natl Cancer Inst, 2003. 95(11): p. 806-12., https://www.ncbi.nlm.nih.gov/pubmed/12783935
63. Hayward, N., New developments in melanoma genetics. Curr Oncol Rep, 2000. 2(4): p. 300-6., https://www.ncbi.nlm.nih.gov/pubmed/11122857
64. Gray-Schopfer, V. C., Cheong, S. C., Chong, H., Chow, J., Moss, T., Abdel-Malek, Z. A., et.al. Cellular senescence in naevi and immortalisation in melanoma: a role for p16?. Br J Cancer, 2006. 95(4): p. 496-505., https://www.ncbi.nlm.nih.gov/pubmed/16880792
65. Bennett, D. C., Human melanocyte senescence and melanoma susceptibility genes. Oncogene, 2003. 22(20): p. 3063-9., https://www.ncbi.nlm.nih.gov/pubmed/12789281
66. Pfeifer, G. P., Besaratinia, A., UV wavelength-dependent DNA damage and human non-melanoma and melanoma skin cancer. Photochem Photobiol Sci, 2012. 11(1): p. 90-7.
67. Haferkamp, S., Becker, T. M., Scurr, L. L., Kefford, R. F., Rizos, H., p16INK4a-induced senescence is disabled by melanoma-associated mutations. Aging Cell, 2008. 7(5): p. 733-45., https://www.ncbi.nlm.nih.gov/pubmed/18843795
68. Demunter, A., Stas, M., Degreef, H., De Wolf-Peeters, C., van den Oord, J. J., Analysis of N- and K-ras mutations in the distinctive tumor progression phases of melanoma. J Invest Dermatol, 2001. 117(6): p. 1483-9., https://www.ncbi.nlm.nih.gov/pubmed/11886512
69. Demunter, A., Ahmadian, M. R., Libbrecht, L., Stas, M., Baens, M., Scheffzek, K., et.al. A novel N-ras mutation in malignant melanoma is associated with excellent prognosis. Cancer Res, 2001. 61(12): p. 4916-22., https://www.ncbi.nlm.nih.gov/pubmed/11406571
70. Omholt, K., Karsberg, S., Platz, A., Kanter, L., Ringborg, U., Hansson, J., Screening of N-ras codon 61 mutations in paired primary and metastatic cutaneous melanomas: mutations occur early and persist throughout tumor progression. Clin Cancer Res, 2002. 8(11): p. 3468-74., https://www.ncbi.nlm.nih.gov/pubmed/12429636
71. Eskandarpour, M., Huang, F., Reeves, K. A., Clark, E., Hansson, J., Oncogenic NRAS has multiple effects on the malignant phenotype of human melanoma cells cultured in vitro. Int J Cancer, 2009. 124(1): p. 16-26., https://www.ncbi.nlm.nih.gov/pubmed/18814281
72. Davies, H., Bignell, G. R., Cox, C., Stephens, P., Edkins, S., Clegg, S., et.al. Mutations of the BRAF gene in human cancer. Nature, 2002. 417(6892): p. 949-54., https://www.ncbi.nlm.nih.gov/pubmed/12068308

73. Brose, M. S., Volpe, P., Feldman, M., Kumar, M., Rishi, I., Gerrero, R., et.al. BRAF and RAS mutations in human lung cancer and melanoma. Cancer Res, 2002. 62(23): p. 6997-7000., https://www.ncbi.nlm.nih.gov/pubmed/12460918
74. Kumar, R., Angelini, S., Snellman, E., Hemminki, K., BRAF mutations are common somatic events in melanocytic nevi. J Invest Dermatol, 2004. 122(2): p. 342-8., https://www.ncbi.nlm.nih.gov/pubmed/15009715
75. Bloethner, S., Snellman, E., Bermejo, J. L., Hiripi, E., Gast, A., Thirumaran, R. K., et.al. Differential gene expression in melanocytic nevi with the V600E BRAF mutation. Genes Chromosomes Cancer, 2007. 46(11): p. 1019-27., https://www.ncbi.nlm.nih.gov/pubmed/17696195
76. Pollock, P. M., Harper, U. L., Hansen, K. S., Yudt, L. M., Stark, M., Robbins, C. M., et.al. High frequency of BRAF mutations in nevi. Nat Genet, 2003. 33(1): p. 19-20., https://www.ncbi.nlm.nih.gov/pubmed/12447372
77. Clark, W. H., Jr., Elder, D. E., Guerry, D. th, Braitman, L. E., Trock, B. J., Schultz, D., et.al. Model predicting survival in stage I melanoma based on tumor progression. J Natl Cancer Inst, 1989. 81(24): p. 1893-904., https://www.ncbi.nlm.nih.gov/pubmed/2593166
78. Schmid-Wendtner, M. H., Baumert, J., Eberle, J., Plewig, G., Volkenandt, M., Sander, C. A., Disease progression in patients with thin cutaneous melanomas (tumour thickness < or = 0.75 mm): clinical and epidemiological data from the Tumour Center Munich 1977-98. Br J Dermatol, 2003. 149(4): p. 788-93., https://www.ncbi.nlm.nih.gov/pubmed/14616371
79. Palmieri, G., Colombino, M., Casula, M., Manca, A., Mandala, M., Cossu, A., et.al. Molecular Pathways in Melanomagenesis: What We Learned from Next-Generation Sequencing Approaches. Curr Oncol Rep, 2018. 20(11): p. 86., https://www.ncbi.nlm.nih.gov/pubmed/30218391
80. Rivers, J. K., Is there more than one road to melanoma?. Lancet, 2004. 363(9410): p. 728-30., https://www.ncbi.nlm.nih.gov/pubmed/15005091
81. Maldonado, J. L., Fridlyand, J., Patel, H., Jain, A. N., Busam, K., Kageshita, T., et.al. Determinants of BRAF mutations in primary melanomas. J Natl Cancer Inst, 2003. 95(24): p. 1878-90., https://www.ncbi.nlm.nih.gov/pubmed/14679157
82. Sondak, V. K., Smalley, K., Targeting mutant BRAF and KIT in metastatic melanoma: ASCO 2009 meeting report. Pigment Cell Melanoma Res, 2009. 22(4): p. 386-7., https://www.ncbi.nlm.nih.gov/pubmed/19624312
83. Esteve-Puig, R., Canals, F., Colome, N., Merlino, G., Recio, J. A., Uncoupling of the LKB1-AMPKalpha energy sensor pathway by growth factors and oncogenic BRAF. PLoS One, 2009. 4(3): p. e4771., https://www.ncbi.nlm.nih.gov/pubmed/19274086
84. Lopez-Bergami, P., The long arm of BRAF V600E gets to mTORC1. Pigment Cell Melanoma Res, 2009. 22(3): p. 244-5., https://www.ncbi.nlm.nih.gov/pubmed/19338646
85. Zheng, B., Jeong, J. H., Asara, J. M., Yuan, Y. Y., Granter, S. R., Chin, L., et.al. Oncogenic B-RAF negatively regulates the tumor suppressor LKB1 to promote melanoma cell proliferation. Mol Cell, 2009. 33(2): p. 237-47., https://www.ncbi.nlm.nih.gov/pubmed/19187764
86. Zerp, S. F., van Elsas, A., Peltenburg, L. T., Schrier, P. I., p53 mutations in human cutaneous melanoma correlate with sun exposure but are not always involved in melanomagenesis. Br J Cancer, 1999. 79(5-6): p. 921-6., https://www.ncbi.nlm.nih.gov/pubmed/10070891
87. Whiteman, D. C., Parsons, P. G., Green, A. C., p53 expression and risk factors for cutaneous melanoma: a case-control study. Int J Cancer, 1998. 77(6): p. 843-8., https://www.ncbi.nlm.nih.gov/pubmed/9714052
88. Hoglund, M., Gisselsson, D., Hansen, G. B., White, V. A., Sall, T., Mitelman, F., et.al. Dissecting karyotypic patterns in malignant melanomas: temporal clustering of losses and gains in melanoma karyotypic evolution. Int J Cancer, 2004. 108(1): p. 57-65., https://www.ncbi.nlm.nih.gov/pubmed/14618616
89. Greinert, R., Breitbart, E.W., Volkmer, B., UV-radiation biology as part of cancer research. Life Science and radiation, 2004.
90. Li, G., Schaider, H., Satyamoorthy, K., Hanakawa, Y., Hashimoto, K., Herlyn, M., Downregulation of E-cadherin and Desmoglein 1 by autocrine hepatocyte growth factor during melanoma

development. Oncogene, 2001. 20(56): p. 8125-35., https://www.ncbi.nlm.nih.gov/pubmed/11781826
91. Healy, E., Rehman, I., Angus, B., Rees, J. L., Loss of heterozygosity in sporadic primary cutaneous melanoma. Genes Chromosomes Cancer, 1995. 12(2): p. 152-6., https://www.ncbi.nlm.nih.gov/pubmed/7535089
92. Celebi, J. T., Shendrik, I., Silvers, D. N., Peacocke, M., Identification of PTEN mutations in metastatic melanoma specimens. J Med Genet, 2000. 37(9): p. 653-7., https://www.ncbi.nlm.nih.gov/pubmed/10978354
93. Pollock, P. M., Walker, G. J., Glendening, J. M., Que Noy, T., Bloch, N. C., Fountain, J. W., et.al. PTEN inactivation is rare in melanoma tumours but occurs frequently in melanoma cell lines. Melanoma Res, 2002. 12(6): p. 565-75., https://www.ncbi.nlm.nih.gov/pubmed/12459646
94. Stambolic, V., Suzuki, A., de la Pompa, J. L., Brothers, G. M., Mirtsos, C., Sasaki, T., et.al. Negative regulation of PKB/Akt-dependent cell survival by the tumor suppressor PTEN. Cell, 1998. 95(1): p. 29-39., https://www.ncbi.nlm.nih.gov/pubmed/9778245
95. Blum, A., Epidemiologie und Risikofaktoren des malignen Melanoms. Onkologe, 2004. 10:
96. International Commission on Non-Ionizing Radiation Protection (ICNIRP), Proceedings Third International Non-Ionizing Radiation Workshop, Baden, Austria. R. Matthes (ed.), 1996.
97. Armstrong, B. K., Kricker, A., The epidemiology of UV induced skin cancer. J Photochem Photobiol B, 2001. 63(1-3): p. 8-18., https://www.ncbi.nlm.nih.gov/pubmed/11684447
98. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, IARC monographs on the evaluation of carcinogenic risks to humans. A review of human carcinogens: Radiation, 2012. 100D:
99. Gallagher, R. P., Hill, G. B., Bajdik, C. D., Fincham, S., Coldman, A. J., McLean, D. I., et.al. Sunlight exposure, pigmentary factors, and risk of nonmelanocytic skin cancer. I. Basal cell carcinoma. Arch Dermatol, 1995. 131(2): p. 157-63.
100. Ikehata, H., Ono, T., The mechanisms of UV mutagenesis. J Radiat Res, 2011. 52(2): p. 115-25., https://www.ncbi.nlm.nih.gov/pubmed/21436607
101. Cadet, J., Douki, T., Ravanat, J. L., Oxidatively generated base damage to cellular DNA. Free Radic Biol Med, 2010. 49(1): p. 9-21., https://www.ncbi.nlm.nih.gov/pubmed/20363317
102. Douki, T., Reynaud-Angelin, A., Cadet, J., Sage, E., Bipyrimidine photoproducts rather than oxidative lesions are the main type of DNA damage involved in the genotoxic effect of solar UVA radiation. Biochemistry, 2003. 42(30): p. 9221-6., https://www.ncbi.nlm.nih.gov/pubmed/12885257
103. Courdavault, S., Baudouin, C., Charveron, M., Favier, A., Cadet, J., Douki, T., Larger yield of cyclobutane dimers than 8-oxo-7,8-dihydroguanine in the DNA of UVA-irradiated human skin cells. Mutat Res, 2004. 556(1-2): p. 135-42., https://www.ncbi.nlm.nih.gov/pubmed/15491641
104. Mouret, S., Baudouin, C., Charveron, M., Favier, A., Cadet, J., Douki, T., Cyclobutane pyrimidine dimers are predominant DNA lesions in whole human skin exposed to UVA radiation. Proc Natl Acad Sci U S A, 2006. 103(37): p. 13765-70., https://www.ncbi.nlm.nih.gov/pubmed/16954188
105. Mouret, S., Forestier, A., Douki, T., The specificity of UVA-induced DNA damage in human melanocytes. Photochem Photobiol Sci, 2012. 11(1): p. 155-62., https://www.ncbi.nlm.nih.gov/pubmed/21986862
106. Kozmin, S. G., Pavlov, Y. I., Kunkel, T. A., Sage, E., Roles of Saccharomyces cerevisiae DNA polymerases Poleta and Polzeta in response to irradiation by simulated sunlight. Nucleic Acids Res, 2003. 31(15): p. 4541-52., https://www.ncbi.nlm.nih.gov/pubmed/12888515
107. Pfeifer, G. P., Besaratinia, A., UV wavelength-dependent DNA damage and human non-melanoma and melanoma skin cancer. Photochem Photobiol Sci, 2012. 11(1): p. 90-7., https://www.ncbi.nlm.nih.gov/pubmed/21804977
108. Tu, Y., Dammann, R., Pfeifer, G. P., Sequence and time-dependent deamination of cytosine bases in UVB-induced cyclobutane pyrimidine dimers in vivo. J Mol Biol, 1998. 284(2): p. 297-311., https://www.ncbi.nlm.nih.gov/pubmed/9813119

109. Cannistraro, V. J., Taylor, J. S., Acceleration of 5-methylcytosine deamination in cyclobutane dimers by G and its implications for UV-induced C-to-T mutation hotspots. J Mol Biol, 2009. 392(5): p. 1145-57., https://www.ncbi.nlm.nih.gov/pubmed/19631218
110. Hendriks, G., Jansen, J. G., Mullenders, L. H., de Wind, N., Transcription-coupled repair and apoptosis provide specific protection against transcription-associated mutagenesis by ultraviolet light. Transcription, 2010. 1(2): p. 95-8., https://www.ncbi.nlm.nih.gov/pubmed/21326899
111. Pleasance, E. D., Cheetham, R. K., Stephens, P. J., McBride, D. J., Humphray, S. J., Greenman, C. D., et.al. A comprehensive catalogue of somatic mutations from a human cancer genome. Nature, 2010. 463(7278): p. 191-6., https://www.ncbi.nlm.nih.gov/pubmed/20016485
112. Armstrong, B. K., Kricker, A., The epidemiology of UV induced skin cancer. J Photochem Photobiol B, 2001. 63(1-3): p. 8-18., https://www.ncbi.nlm.nih.gov/pubmed/11684447
113. Kricker, A., Armstrong, B. K., English, D. R., Heenan, P. J., Pigmentary and cutaneous risk factors for non-melanocytic skin cancer—a case-control study. Int J Cancer, 1991. 48(5): p. 650-62., https://www.ncbi.nlm.nih.gov/pubmed/2071226
114. Kricker, A., Armstrong, B. K., English, D. R., Heenan, P. J., A dose-response curve for sun exposure and basal cell carcinoma. Int J Cancer, 1995. 60(4): p. 482-8., https://www.ncbi.nlm.nih.gov/pubmed/7829261
115. Kricker, A., Armstrong, B. K., English, D. R., Heenan, P. J., Does intermittent sun exposure cause basal cell carcinoma? a case-control study in Western Australia. Int J Cancer, 1995. 60(4): p. 489-94., https://www.ncbi.nlm.nih.gov/pubmed/7829262
116. Rosso, S., Zanetti, R., Martinez, C., Tormo, M. J., Schraub, S., Sancho-Garnier, H., et.al. The multicentre south European study ‚Helios'. II: Different sun exposure patterns in the aetiology of basal cell and squamous cell carcinomas of the skin. Br J Cancer, 1996. 73(11): p. 1447-54., https://www.ncbi.nlm.nih.gov/pubmed/8645596
117. Vitasa, B. C., Taylor, H. R., Strickland, P. T., Rosenthal, F. S., West, S., Abbey, H., et.al. Association of nonmelanoma skin cancer and actinic keratosis with cumulative solar ultraviolet exposure in Maryland watermen. Cancer, 1990. 65(12): p. 2811-7., https://www.ncbi.nlm.nih.gov/pubmed/2340474
118. El Ghissassi, F., Baan, R., Straif, K., Grosse, Y., Secretan, B., Bouvard, V., et.al. A review of human carcinogens—part D: radiation. Lancet Oncol, 2009. 10(8): p. 751-2.
119. Zanetti, R., Rosso, S., Martinez, C., Navarro, C., Schraub, S., Sancho-Garnier, H., et.al. The multicentre south European study ‚Helios'. I: Skin characteristics and sunburns in basal cell and squamous cell carcinomas of the skin. Br J Cancer, 1996. 73(11): p. 1440-6., https://www.ncbi.nlm.nih.gov/pubmed/8645595
120. Kimonis, V. E., Goldstein, A. M., Pastakia, B., Yang, M. L., Kase, R., DiGiovanna, J. J., et.al. Clinical manifestations in 105 persons with nevoid basal cell carcinoma syndrome. Am J Med Genet, 1997. 69(3): p. 299-308., https://www.ncbi.nlm.nih.gov/pubmed/9096761
121. Shanley, S., Ratcliffe, J., Hockey, A., Haan, E., Oley, C., Ravine, D., et.al. Nevoid basal cell carcinoma syndrome: review of 118 affected individuals. Am J Med Genet, 1994. 50(3): p. 282-90., https://www.ncbi.nlm.nih.gov/pubmed/8042673
122. Hahn, H., Wicking, C., Zaphiropoulous, P. G., Gailani, M. R., Shanley, S., Chidambaram, A., et.al. Mutations of the human homolog of Drosophila patched in the nevoid basal cell carcinoma syndrome. Cell, 1996. 85(6): p. 841-51., https://www.ncbi.nlm.nih.gov/pubmed/8681379
123. Stone, D. M., Hynes, M., Armanini, M., Swanson, T. A., Gu, Q., Johnson, R. L., et.al. The tumour-suppressor gene patched encodes a candidate receptor for Sonic hedgehog. Nature, 1996. 384(6605): p. 129-34., https://www.ncbi.nlm.nih.gov/pubmed/8906787
124. Johnson, R. L., Rothman, A. L., Xie, J., Goodrich, L. V., Bare, J. W., Bonifas, J. M., et.al. Human homolog of patched, a candidate gene for the basal cell nevus syndrome. Science, 1996. 272(5268): p. 1668-71., https://www.ncbi.nlm.nih.gov/pubmed/8658145
125. Brellier, F., Marionnet, C., Chevallier-Lagente, O., Toftgard, R., Mauviel, A., Sarasin, A., et.al. Ultraviolet irradiation represses PATCHED gene transcription in human epidermal keratinocytes

through an activator protein-1-dependent process. Cancer Res, 2004. 64(8): p. 2699-704., https://www.ncbi.nlm.nih.gov/pubmed/15087382
126. Fan, H., Khavari, P. A., Sonic hedgehog opposes epithelial cell cycle arrest. J Cell Biol, 1999. 147(1): p. 71-6., https://www.ncbi.nlm.nih.gov/pubmed/10508856
127. Aszterbaum, M., Beech, J., Epstein, E. H., Jr., Ultraviolet radiation mutagenesis of hedgehog pathway genes in basal cell carcinomas. J Investig Dermatol Symp Proc, 1999. 4(1): p. 41-5., https://www.ncbi.nlm.nih.gov/pubmed/10537006
128. Grachtchouk, M., Mo, R., Yu, S., Zhang, X., Sasaki, H., Hui, C. C., et.al. Basal cell carcinomas in mice overexpressing Gli2 in skin. Nat Genet, 2000. 24(3): p. 216-7., https://www.ncbi.nlm.nih.gov/pubmed/10700170
129. Nilsson, M., Unden, A. B., Krause, D., Malmqwist, U., Raza, K., Zaphiropoulos, P. G., et.al. Induction of basal cell carcinomas and trichoepitheliomas in mice overexpressing GLI-1. Proc Natl Acad Sci U S A, 2000. 97(7): p. 3438-43., https://www.ncbi.nlm.nih.gov/pubmed/10725363
130. Oro, A. E., Higgins, K. M., Hu, Z., Bonifas, J. M., Epstein, E. H., Jr., Scott, M. P., Basal cell carcinomas in mice overexpressing sonic hedgehog. Science, 1997. 276(5313): p. 817-21., https://www.ncbi.nlm.nih.gov/pubmed/9115210
131. Grachtchouk, M., Pero, J., Yang, S. H., Ermilov, A. N., Michael, L. E., Wang, A., et.al. Basal cell carcinomas in mice arise from hair follicle stem cells and multiple epithelial progenitor populations. J Clin Invest, 2011. 121(5): p. 1768-81., https://www.ncbi.nlm.nih.gov/pubmed/21519145
132. Wang, G. Y., Wang, J., Mancianti, M. L., Epstein, E. H., Jr., Basal cell carcinomas arise from hair follicle stem cells in Ptch1(+/-) mice. Cancer Cell, 2011. 19(1): p. 114-24., https://www.ncbi.nlm.nih.gov/pubmed/21215705
133. Gailani, M. R., Stahle-Backdahl, M., Leffell, D. J., Glynn, M., Zaphiropoulos, P. G., Pressman, C., et.al. The role of the human homologue of Drosophila patched in sporadic basal cell carcinomas. Nat Genet, 1996. 14(1): p. 78-81., https://www.ncbi.nlm.nih.gov/pubmed/8782823
134. Xie, J., Murone, M., Luoh, S. M., Ryan, A., Gu, Q., Zhang, C., et.al. Activating Smoothened mutations in sporadic basal-cell carcinoma. Nature, 1998. 391(6662): p. 90-2., https://www.ncbi.nlm.nih.gov/pubmed/9422511
135. Lupi, O., Correlations between the Sonic Hedgehog pathway and basal cell carcinoma. Int J Dermatol, 2007. 46(11): p. 1113-7., https://www.ncbi.nlm.nih.gov/pubmed/17988327
136. Reifenberger, J., Wolter, M., Knobbe, C. B., Kohler, B., Schonicke, A., Scharwachter, C., et.al. Somatic mutations in the PTCH, SMOH, SUFUH and TP53 genes in sporadic basal cell carcinomas. Br J Dermatol, 2005. 152(1): p. 43-51., https://www.ncbi.nlm.nih.gov/pubmed/15656799
137. Bakshi, A., Chaudhary, S. C., Rana, M., Elmets, C. A., Athar, M., Basal cell carcinoma pathogenesis and therapy involving hedgehog signaling and beyond. Mol Carcinog, 2017. 56(12): p. 2543-2557., https://www.ncbi.nlm.nih.gov/pubmed/28574612
138. Aszterbaum, M., Epstein, J., Oro, A., Douglas, V., LeBoit, P. E., Scott, M. P., et.al. Ultraviolet and ionizing radiation enhance the growth of BCCs and trichoblastomas in patched heterozygous knockout mice. Nat Med, 1999. 5(11): p. 1285-91., https://www.ncbi.nlm.nih.gov/pubmed/10545995
139. Ridley, A. J., Whiteside, J. R., McMillan, T. J., Allinson, S. L., Cellular and sub-cellular responses to UVA in relation to carcinogenesis. Int J Radiat Biol, 2009. 85(3): p. 177-95., https://www.ncbi.nlm.nih.gov/pubmed/19296341
140. Daya-Grosjean, L., Couve-Privat, S., Sonic hedgehog signaling in basal cell carcinomas. Cancer Lett, 2005. 225(2): p. 181-92., https://www.ncbi.nlm.nih.gov/pubmed/15978322
141. Couve-Privat, S., Le Bret, M., Traiffort, E., Queille, S., Coulombe, J., Bouadjar, B., et.al. Functional analysis of novel sonic hedgehog gene mutations identified in basal cell carcinomas from xeroderma pigmentosum patients. Cancer Res, 2004. 64(10): p. 3559-65., https://www.ncbi.nlm.nih.gov/pubmed/15150112
142. Couve-Privat, S., Bouadjar, B., Avril, M. F., Sarasin, A., Daya-Grosjean, L., Significantly high levels of ultraviolet-specific mutations in the smoothened gene in basal cell carcinomas from DNA

repair-deficient xeroderma pigmentosum patients. Cancer Res, 2002. 62(24): p. 7186-9., https://www.ncbi.nlm.nih.gov/pubmed/12499255
143. Daya-Grosjean, L., Sarasin, A., UV-specific mutations of the human patched gene in basal cell carcinomas from normal individuals and xeroderma pigmentosum patients. Mutat Res, 2000. 450(1-2): p. 193-9., https://www.ncbi.nlm.nih.gov/pubmed/10838143
144. Evans, T., Boonchai, W., Shanley, S., Smyth, I., Gillies, S., Georgas, K., et.al. The spectrum of patched mutations in a collection of Australian basal cell carcinomas. Hum Mutat, 2000. 16(1): p. 43-8., https://www.ncbi.nlm.nih.gov/pubmed/10874304
145. Kim, M. Y., Park, H. J., Baek, S. C., Byun, D. G., Houh, D., Mutations of the p53 and PTCH gene in basal cell carcinomas: UV mutation signature and strand bias. J Dermatol Sci, 2002. 29(1): p. 1-9., https://www.ncbi.nlm.nih.gov/pubmed/12007715
146. Ratner, D., Peacocke, M., Zhang, H., Ping, X. L., Tsou, H. C., UV-specific p53 and PTCH mutations in sporadic basal cell carcinoma of sun-exposed skin. J Am Acad Dermatol, 2001. 44(2): p. 293-7., https://www.ncbi.nlm.nih.gov/pubmed/11174390
147. Bolshakov, S., Walker, C. M., Strom, S. S., Selvan, M. S., Clayman, G. L., El-Naggar, A., et.al. p53 mutations in human aggressive and nonaggressive basal and squamous cell carcinomas. Clin Cancer Res, 2003. 9(1): p. 228-34., https://www.ncbi.nlm.nih.gov/pubmed/12538474
148. Boehnke, K., Falkowska-Hansen, B., Stark, H. J., Boukamp, P., Stem cells of the human epidermis and their niche: composition and function in epidermal regeneration and carcinogenesis. Carcinogenesis, 2012. 33(7): p. 1247-58., https://www.ncbi.nlm.nih.gov/pubmed/22461521
149. Jin, Y., Mertens, F., Persson, B., Warloe, T., Gullestad, H. P., Salemark, L., et.al. Nonrandom numerical chromosome abnormalities in basal cell carcinomas. Cancer Genet Cytogenet, 1998. 103(1): p. 35-42., https://www.ncbi.nlm.nih.gov/pubmed/9595042
150. Jin, Y., Martins, C., Salemark, L., Persson, B., Jin, C., Miranda, J., et.al. Nonrandom karyotypic features in basal cell carcinomas of the skin. Cancer Genet Cytogenet, 2001. 131(2): p. 109-19., https://www.ncbi.nlm.nih.gov/pubmed/11750050
151. Karagas, M. R., Zens, M. S., Nelson, H. H., Mabuchi, K., Perry, A. E., Stukel, T. A., et.al. Measures of cumulative exposure from a standardized sun exposure history questionnaire: a comparison with histologic assessment of solar skin damage. Am J Epidemiol, 2007. 165(6): p. 719-26., https://www.ncbi.nlm.nih.gov/pubmed/17204514
152. Kennedy, C., Bajdik, C. D., Willemze, R., De Gruijl, F. R., Bouwes Bavinck, J. N., Leiden Skin Cancer, Study, The influence of painful sunburns and lifetime sun exposure on the risk of actinic keratoses, seborrheic warts, melanocytic nevi, atypical nevi, and skin cancer. J Invest Dermatol, 2003. 120(6): p. 1087-93., https://www.ncbi.nlm.nih.gov/pubmed/12787139
153. Salasche, S. J., Epidemiology of actinic keratoses and squamous cell carcinoma. J Am Acad Dermatol, 2000. 42(1 Pt 2): p. 4-7., https://www.ncbi.nlm.nih.gov/pubmed/10607349
154. Cockerell, C. J., Histopathology of incipient intraepidermal squamous cell carcinoma (‚actinic keratosis'). Journal of the American Academy of Dermatology, 2000. p. 42(1 II)(pp S11-S17), 2000., https://www.ncbi.nlm.nih.gov/pubmed/10607351
155. Dodson, J. M., DeSpain, J., Hewett, J. E., Clark, D. P., Malignant potential of actinic keratoses and the controversy over treatment. A patient-oriented perspective. Arch Dermatol, 1991. 127(7): p. 1029-31., https://www.ncbi.nlm.nih.gov/pubmed/2064402
156. Glogau, R. G., The risk of progression to invasive disease. J Am Acad Dermatol, 2000. 42(1 Pt 2): p. 23-4., https://www.ncbi.nlm.nih.gov/pubmed/10607353
157. Marks, R., Rennie, G., Selwood, T., The relationship of basal cell carcinomas and squamous cell carcinomas to solar keratoses. Arch Dermatol, 1988. 124(7): p. 1039-42., https://www.ncbi.nlm.nih.gov/pubmed/3389848
158. Marks, R., Rennie, G., Selwood, T. S., Malignant transformation of solar keratoses to squamous cell carcinoma. Lancet, 1988. 1(8589): p. 795-7., https://www.ncbi.nlm.nih.gov/pubmed/2895318

159. Czarnecki, D., Meehan, C. J., Bruce, F., Culjak, G., The majority of cutaneous squamous cell carcinomas arise in actinic keratoses. J Cutan Med Surg, 2002. 6(3): p. 207-9., https://www.ncbi.nlm.nih.gov/pubmed/11951126
160. Criscione, V. D., Weinstock, M. A., Naylor, M. F., Luque, C., Eide, M. J., Bingham, S. F., et.al. Actinic keratoses: Natural history and risk of malignant transformation in the Veterans Affairs Topical Tretinoin Chemoprevention Trial. Cancer, 2009. 115(11): p. 2523-30., https://www.ncbi.nlm.nih.gov/pubmed/19382202
161. Chen, G. J., Feldman, S. R., Williford, P. M., Hester, E. J., Kiang, S. H., Gill, I., et.al. Clinical diagnosis of actinic keratosis identifies an elderly population at high risk of developing skin cancer. Dermatol Surg, 2005. 31(1): p. 43-7., https://www.ncbi.nlm.nih.gov/pubmed/15720095
162. Quaedvlieg, P. J., Tirsi, E., Thissen, M. R., Krekels, G. A., Actinic keratosis: how to differentiate the good from the bad ones?. Eur J Dermatol, 2006. 16(4): p. 335-9., https://www.ncbi.nlm.nih.gov/pubmed/16935787
163. Feldman, S. R., Fleischer, A. B., Jr., Progression of actinic keratosis to squamous cell carcinoma revisited: clinical and treatment implications. Cutis, 2011. 87(4): p. 201-7., https://www.ncbi.nlm.nih.gov/pubmed/21644496
164. Padilla, R. S., Sebastian, S., Jiang, Z., Nindl, I., Larson, R., Gene expression patterns of normal human skin, actinic keratosis, and squamous cell carcinoma: a spectrum of disease progression. Arch Dermatol, 2010. 146(3): p. 288-93., https://www.ncbi.nlm.nih.gov/pubmed/20231500
165. Kanellou, P., Zaravinos, A., Zioga, M., Stratigos, A., Baritaki, S., Soufla, G., et.al. Genomic instability, mutations and expression analysis of the tumour suppressor genes p14(ARF), p15(INK4b), p16(INK4a) and p53 in actinic keratosis. Cancer Lett, 2008. 264(1): p. 145-61., https://www.ncbi.nlm.nih.gov/pubmed/18331779
166. Drake, L. A., Ceilley, R. I., Cornelison, R. L., Dobes, W. L., Dorner, W., Goltz, R. W., et.al. Guidelines of care for actinic keratoses. Committee on Guidelines of Care. J Am Acad Dermatol, 1995. 32(1): p. 95-8., https://www.ncbi.nlm.nih.gov/pubmed/7529779
167. Lober, B. A., Lober, C. W., Actinic keratosis is squamous cell carcinoma. South Med J, 2000. 93(7): p. 650-5., https://www.ncbi.nlm.nih.gov/pubmed/10923948
168. Stulberg, D. L., Crandell, B., Fawcett, R. S., Diagnosis and treatment of basal cell and squamous cell carcinomas. Am Fam Physician, 2004. 70(8): p. 1481-8., https://www.ncbi.nlm.nih.gov/pubmed/15526735
169. Ackerman, A. B., Mones, J. M., Solar (actinic) keratosis is squamous cell carcinoma. Br J Dermatol, 2006. 155(1): p. 9-22., https://www.ncbi.nlm.nih.gov/pubmed/16792746
170. Anwar, J., Wrone, D. A., Kimyai-Asadi, A., Alam, M., The development of actinic keratosis into invasive squamous cell carcinoma: evidence and evolving classification schemes. Clin Dermatol, 2004. 22(3): p. 189-96., https://www.ncbi.nlm.nih.gov/pubmed/15262304
171. Roewert-Huber, J., Stockfleth, E., Kerl, H., Pathology and pathobiology of actinic (solar) keratosis - an update. Br J Dermatol, 2007. 157 Suppl 2: p. 18-20., https://www.ncbi.nlm.nih.gov/pubmed/18067626
172. Fernandez-Figueras, M. T., Carrato, C., Saenz, X., Puig, L., Musulen, E., Ferrandiz, C., et.al. Actinic keratosis with atypical basal cells (AK I) is the most common lesion associated with invasive squamous cell carcinoma of the skin. J Eur Acad Dermatol Venereol, 2015. 29(5): p. 991-7., https://www.ncbi.nlm.nih.gov/pubmed/25428612
173. Brash, D. E., Sunlight and the onset of skin cancer. Trends Genet, 1997. 13(10): p. 410-4., https://www.ncbi.nlm.nih.gov/pubmed/9351343
174. Cleaver, J. E., Crowley, E., UV damage, DNA repair and skin carcinogenesis. Front Biosci, 2002. 7: p. d1024-43., https://www.ncbi.nlm.nih.gov/pubmed/11897551
175. Ziegler, A., Jonason, A. S., Leffell, D. J., Simon, J. A., Sharma, H. W., Kimmelman, J., et.al. Sunburn and p53 in the onset of skin cancer. Nature, 1994. 372(6508): p. 773-6., https://www.ncbi.nlm.nih.gov/pubmed/7997263
176. Park, W. S., Lee, H. K., Lee, J. Y., Yoo, N. J., Kim, C. S., Kim, S. H., p53 mutations in solar keratoses. Hum Pathol, 1996. 27(11): p. 1180-4., https://www.ncbi.nlm.nih.gov/pubmed/8912828

177. Ortonne, J. P., From actinic keratosis to squamous cell carcinoma. Br J Dermatol, 2002. 146 Suppl 61: p. 20-3., https://www.ncbi.nlm.nih.gov/pubmed/11966728
178. Mitchell, D. L., The relative cytotoxicity of (6-4) photoproducts and cyclobutane dimers in mammalian cells. Photochem Photobiol, 1988. 48(1): p. 51-7., https://www.ncbi.nlm.nih.gov/pubmed/3217442
179. Greinert, R., Boguhn, O., Harder, D., Breitbart, E. W., Mitchell, D. L., Volkmer, B., The dose dependence of cyclobutane dimer induction and repair in UVB-irradiated human keratinocytes. Photochem Photobiol, 2000. 72(5): p. 701-8., https://www.ncbi.nlm.nih.gov/pubmed/11107858
180. Robinson, J. K., Dahiya, M., Basal cell carcinoma with pulmonary and lymph node metastasis causing death. Arch Dermatol, 2003. 139(5): p. 643-8., https://www.ncbi.nlm.nih.gov/pubmed/12756102
181. LeBoit, P.E., Burg, G., Weedon, D., Sarasain, A., World Health Organization Classification of Tumours. Pathology and Genetics of Skin TumoursIARC Press, 2006., http://www.iarc.fr/en/publications/pdfs-online/pat-gen/bb6/index.php
182. Scrivener, Y., Grosshans, E., Cribier, B., Variations of basal cell carcinomas according to gender, age, location and histopathological subtype. Br J Dermatol, 2002. 147(1): p. 41-7., https://www.ncbi.nlm.nih.gov/pubmed/12100183
183. Union For International Cancer Control (UICC), John Wiley & Sons, Ltd., TNM-Klassifikation maligner Tumoren. Achte AuflageWILEY-VCH Verlag GmbH & Co. KGaA, Herausgegeben von Ch. Wittekind, 2017.
184. Karagas, M. R., Greenberg, E. R., Spencer, S. K., Stukel, T. A., Mott, L. A., Increase in incidence rates of basal cell and squamous cell skin cancer in New Hampshire, USA. New Hampshire Skin Cancer Study Group. Int J Cancer, 1999. 81(4): p. 555-9., https://www.ncbi.nlm.nih.gov/pubmed/10225444
185. Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V., GEKID-Atlas „Inzidenz und Mortalität von Krebserkrankungen in den Bundesländern; interaktiver Atlas der Gesellschaft für epidemiologische Krebsregister in Deutschland, 2019., http://www.ekr.med.uni-erlangen.de/GEKID/Atlas/CurrentVersion/Inzidenz/atlas.html
186. Eisemann, N., Jansen, L., Holleczek, B., Waldmann, A., Luttmann, S., Emrich, K., et.al. Up-to-date results on survival of patients with melanoma in Germany. Br J Dermatol, 2012. 167(3): p. 606-12., https://www.ncbi.nlm.nih.gov/pubmed/22564081
187. Zentrum für Krebsregisterdaten und Gesellschaft der epidemiologischen Krebsregister in Deutschland e. V., Krebs in Deutschland 2013/2014Robert Koch-Institut. Gesundheitsberichterstattung des Bundes, 2017.
188. Robert Koch-Institut, Bericht zum Krebsgeschehen in Deutschland 2016, 2016.
189. Statistisches Bundesamt, Sterbefälle, Sterbeziffern (je 100.000 Einwohner, altersstandardisiert) (ab 1998). Gesundheitsberichterstattung des Bundes. Elektronische RessourceStatistisches Bundesamt, 2012. 2012:, http://www.gbe-bund.de
190. International Agency for Research on Cancer, Cancer Today. Data visualization tolls for exploring the global cancer burden in 2018, gco.iarc.fr/today/home
191. Arnold, M., Holterhues, C., Hollestein, L. M., Coebergh, J. W., Nijsten, T., Pukkala, E., et.al. Trends in incidence and predictions of cutaneous melanoma across Europe up to 2015. J Eur Acad Dermatol Venereol, 2014. 28(9): p. 1170-8., https://www.ncbi.nlm.nih.gov/pubmed/23962170
192. Brunssen, A., Jansen, L., Eisemann, N., Waldmann, A., Weberpals, J., Kraywinkel, K., et.al. Long-term relative survival from melanoma in Germany 1997-2013. Melanoma Res, 2020. 30(4): p. 386-395., https://www.ncbi.nlm.nih.gov/pubmed/30020195
193. Erdmann, F., Lortet-Tieulent, J., Schuz, J., Zeeb, H., Greinert, R., Breitbart, E. W., et.al. International trends in the incidence of malignant melanoma 1953-2008--are recent generations at higher or lower risk?. Int J Cancer, 2013. 132(2): p. 385-400., https://www.ncbi.nlm.nih.gov/pubmed/22532371

194. Australian Government: Cancer Australia, Cancer incidence, https://ncci.canceraustralia.gov.au/diagnosis/cancer-incidence/cancer-incidence
195. Baade, P., Coory, M., Trends in melanoma mortality in Australia: 1950-2002 and their implications for melanoma control. Aust N Z J Public Health, 2005. 29(4): p. 383-6., https://www.ncbi.nlm.nih.gov/pubmed/16222938
196. Aitken, J. F., Youlden, D. R., Baade, P. D., Soyer, H. P., Green, A. C., Smithers, B. M., Generational shift in melanoma incidence and mortality in Queensland, Australia, 1995-2014. Int J Cancer, 2018. 142(8): p. 1528-1535., https://www.ncbi.nlm.nih.gov/pubmed/29105744
197. Katalinic, A., Waldmann, A., Weinstock, M. A., Geller, A. C., Eisemann, N., Greinert, R., et.al. Does skin cancer screening save lives?: an observational study comparing trends in melanoma mortality in regions with and without screening. Cancer, 2012. 118(21): p. 5395-402., https://www.ncbi.nlm.nih.gov/pubmed/22517033
198. Katalinic, A., Eisemann, N., Waldmann, A., Hautkrebsscreening in Deutschland. Erfassung der Melanominzidenz und -sterblichkeit von 2008 bis 2013. Skin Cancer Screening in Germany - Documenting Melanoma Incidence and Mortality From 2008 to 2013. Deutsches Ärzteblatt : Ausgabe A, Praxis-Ausgabe : niedergelassene Ärzte, 2015. 112(38):, http://www.zbmed.de/ccmedimages/2015/ZBMED-20159195155-3.pdf
199. Veit, Ch., Lüken, F., Melsheimer, O., Evaluation der Screeninguntersuchungen auf Hautkrebs gemäß Krebsfrüherkennungs-Richtlinie des Gemeinsamen Bundesausschusses. Abschlussbericht 2009 –2010im Auftrag des Gemeinsamen Bundesausschusses, 2015.
200. Evaluation des bundesweiten Hautkrebsscreenings - Innovationsausschuss fördert Projekt EvaSCaUniversitätsklinikum Essen, 2019., https://www.uni-due.de/med/meldung.php?id=802
201. Katalinic, Alexander, Kunze, Uta, Schäfer, Torsten, Epidemiology of cutaneous melanoma and non-melanoma skin cancer in Schleswig-Holstein, Germany: incidence, clinical subtypes, tumour stages and localization (epidemiology of skin cancer). The British Journal of Dermatology, 2003. 149: p. 1200-1206.
202. Demers, A. A., Nugent, Z., Mihalcioiu, C., Wiseman, M. C., Kliewer, E. V., Trends of nonmelanoma skin cancer from 1960 through 2000 in a Canadian population. J Am Acad Dermatol, 2005. 53(2): p. 320-8., https://www.ncbi.nlm.nih.gov/pubmed/16021129
203. Brewster, D. H., Bhatti, L. A., Inglis, J. H., Nairn, E. R., Doherty, V. R., Recent trends in incidence of nonmelanoma skin cancers in the East of Scotland, 1992-2003. Br J Dermatol, 2007. 156(6): p. 1295-300., https://www.ncbi.nlm.nih.gov/pubmed/17535229
204. Bath-Hextall, F., Leonardi-Bee, J., Smith, C., Meal, A., Hubbard, R., Trends in incidence of skin basal cell carcinoma. Additional evidence from a UK primary care database study. Int J Cancer, 2007. 121(9): p. 2105-8., https://www.ncbi.nlm.nih.gov/pubmed/17640064
205. Breitbart, E. W., Waldmann, A., Nolte, S., Capellaro, M., Greinert, R., Volkmer, B., et.al. Systematic skin cancer screening in Northern Germany. J Am Acad Dermatol, 2012. 66(2): p. 201-11., https://www.ncbi.nlm.nih.gov/pubmed/22074699
206. Waldmann, A., Nolte, S., Weinstock, M. A., Breitbart, E. W., Eisemann, N., Geller, A. C., et.al. Skin cancer screening participation and impact on melanoma incidence in Germany—an observational study on incidence trends in regions with and without population-based screening. Br J Cancer, 2012. 106(5): p. 970-4., https://www.ncbi.nlm.nih.gov/pubmed/22294187
207. Hübner, J., Hübner, Franziska, Terheyden, Peter, Katalinic, A., Trendwende bei der Hautkrebsmortalität. Eine Analyse der Entwicklung in Deutschland 1998 bis 2017. Der Hautarzt, 2019. 70: p. 989–992.
208. Gallagher, R. P., Hill, G. B., Bajdik, C. D., Coldman, A. J., Fincham, S., McLean, D. I., et.al. Sunlight exposure, pigmentation factors, and risk of nonmelanocytic skin cancer. II. Squamous cell carcinoma. Arch Dermatol, 1995. 131(2): p. 164-9.
209. Gandini, S., Sera, F., Cattaruzza, M. S., Pasquini, P., Zanetti, R., Masini, C., et.al. Meta-analysis of risk factors for cutaneous melanoma: III. Family history, actinic damage and phenotypic factors. Eur J Cancer, 2005. 41(14): p. 2040-59., https://www.ncbi.nlm.nih.gov/pubmed/16125929

210. Kinsler, V. A., Birley, J., Atherton, D. J., Great Ormond Street Hospital for Children Registry for congenital melanocytic naevi: prospective study 1988-2007. Part 1-epidemiology, phenotype and outcomes. Br J Dermatol, 2009. 160(1): p. 143-50., https://www.ncbi.nlm.nih.gov/pubmed/18811688
211. Krengel, S., Hauschild, A., Schafer, T., Melanoma risk in congenital melanocytic naevi: a systematic review. Br J Dermatol, 2006. 155(1): p. 1-8., https://www.ncbi.nlm.nih.gov/pubmed/16792745
212. Krengel, S., Scope, A., Dusza, S. W., Vonthein, R., Marghoob, A. A., New recommendations for the categorization of cutaneous features of congenital melanocytic nevi. J Am Acad Dermatol, 2013. 68(3): p. 441-51., https://www.ncbi.nlm.nih.gov/pubmed/22982004
213. Price, H. N., Schaffer, J. V., Congenital melanocytic nevi-when to worry and how to treat: Facts and controversies. Clin Dermatol, 2010. 28(3): p. 293-302.
214. Castilla, E. E., da Graca Dutra, M., Orioli-Parreiras, I. M., Epidemiology of congenital pigmented naevi: II. Risk factors. Br J Dermatol, 1981. 104(4): p. 421-7.
215. Illig, L., Weidner, F., Hundeiker, M., Gartmann, H., Biess, B., Leyh, F., et.al. Congenital nevi less than or equal to 10 cm as precursors to melanoma. 52 cases, a review, and a new conception. Arch Dermatol, 1985. 121(10): p. 1274-81., https://www.ncbi.nlm.nih.gov/pubmed/4037820
216. Kinsler, V. A., Thomas, A. C., Ishida, M., Bulstrode, N. W., Loughlin, S., Hing, S., et.al. Multiple congenital melanocytic nevi and neurocutaneous melanosis are caused by postzygotic mutations in codon 61 of NRAS. J Invest Dermatol, 2013. 133(9): p. 2229-36.
217. Bastian, B. C., Xiong, J., Frieden, I. J., Williams, M. L., Chou, P., Busam, K., et.al. Genetic changes in neoplasms arising in congenital melanocytic nevi: differences between nodular proliferations and melanomas. Am J Pathol, 2002. 161(4): p. 1163-9.
218. Gallagher, R. P., Hill, G. B., Bajdik, C. D., Fincham, S., Coldman, A. J., McLean, D. I., et.al. Sunlight exposure, pigmentary factors, and risk of nonmelanocytic skin cancer. I. Basal cell carcinoma. Arch Dermatol, 1995. 131(2): p. 157-63., https://www.ncbi.nlm.nih.gov/pubmed/7857111
219. Dulon, M., Weichenthal, M., Blettner, M., Breitbart, M., Hetzer, M., Greinert, R., et.al. Sun exposure and number of nevi in 5- to 6-year-old European children. J Clin Epidemiol, 2002. 55(11): p. 1075-81.
220. Marcil, I., Stern, R. S., Risk of developing a subsequent nonmelanoma skin cancer in patients with a history of nonmelanoma skin cancer: a critical review of the literature and meta-analysis. Arch Dermatol, 2000. 136(12): p. 1524-30.
221. Frankel, D. H., Hanusa, B. H., Zitelli, J. A., New primary nonmelanoma skin cancer in patients with a history of squamous cell carcinoma of the skin. Implications and recommendations for follow-up. J Am Acad Dermatol, 1992. 26(5 Pt 1): p. 720-6., https://www.ncbi.nlm.nih.gov/pubmed/1583171
222. DiGiovanna, J. J., Posttransplantation skin cancer: scope of the problem, management, and role for systemic retinoid chemoprevention. Transplant Proc, 1998. 30(6): p. 2771-5; discussion 2776-8., https://www.ncbi.nlm.nih.gov/pubmed/9745564
223. Berg, D., Otley, C. C., Skin cancer in organ transplant recipients: Epidemiology, pathogenesis, and management. J Am Acad Dermatol, 2002. 47(1): p. 1-17; quiz 18-20., https://www.ncbi.nlm.nih.gov/pubmed/12077575
224. Dantal, J., Hourmant, M., Cantarovich, D., Giral, M., Blancho, G., Dreno, B., et.al. Effect of long-term immunosuppression in kidney-graft recipients on cancer incidence: randomised comparison of two cyclosporin regimens. Lancet, 1998. 351(9103): p. 623-8., https://www.ncbi.nlm.nih.gov/pubmed/9500317
225. Espana, A., Redondo, P., Fernandez, A. L., Zabala, M., Herreros, J., Llorens, R., et.al. Skin cancer in heart transplant recipients. J Am Acad Dermatol, 1995. 32(3): p. 458-65., https://www.ncbi.nlm.nih.gov/pubmed/7868716
226. Jensen, P., Hansen, S., Moller, B., Leivestad, T., Pfeffer, P., Geiran, O., et.al. Skin cancer in kidney and heart transplant recipients and different long-term immunosuppressive therapy

regimens. J Am Acad Dermatol, 1999. 40(2 Pt 1): p. 177-86., https://www.ncbi.nlm.nih.gov/pubmed/10025742
227. Otley, C. C., Immunosuppression and skin cancer: pathogenetic insights, therapeutic challenges, and opportunities for innovation. Arch Dermatol, 2002. 138(6): p. 827-8., https://www.ncbi.nlm.nih.gov/pubmed/12056967
228. Preciado, D. A., Matas, A., Adams, G. L., Squamous cell carcinoma of the head and neck in solid organ transplant recipients. Head Neck, 2002. 24(4): p. 319-25., https://www.ncbi.nlm.nih.gov/pubmed/11933172
229. Marshall, V., Premalignant and malignant skin tumours in immunosuppressed patients. Transplantation, 1974. 17(3): p. 272-5., https://www.ncbi.nlm.nih.gov/pubmed/4592184
230. Euvrard, S., Kanitakis, J., Pouteil-Noble, C., Dureau, G., Touraine, J. L., Faure, M., et.al. Comparative epidemiologic study of premalignant and malignant epithelial cutaneous lesions developing after kidney and heart transplantation. J Am Acad Dermatol, 1995. 33(2 Pt 1): p. 222-9.
231. Fortina, A. B., Caforio, A. L., Piaserico, S., Alaibac, M., Tona, F., Feltrin, G., et.al. Skin cancer in heart transplant recipients: frequency and risk factor analysis. J Heart Lung Transplant, 2000. 19(3): p. 249-55., https://www.ncbi.nlm.nih.gov/pubmed/10713249
232. Gjersvik, P., Hansen, S., Moller, B., Leivestad, T., Geiran, O., Simonsen, S., et.al. Are heart transplant recipients more likely to develop skin cancer than kidney transplant recipients?. Transpl Int, 2000. 13 Suppl 1: p. S380-1., https://www.ncbi.nlm.nih.gov/pubmed/11112037
233. Naldi, L., Fortina, A. B., Lovati, S., Barba, A., Gotti, E., Tessari, G., et.al. Risk of nonmelanoma skin cancer in Italian organ transplant recipients. A registry-based study. Transplantation, 2000. 70(10): p. 1479-84.
234. Tessari, G., Naldi, L., Boschiero, L., Nacchia, F., Fior, F., Forni, A., et.al. Incidence and clinical predictors of a subsequent nonmelanoma skin cancer in solid organ transplant recipients with a first nonmelanoma skin cancer: a multicenter cohort study. Arch Dermatol, 2010. 146(3): p. 294-9.
235. Ong, C. S., Keogh, A. M., Kossard, S., Macdonald, P. S., Spratt, P. M., Skin cancer in Australian heart transplant recipients. J Am Acad Dermatol, 1999. 40(1): p. 27-34., https://www.ncbi.nlm.nih.gov/pubmed/9922009
236. Nguyen, P., Vin-Christian, K., Ming, M. E., Berger, T., Aggressive squamous cell carcinomas in persons infected with the human immunodeficiency virus. Arch Dermatol, 2002. 138(6): p. 758-63.
237. Lobo, D. V., Chu, P., Grekin, R. C., Berger, T. G., Nonmelanoma skin cancers and infection with the human immunodeficiency virus. Arch Dermatol, 1992. 128(5): p. 623-7.
238. Maurer, T. A., Christian, K. V., Kerschmann, R. L., Berzin, B., Palefsky, J. M., Payne, D., et.al. Cutaneous squamous cell carcinoma in human immunodeficiency virus-infected patients. A study of epidemiologic risk factors, human papillomavirus, and p53 expression. Arch Dermatol, 1997. 133(5): p. 577-83.
239. Wilkins, K., Turner, R., Dolev, J. C., LeBoit, P. E., Berger, T. G., Maurer, T. A., Cutaneous malignancy and human immunodeficiency virus disease. J Am Acad Dermatol, 2006. 54(2): p. 189-206; quiz 207-10.
240. Travis, L. B., Arndt, K. A., Occupational skin cancer. Four major carcinogens that put workers at risk. Postgrad Med, 1986. 79(6): p. 211-4, 217.
241. Karagas, M. R., McDonald, J. A., Greenberg, E. R., Stukel, T. A., Weiss, J. E., Baron, J. A., et.al. Risk of basal cell and squamous cell skin cancers after ionizing radiation therapy. For The Skin Cancer Prevention Study Group. J Natl Cancer Inst, 1996. 88(24): p. 1848-53.
242. Lichter, M. D., Karagas, M. R., Mott, L. A., Spencer, S. K., Stukel, T. A., Greenberg, E. R., Therapeutic ionizing radiation and the incidence of basal cell carcinoma and squamous cell carcinoma. The New Hampshire Skin Cancer Study Group. Arch Dermatol, 2000. 136(8): p. 1007-11.
243. Gandini, S., Sera, F., Cattaruzza, M. S., Pasquini, P., Abeni, D., Boyle, P., et.al. Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi. Eur J Cancer, 2005. 41(1): p. 28-44., https://www.ncbi.nlm.nih.gov/pubmed/15617989

244. Gandini, S., Sera, F., Cattaruzza, M. S., Pasquini, P., Picconi, O., Boyle, P., et.al. Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure. Eur J Cancer, 2005. 41(1): p. 45-60., https://www.ncbi.nlm.nih.gov/pubmed/15617990
245. Tucker, M. A., Boice, J. D., Jr., Hoffman, D. A., Second cancer following cutaneous melanoma and cancers of the brain, thyroid, connective tissue, bone, and eye in Connecticut, 1935-82. Natl Cancer Inst Monogr, 1985. 68: p. 161-89.
246. Ford, D., Bliss, J. M., Swerdlow, A. J., Armstrong, B. K., Franceschi, S., Green, A., et.al. Risk of cutaneous melanoma associated with a family history of the disease. The International Melanoma Analysis Group (IMAGE). Int J Cancer, 1995. 62(4): p. 377-81.
247. Hemminki, K., Lonnstedt, I., Vaittinen, P., A population-based study of familial cutaneous melanoma. Melanoma Res, 2001. 11(2): p. 133-40.
248. Brobeil, A., Rapaport, D., Wells, K., Cruse, C. W., Glass, F., Fenske, N., et.al. Multiple primary melanomas: implications for screening and follow-up programs for melanoma. Ann Surg Oncol, 1997. 4(1): p. 19-23.
249. Hubner, J., Waldmann, A., Eisemann, N., Noftz, M., Geller, A. C., Weinstock, M. A., et.al. Association between risk factors and detection of cutaneous melanoma in the setting of a population-based skin cancer screening. Eur J Cancer Prev, 2018. 27(6): p. 563-569., https://www.ncbi.nlm.nih.gov/pubmed/28692584
250. Schmid-Wendtner, M. H., Baumert, J., Wendtner, C. M., Plewig, G., Volkenandt, M., Risk of second primary malignancies in patients with cutaneous melanoma. Br J Dermatol, 2001. 145(6): p. 981-5.
251. Bhatia, S., Estrada-Batres, L., Maryon, T., Bogue, M., Chu, D., Second primary tumors in patients with cutaneous malignant melanoma. Cancer, 1999. 86(10): p. 2014-20.
252. Wassberg, C., Thorn, M., Yuen, J., Ringborg, U., Hakulinen, T., Second primary cancers in patients with cutaneous malignant melanoma: a population-based study in Sweden. Br J Cancer, 1996. 73(2): p. 255-9.
253. Goldstein, A. M., Tucker, M. A., Genetic epidemiology of familial melanoma. Dermatol Clin, 1995. 13(3): p. 605-12.
254. Bauer, J., Garbe, C., Acquired melanocytic nevi as risk factor for melanoma development. A comprehensive review of epidemiological data. Pigment Cell Res, 2003. 16(3): p. 297-306., https://www.ncbi.nlm.nih.gov/pubmed/12753404
255. Bataille, V., Bishop, J. A., Sasieni, P., Swerdlow, A. J., Pinney, E., Griffiths, K., et.al. Risk of cutaneous melanoma in relation to the numbers, types and sites of naevi: a case-control study. Br J Cancer, 1996. 73(12): p. 1605-11.
256. Chang, Y. M., Newton-Bishop, J. A., Bishop, D. T., Armstrong, B. K., Bataille, V., Bergman, W., et.al. A pooled analysis of melanocytic nevus phenotype and the risk of cutaneous melanoma at different latitudes. Int J Cancer, 2009. 124(2): p. 420-8.
257. Olsen, C. M., Zens, M. S., Green, A. C., Stukel, T. A., Holman, C. D., Mack, T., et.al. Biologic markers of sun exposure and melanoma risk in women: pooled case-control analysis. Int J Cancer, 2011. 129(3): p. 713-23.
258. Olsen, C. M., Zens, M. S., Stukel, T. A., Sacerdote, C., Chang, Y. M., Armstrong, B. K., et.al. Nevus density and melanoma risk in women: a pooled analysis to test the divergent pathway hypothesis. Int J Cancer, 2009. 124(4): p. 937-44., https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3035752
259. Breitbart, M., Garbe, C., Buttner, P., Weiss, J., Soyer, H. P., Stocker, U., et.al. Ultraviolet light exposure, pigmentary traits and the development of melanocytic naevi and cutaneous melanoma. A case-control study of the German Central Malignant Melanoma Registry. Acta Derm Venereol, 1997. 77(5): p. 374-8.
260. Garbe, C., Buttner, P., Weiss, J., Soyer, H. P., Stocker, U., Kruger, S., et.al. Associated factors in the prevalence of more than 50 common melanocytic nevi, atypical melanocytic nevi, and actinic lentigines: multicenter case-control study of the Central Malignant Melanoma Registry of the German Dermatological Society. J Invest Dermatol, 1994. 102(5): p. 700-5.

261. Garbe, C., Buttner, P., Weiss, J., Soyer, H. P., Stocker, U., Kruger, S., et.al. Risk factors for developing cutaneous melanoma and criteria for identifying persons at risk: multicenter case-control study of the Central Malignant Melanoma Registry of the German Dermatological Society. J Invest Dermatol, 1994. 102(5): p. 695-9.
262. Grulich, A. E., Bataille, V., Swerdlow, A. J., Newton-Bishop, J. A., Cuzick, J., Hersey, P., et.al. Naevi and pigmentary characteristics as risk factors for melanoma in a high-risk population: a case-control study in New South Wales, Australia. Int J Cancer, 1996. 67(4): p. 485-91.
263. Naldi, L., Lorenzo Imberti, G., Parazzini, F., Gallus, S., La Vecchia, C., Pigmentary traits, modalities of sun reaction, history of sunburns, and melanocytic nevi as risk factors for cutaneous malignant melanoma in the Italian population: results of a collaborative case-control study. Cancer, 2000. 88(12): p. 2703-10., https://www.ncbi.nlm.nih.gov/pubmed/8759605
264. Rodenas, J. M., Delgado-Rodriguez, M., Herranz, M. T., Tercedor, J., Serrano, S., Sun exposure, pigmentary traits, and risk of cutaneous malignant melanoma: a case-control study in a Mediterranean population. Cancer Causes Control, 1996. 7(2): p. 275-83.
265. White, E., Kirkpatrick, C. S., Lee, J. A., Case-control study of malignant melanoma in Washington State. I. Constitutional factors and sun exposure. Am J Epidemiol, 1994. 139(9): p. 857-68.
266. Bataille, V., Snieder, H., MacGregor, A. J., Sasieni, P., Spector, T. D., Genetics of risk factors for melanoma: an adult twin study of nevi and freckles. J Natl Cancer Inst, 2000. 92(6): p. 457-63.
267. Easton, D. F., Cox, G. M., Macdonald, A. M., Ponder, B. A., Genetic susceptibility to naevi—a twin study. Br J Cancer, 1991. 64(6): p. 1164-7.
268. Green, A., Siskind, V., Hansen, M. E., Hanson, L., Leech, P., Melanocytic nevi in schoolchildren in Queensland. J Am Acad Dermatol, 1989. 20(6): p. 1054-60.
269. Gallagher, R. P., McLean, D. I., Yang, C. P., Coldman, A. J., Silver, H. K., Spinelli, J. J., et.al. Suntan, sunburn, and pigmentation factors and the frequency of acquired melanocytic nevi in children. Similarities to melanoma: the Vancouver Mole Study. Arch Dermatol, 1990. 126(6): p. 770-6., https://www.ncbi.nlm.nih.gov/pubmed/2346321
270. Green, A. C., Wallingford, S. C., McBride, P., Childhood exposure to ultraviolet radiation and harmful skin effects: epidemiological evidence. Prog Biophys Mol Biol, 2011. 107(3): p. 349-55.
271. Harrison, S. L., MacLennan, R., Buettner, P. G., Sun exposure and the incidence of melanocytic nevi in young Australian children. Cancer Epidemiol Biomarkers Prev, 2008. 17(9): p. 2318-24.
272. Kelly, J. W., Rivers, J. K., MacLennan, R., Harrison, S., Lewis, A. E., Tate, B. J., Sunlight: a major factor associated with the development of melanocytic nevi in Australian schoolchildren. J Am Acad Dermatol, 1994. 30(1): p. 40-8.
273. Richard, M. A., Grob, J. J., Gouvernet, J., Culat, J., Normand, P., Zarour, H., et.al. Role of sun exposure on nevus. First study in age-sex phenotype-controlled populations. Arch Dermatol, 1993. 129(10): p. 1280-5.
274. Wiecker, T. S., Luther, H., Buettner, P., Bauer, J., Garbe, C., Moderate sun exposure and nevus counts in parents are associated with development of melanocytic nevi in childhood: a risk factor study in 1,812 kindergarten children. Cancer, 2003. 97(3): p. 628-38.
275. Grob, J. J., Gouvernet, J., Aymar, D., Mostaque, A., Romano, M. H., Collet, A. M., et.al. Count of benign melanocytic nevi as a major indicator of risk for nonfamilial nodular and superficial spreading melanoma. Cancer, 1990. 66(2): p. 387-95.
276. Holly, E. A., Kelly, J. W., Shpall, S. N., Chiu, S. H., Number of melanocytic nevi as a major risk factor for malignant melanoma. J Am Acad Dermatol, 1987. 17(3): p. 459-68.
277. Halpern, A. C., Guerry, D. th, Elder, D. E., Clark, W. H., Jr., Synnestvedt, M., Norman, S., et.al. Dysplastic nevi as risk markers of sporadic (nonfamilial) melanoma. A case-control study. Arch Dermatol, 1991. 127(7): p. 995-9.
278. Hübner, J., Eisemann, N., Brunßen, A., Katalinic, A., Hautkrebsscreening in Deutschland: Bilanz nach zehn Jahren. Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz, 2018.
279. Savoye, I., Olsen, C. M., Whiteman, D. C., Bijon, A., Wald, L., Dartois, L., et.al. Patterns of Ultraviolet Radiation Exposure and Skin Cancer Risk: the E3N-SunExp Study. J Epidemiol, 2018. 28(1): p. 27-33., https://www.ncbi.nlm.nih.gov/pubmed/29176271

280. de Gruijl, F. R., van Kranen, H. J., Mullenders, L. H., UV-induced DNA damage, repair, mutations and oncogenic pathways in skin cancer. J Photochem Photobiol B, 2001. 63(1-3): p. 19-27.
281. Schmitt, J., Haufe, E., Trautmann, F., Schulze, H. J., Elsner, P., Drexler, H., et.al. Is ultraviolet exposure acquired at work the most important risk factor for cutaneous squamous cell carcinoma? Results of the population-based case-control study FB-181. Br J Dermatol, 2018. 178(2): p. 462-472., https://www.ncbi.nlm.nih.gov/pubmed/28845516
282. Iannacone, M. R., Wang, W., Stockwell, H. G., O'Rourke, K., Giuliano, A. R., Sondak, V. K., et.al. Patterns and timing of sunlight exposure and risk of basal cell and squamous cell carcinomas of the skin—a case-control study. BMC Cancer, 2012. 12: p. 417., https://www.ncbi.nlm.nih.gov/pubmed/22994655
283. National Institutes of Health summary of the Consensus Development Conference on Sunlight, U.R., and the Skin, Bethesda, Maryland, May 8-10, 1989. Consensus Development Panel,, J Am Acad Dermatol, 1991. 24(4): p. 608-12., 1991.
284. Schmitt, J., Haufe, E., Trautmann, F., Schulze, H. J., Elsner, P., Drexler, H., et.al. Occupational UV-Exposure is a Major Risk Factor for Basal Cell Carcinoma: Results of the Population-Based Case-Control Study FB-181. J Occup Environ Med, 2018. 60(1): p. 36-43., https://www.ncbi.nlm.nih.gov/pubmed/29111985
285. Dubin, N., Moseson, M., Pasternack, B. S., Sun exposure and malignant melanoma among susceptible individuals. Environ Health Perspect, 1989. 81: p. 139-51., https://www.ncbi.nlm.nih.gov/pubmed/2759056
286. Whiteman, D., Green, A., Melanoma and sunburn. Cancer Causes Control, 1994. 5(6): p. 564-72., https://www.ncbi.nlm.nih.gov/pubmed/7827244
287. Greenland, S., Quantitative methods in the review of epidemiologic literature. Epidemiol Rev, 1987. 9: p. 1-30., https://www.ncbi.nlm.nih.gov/pubmed/3678409
288. Elwood, J. M., Jopson, J., Melanoma and sun exposure: an overview of published studies. Int J Cancer, 1997. 73(2): p. 198-203., https://www.ncbi.nlm.nih.gov/pubmed/9335442
289. Nelemans, P. J., Rampen, F. H., Ruiter, D. J., Verbeek, A. L., An addition to the controversy on sunlight exposure and melanoma risk: a meta-analytical approach. J Clin Epidemiol, 1995. 48(11): p. 1331-42., https://www.ncbi.nlm.nih.gov/pubmed/7490596
290. Stang, A., Pukkala, E., Sankila, R., Soderman, B., Hakulinen, T., Time trend analysis of the skin melanoma incidence of Finland from 1953 through 2003 including 16,414 cases. Int J Cancer, 2006. 119(2): p. 380-4., https://www.ncbi.nlm.nih.gov/pubmed/16477634
291. Stang, A., Valiukeviciene, S., Aleknaviciene, B., Kurtinaitis, J., Time trends of incidence, mortality, and relative survival of invasive skin melanoma in Lithuania. Eur J Cancer, 2006. 42(5): p. 660-7., https://www.ncbi.nlm.nih.gov/pubmed/16510281
292. Cullen, A. P., Photokeratitis and other phototoxic effects on the cornea and conjunctiva. Int J Toxicol, 2002. 21(6): p. 455-64., https://www.ncbi.nlm.nih.gov/pubmed/12537642
293. Ren, H., Wilson, G., The effect of ultraviolet-B irradiation on the cell shedding rate of the corneal epithelium. Acta Ophthalmol (Copenh), 1994. 72(4): p. 447-52., https://www.ncbi.nlm.nih.gov/pubmed/7825410
294. Oliva, M. S., Taylor, H., Ultraviolet radiation and the eye. Int Ophthalmol Clin, 2005. 45(1): p. 1-17., https://www.ncbi.nlm.nih.gov/pubmed/15632523
295. Comander, J., Gardiner, M., Loewenstein, J., High-resolution optical coherence tomography findings in solar maculopathy and the differential diagnosis of outer retinal holes. Am J Ophthalmol, 2011. 152(3): p. 413-419 e6., https://www.ncbi.nlm.nih.gov/pubmed/21708377
296. Chen, K. C., Jung, J. J., Aizman, A., High definition spectral domain optical coherence tomography findings in three patients with solar retinopathy and review of the literature. Open Ophthalmol J, 2012. 6: p. 29-35., https://www.ncbi.nlm.nih.gov/pubmed/22798967
297. Cameron, M, Pterygium throughout the worldCharles C. Thomas, 1992.
298. Mackenzie, F. D., Hirst, L. W., Battistutta, D., Green, A., Risk analysis in the development of pterygia. Ophthalmology, 1992. 99(7): p. 1056-61., https://www.ncbi.nlm.nih.gov/pubmed/1495784

299. Moran, D. J., Hollows, F. C., Pterygium and ultraviolet radiation: a positive correlation. Br J Ophthalmol, 1984. 68(5): p. 343-6., https://www.ncbi.nlm.nih.gov/pubmed/6712914
300. Taylor, H. R., West, S. K., Rosenthal, F. S., Munoz, B., Newland, H. S., Emmett, E. A., Corneal changes associated with chronic UV irradiation. Arch Ophthalmol, 1989. 107(10): p. 1481-4., https://www.ncbi.nlm.nih.gov/pubmed/2803097
301. Norn, M. S., Spheroid degeneration, pinguecula, and pterygium among Arabs in the Red Sea territory, Jordan. Acta Ophthalmol (Copenh), 1982. 60(6): p. 949-54., https://www.ncbi.nlm.nih.gov/pubmed/7170936
302. Gray, R. H., Johnson, G. J., Freedman, A., Climatic droplet keratopathy. Surv Ophthalmol, 1992. 36(4): p. 241-53., https://www.ncbi.nlm.nih.gov/pubmed/1549808
303. Klintworth, G. K., Chronic actinic keratopathy—a condition associated with conjunctival elastosis (pingueculae) and typified by characteristic extracellular concretions. Am J Pathol, 1972. 67(2): p. 327-48., https://www.ncbi.nlm.nih.gov/pubmed/5021106
304. Johnson, G. J., Aetiology of spheroidal degeneration of the cornea in Labrador. Br J Ophthalmol, 1981. 65(4): p. 270-83., https://www.ncbi.nlm.nih.gov/pubmed/7236572
305. Pe'er, J., Ocular surface squamous neoplasia: evidence for topical chemotherapy. Int Ophthalmol Clin, 2015. 55(1): p. 9-21., https://www.ncbi.nlm.nih.gov/pubmed/25436490
306. Templeton, A. C., Tumors of the eye and adnexa in Africans of Uganda. Cancer, 1967. 20(10): p. 1689-98., https://www.ncbi.nlm.nih.gov/pubmed/6058176
307. Malik, M. O., El Sheikh, E. H., Tumors of the eye and adnexa in the Sudan. Cancer, 1979. 44(1): p. 293-303., https://www.ncbi.nlm.nih.gov/pubmed/455254
308. Sun, E. C., Fears, T. R., Goedert, J. J., Epidemiology of squamous cell conjunctival cancer. Cancer Epidemiol Biomarkers Prev, 1997. 6(2): p. 73-7., https://www.ncbi.nlm.nih.gov/pubmed/9037556
309. Pola, E. C., Masanganise, R., Rusakaniko, S., The trend of ocular surface squamous neoplasia among ocular surface tumour biopsies submitted for histology from Sekuru Kaguvi Eye Unit, Harare between 1996 and 2000. Cent Afr J Med, 2003. 49(1-2): p. 1-4., https://www.ncbi.nlm.nih.gov/pubmed/14562592
310. Lee, G. A., Hirst, L. W., Incidence of ocular surface epithelial dysplasia in metropolitan Brisbane. A 10-year survey. Arch Ophthalmol, 1992. 110(4): p. 525-7., https://www.ncbi.nlm.nih.gov/pubmed/1562262
311. Newton, R., Ferlay, J., Reeves, G., Beral, V., Parkin, D. M., Effect of ambient solar ultraviolet radiation on incidence of squamous-cell carcinoma of the eye. Lancet, 1996. 347(9013): p. 1450-1., https://www.ncbi.nlm.nih.gov/pubmed/8676629
312. El-Shabrawi, Y., Radner, H., Muellner, K., Langmann, G., Hoefler, G., The role of UV-radiation in the development of conjunctival malignant melanoma. Acta Ophthalmol Scand, 1999. 77(1): p. 31-2., https://www.ncbi.nlm.nih.gov/pubmed/10071144
313. Taylor, H. R., The environment and the lens. Br J Ophthalmol, 1980. 64(5): p. 303-10., https://www.ncbi.nlm.nih.gov/pubmed/7437389
314. Hollows, F., Moran, D., Cataract—the ultraviolet risk factor. Lancet, 1981. 2(8258): p. 1249-50., https://www.ncbi.nlm.nih.gov/pubmed/6118668
315. Chatterjee, A., Milton, R. C., Thyle, S., Prevalence and aetiology of cataract in Punjab. Br J Ophthalmol, 1982. 66(1): p. 35-42., https://www.ncbi.nlm.nih.gov/pubmed/7055541
316. Brilliant, L. B., Grasset, N. C., Pokhrel, R. P., Kolstad, A., Lepkowski, J. M., Brilliant, G. E., et.al. Associations among cataract prevalence, sunlight hours, and altitude in the Himalayas. Am J Epidemiol, 1983. 118(2): p. 250-64., https://www.ncbi.nlm.nih.gov/pubmed/6603790
317. Wong, L., Ho, S. C., Coggon, D., Cruddas, A. M., Hwang, C. H., Ho, C. P., et.al. Sunlight exposure, antioxidant status, and cataract in Hong Kong fishermen. J Epidemiol Community Health, 1993. 47(1): p. 46-9., https://www.ncbi.nlm.nih.gov/pubmed/8436894
318. Bochow, T. W., West, S. K., Azar, A., Munoz, B., Sommer, A., Taylor, H. R., Ultraviolet light exposure and risk of posterior subcapsular cataracts. Arch Ophthalmol, 1989. 107(3): p. 369-72., https://www.ncbi.nlm.nih.gov/pubmed/2923558

319. Cruickshanks, K. J., Klein, B. E., Klein, R., Ultraviolet light exposure and lens opacities: the Beaver Dam Eye Study. Am J Public Health, 1992. 82(12): p. 1658-62., https://www.ncbi.nlm.nih.gov/pubmed/1456342
320. Hyman, L. G., Lilienfeld, A. M., Ferris, F. L., 3rd, Fine, S. L., Senile macular degeneration: a case-control study. Am J Epidemiol, 1983. 118(2): p. 213-27., https://www.ncbi.nlm.nih.gov/pubmed/6881127
321. Risk factors for neovascular age-related macular degeneration. The Eye Disease Case-Control Study Group. Arch Ophthalmol, 1992. 110(12): p. 1701-8., https://www.ncbi.nlm.nih.gov/pubmed/1281403
322. Darzins, P., Mitchell, P., Heller, R. F., Sun exposure and age-related macular degeneration. An Australian case-control study. Ophthalmology, 1997. 104(5): p. 770-6., https://www.ncbi.nlm.nih.gov/pubmed/9160021
323. West, S. K., Rosenthal, F. S., Bressler, N. M., Bressler, S. B., Munoz, B., Fine, S. L., et.al. Exposure to sunlight and other risk factors for age-related macular degeneration. Arch Ophthalmol, 1989. 107(6): p. 875-9., https://www.ncbi.nlm.nih.gov/pubmed/2786410
324. Taylor, H. R., West, S., Munoz, B., Rosenthal, F. S., Bressler, S. B., Bressler, N. M., The long-term effects of visible light on the eye. Arch Ophthalmol, 1992. 110(1): p. 99-104., https://www.ncbi.nlm.nih.gov/pubmed/1731731
325. Sui, G. Y., Liu, G. C., Liu, G. Y., Gao, Y. Y., Deng, Y., Wang, W. Y., et.al. Is sunlight exposure a risk factor for age-related macular degeneration? A systematic review and meta-analysis. Br J Ophthalmol, 2013. 97(4): p. 389-94., https://www.ncbi.nlm.nih.gov/pubmed/23143904
326. Wang, J. J., Klein, R., Smith, W., Klein, B. E., Tomany, S., Mitchell, P., Cataract surgery and the 5-year incidence of late-stage age-related maculopathy: pooled findings from the Beaver Dam and Blue Mountains eye studies. Ophthalmology, 2003. 110(10): p. 1960-7., https://www.ncbi.nlm.nih.gov/pubmed/14522772
327. Downie, L. E., Busija, L., Keller, P. R., Blue-light filtering intraocular lenses (IOLs) for protecting macular health. Cochrane Database Syst Rev, 2018. 5: p. CD011977., https://www.ncbi.nlm.nih.gov/pubmed/29786830
328. Partanen, T., Boffetta, P., Cancer risk in asphalt workers and roofers: review and meta-analysis of epidemiologic studies. Am J Ind Med, 1994. 26(6): p. 721-40., https://www.ncbi.nlm.nih.gov/pubmed/7892824
329. Tsai, P. J., Shieh, H. Y., Lee, W. J., Lai, S. O., Health-risk assessment for workers exposed to polycyclic aromatic hydrocarbons (PAHs) in a carbon black manufacturing industry. Sci Total Environ, 2001. 278(1-3): p. 137-50., https://www.ncbi.nlm.nih.gov/pubmed/11669262
330. Roelofzen, J. H., Aben, K. K., Oldenhof, U. T., Coenraads, P. J., Alkemade, H. A., van de Kerkhof, P. C., et.al. No increased risk of cancer after coal tar treatment in patients with psoriasis or eczema. J Invest Dermatol, 2010. 130(4): p. 953-61., https://www.ncbi.nlm.nih.gov/pubmed/20016499
331. Forslund, O., Iftner, T., Andersson, K., Lindelof, B., Hradil, E., Nordin, P., et.al. Cutaneous human papillomaviruses found in sun-exposed skin: Beta-papillomavirus species 2 predominates in squamous cell carcinoma. J Infect Dis, 2007. 196(6): p. 876-83., https://www.ncbi.nlm.nih.gov/pubmed/17703418
332. Kelly, D. A., Young, A. R., McGregor, J. M., Seed, P. T., Potten, C. S., Walker, S. L., Sensitivity to sunburn is associated with susceptibility to ultraviolet radiation-induced suppression of cutaneous cell-mediated immunity. J Exp Med, 2000. 191(3): p. 561-6., https://www.ncbi.nlm.nih.gov/pubmed/10662801
333. Pedersen, S. A., Gaist, D., Schmidt, S. A. J., Holmich, L. R., Friis, S., Pottegard, A., Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark. J Am Acad Dermatol, 2018. 78(4): p. 673-681 e9., https://www.ncbi.nlm.nih.gov/pubmed/29217346

334. Pottegard, A., Hallas, J., Olesen, M., Svendsen, M. T., Habel, L. A., Friedman, G. D., et.al. Hydrochlorothiazide use is strongly associated with risk of lip cancer. J Intern Med, 2017. 282(4): p. 322-331., https://www.ncbi.nlm.nih.gov/pubmed/28480532
335. Ludwig, J. A., Weinstein, J. N., Biomarkers in cancer staging, prognosis and treatment selection. Nat Rev Cancer, 2005. 5(11): p. 845-56., https://www.ncbi.nlm.nih.gov/pubmed/16239904
336. Kulasingam, V., Diamandis, E. P., Strategies for discovering novel cancer biomarkers through utilization of emerging technologies. Nat Clin Pract Oncol, 2008. 5(10): p. 588-99., https://www.ncbi.nlm.nih.gov/pubmed/18695711
337. Weinstein, D., Leininger, J., Hamby, C., Safai, B., Diagnostic and prognostic biomarkers in melanoma. J Clin Aesthet Dermatol, 2014. 7(6): p. 13-24., https://www.ncbi.nlm.nih.gov/pubmed/25013535
338. Neagu, M., Constantin, C., Cretoiu, S. M., Zurac, S., miRNAs in the Diagnosis and Prognosis of Skin Cancer. Front Cell Dev Biol, 2020. 8: p. 71., https://www.ncbi.nlm.nih.gov/pubmed/32185171
339. Chen, J. J., Lu, T. P., Chen, Y. C., Lin, W. J., Predictive biomarkers for treatment selection: statistical considerations. Biomark Med, 2015. 9(11): p. 1121-35., https://www.ncbi.nlm.nih.gov/pubmed/26507127
340. Kalia, M., Biomarkers for personalized oncology: recent advances and future challenges. Metabolism, 2015. 64(3 Suppl 1): p. S16-21., https://www.ncbi.nlm.nih.gov/pubmed/25468140
341. Chen, G., Huang, A. C., Zhang, W., Zhang, G., Wu, M., Xu, W., et.al. Exosomal PD-L1 contributes to immunosuppression and is associated with anti-PD-1 response. Nature, 2018. 560(7718): p. 382-386., https://www.ncbi.nlm.nih.gov/pubmed/30089911
342. Reimers, N., Pantel, K., Liquid biopsy: novel technologies and clinical applications. Clin Chem Lab Med, 2019. 57(3): p. 312-316., https://www.ncbi.nlm.nih.gov/pubmed/30465714
343. Lianidou, E., Pantel, K., Liquid biopsies. Genes Chromosomes Cancer, 2019. 58(4): p. 219-232., https://www.ncbi.nlm.nih.gov/pubmed/30382599
344. Gaiser, M. R., von Bubnoff, N., Gebhardt, C., Utikal, J. S., Liquid biopsy to monitor melanoma patients. J Dtsch Dermatol Ges, 2018. 16(4): p. 405-414., https://www.ncbi.nlm.nih.gov/pubmed/29512873
345. Quandt, D., Dieter Zucht, H., Amann, A., Wulf-Goldenberg, A., Borrebaeck, C., Cannarile, M., et.al. Implementing liquid biopsies into clinical decision making for cancer immunotherapy. Oncotarget, 2017. 8(29): p. 48507-48520., https://www.ncbi.nlm.nih.gov/pubmed/28501851
346. Dragomir, M., Mafra, A. C. P., Dias, S. M. G., Vasilescu, C., Calin, G. A., Using microRNA Networks to Understand Cancer. Int J Mol Sci, 2018. 19(7):, https://www.ncbi.nlm.nih.gov/pubmed/29949872
347. Whiteside, T. L., Tumor-Derived Exosomes and Their Role in Cancer Progression. Adv Clin Chem, 2016. 74: p. 103-41., https://www.ncbi.nlm.nih.gov/pubmed/27117662
348. Lim, S. Y., Lee, J. H., Diefenbach, R. J., Kefford, R. F., Rizos, H., Liquid biomarkers in melanoma: detection and discovery. Mol Cancer, 2018. 17(1): p. 8., https://www.ncbi.nlm.nih.gov/pubmed/29343260
349. Zhang, Y., Liu, Y., Liu, H., Tang, W. H., Exosomes: biogenesis, biologic function and clinical potential. Cell Biosci, 2019. 9: p. 19., https://www.ncbi.nlm.nih.gov/pubmed/30815248
350. Mumford, S. L., Towler, B. P., Pashler, A. L., Gilleard, O., Martin, Y., Newbury, S. F., Circulating MicroRNA Biomarkers in Melanoma: Tools and Challenges in Personalised Medicine. Biomolecules, 2018. 8(2):, https://www.ncbi.nlm.nih.gov/pubmed/29701682
351. Sharma, P., Diergaarde, B., Ferrone, S., Kirkwood, J. M., Whiteside, T. L., Melanoma cell-derived exosomes in plasma of melanoma patients suppress functions of immune effector cells. Sci Rep, 2020. 10(1): p. 92., https://www.ncbi.nlm.nih.gov/pubmed/31919420
352. Gandini, S., Sera, F., Cattaruzza, M. S., Pasquini, P., Zanetti, R., Masini, C., et.al. Meta-analysis of risk factors for cutaneous melanoma: III. Family history, actinic damage and phenotypic factors. Eur J Cancer, 2005. 41(14): p. 2040-59., https://www.ncbi.nlm.nih.gov/pubmed/16125929

353. Gandini, S., Sera, F., Cattaruzza, M. S., Pasquini, P., Picconi, O., Boyle, P., et.al. Meta-analysis of risk factors for cutaneous melanoma: II. Sun exposure. Eur J Cancer, 2005. 41(1): p. 45-60., https://www.ncbi.nlm.nih.gov/pubmed/15617990
354. Neale, R. E., Davis, M., Pandeya, N., Whiteman, D. C., Green, A. C., Basal cell carcinoma on the trunk is associated with excessive sun exposure. J Am Acad Dermatol, 2007. 56(3): p. 380-6., https://www.ncbi.nlm.nih.gov/pubmed/17097387
355. World Health Organization, Global Solar UV Index: A Practical Guide., 2002.
356. Autier, P., Boniol, M., Dore, J. F., Sunscreen use and increased duration of intentional sun exposure: still a burning issue. Int J Cancer, 2007. 121(1): p. 1-5., https://www.ncbi.nlm.nih.gov/pubmed/17415716
357. Autier, P., Dore, J. F., Reis, A. C., Grivegnee, A., Ollivaud, L., Truchetet, F., et.al. Sunscreen use and intentional exposure to ultraviolet A and B radiation: A double blind randomized trial using personal dosimeters. British Journal of Cancer, 2000. p. 83(9)(pp 1243-1248).
358. Autier, P., Dore, J. F., Schifflers, E., Cesarini, J. P., Bollaerts, A., Koelmel, K. F., et.al. Melanoma and use of sunscreens: an Eortc case-control study in Germany, Belgium and France. The EORTC Melanoma Cooperative Group. Int J Cancer, 1995. 61(6): p. 749-55., https://www.ncbi.nlm.nih.gov/pubmed/7790106
359. Gorham, E. D., Mohr, S. B., Garland, C. F., Chaplin, G., Garland, F. C., Do sunscreens increase risk of melanoma in populations residing at higher latitudes?. Ann Epidemiol, 2007. 17(12): p. 956-63., https://www.ncbi.nlm.nih.gov/pubmed/18022535
360. Green, A. C., Williams, G. M., Logan, V., Strutton, G. M., Reduced melanoma after regular sunscreen use: randomized trial follow-up. J Clin Oncol, 2011. 29(3): p. 257-63., https://www.ncbi.nlm.nih.gov/pubmed/21135266
361. Lin, J. S., Eder, M., Weinmann, S., Behavioral counseling to prevent skin cancer: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med, 2011. 154(3): p. 190-201., https://www.ncbi.nlm.nih.gov/pubmed/21282699
362. Darlington, S., Williams, G., Neale, R., Frost, C., Green, A., A randomized controlled trial to assess sunscreen application and beta carotene supplementation in the prevention of solar keratoses. Arch Dermatol, 2003. 139(4): p. 451-5., https://www.ncbi.nlm.nih.gov/pubmed/12707092
363. Dennis, L. K., Beane Freeman, L. E., VanBeek, M. J., Sunscreen use and the risk for melanoma: a quantitative review. Ann Intern Med, 2003. 139(12): p. 966-78., https://www.ncbi.nlm.nih.gov/pubmed/14678916
364. Kulichova, D., Danova, J., Kunte, C., Ruzicka, T., Celko, A. M., Risk factors for malignant melanoma and preventive methods. Cutis, 2014. 94(5): p. 241-8., https://www.ncbi.nlm.nih.gov/pubmed/25474453
365. Ghiasvand, R., Weiderpass, E., Green, A. C., Lund, E., Veierod, M. B., Sunscreen Use and Subsequent Melanoma Risk: A Population-Based Cohort Study. J Clin Oncol, 2016. 34(33): p. 3976-3983., https://www.ncbi.nlm.nih.gov/pubmed/27621396
366. Autier, P., Dore, J. F., Reis, A. C., Grivegnee, A., Ollivaud, L., Truchetet, F., et.al. Sunscreen use and intentional exposure to ultraviolet A and B radiation: A double blind randomized trial using personal dosimeters. British Journal of Cancer, 2000. p. 83(9)(pp 1243-1248), 2000., https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2363574
367. European Commission, Policies, information and services: Sunscreen products, https://ec.europa.eu/growth/sectors/cosmetics/products/sunscreen_en
368. Huncharek, M., Kupelnick, B., Use of topical sunscreens and the risk of malignant melanoma: a meta-analysis of 9067 patients from 11 case-control studies. Am J Public Health, 2002. 92(7): p. 1173-7., https://www.ncbi.nlm.nih.gov/pubmed/12084704
369. Matta, M. K., Zusterzeel, R., Pilli, N. R., Patel, V., Volpe, D. A., Florian, J., et.al. Effect of Sunscreen Application Under Maximal Use Conditions on Plasma Concentration of Sunscreen Active Ingredients: A Randomized Clinical Trial. JAMA, 2019. 321(21): p. 2082-2091., https://www.ncbi.nlm.nih.gov/pubmed/31058986

370. Burgard, B., Schope, J., Holzschuh, I., Schiekofer, C., Reichrath, S., Stefan, W., et.al. Solarium Use and Risk for Malignant Melanoma: Meta-analysis and Evidence-based Medicine Systematic Review. Anticancer Res, 2018. 38(2): p. 1187-1199., https://www.ncbi.nlm.nih.gov/pubmed/29374757
371. Colantonio, S., Bracken, M. B., Beecker, J., The association of indoor tanning and melanoma in adults: systematic review and meta-analysis. J Am Acad Dermatol, 2014. 70(5): p. 847-57 e1-18., https://www.ncbi.nlm.nih.gov/pubmed/24629998
372. Boniol, M., Autier, P., Boyle, P., Gandini, S., Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. BMJ, 2012. 345: p. e4757., https://www.ncbi.nlm.nih.gov/pubmed/22833605
373. Ghiasvand, R., Rueegg, C. S., Weiderpass, E., Green, A. C., Lund, E., Veierod, M. B., Indoor Tanning and Melanoma Risk: Long-Term Evidence From a Prospective Population-Based Cohort Study. Am J Epidemiol, 2017. 185(3): p. 147-156., https://www.ncbi.nlm.nih.gov/pubmed/28077359
374. Karagas, M. R., Zens, M. S., Li, Z., Stukel, T. A., Perry, A. E., Gilbert-Diamond, D., et.al. Early-onset basal cell carcinoma and indoor tanning: a population-based study. Pediatrics, 2014. 134(1): p. e4-12., https://www.ncbi.nlm.nih.gov/pubmed/24958589
375. Wehner, M. R., Shive, M. L., Chren, M. M., Han, J., Qureshi, A. A., Linos, E., Indoor tanning and non-melanoma skin cancer: systematic review and meta-analysis. BMJ, 2012. 345: p. e5909., https://www.ncbi.nlm.nih.gov/pubmed/23033409
376. Green, A., Williams, G., Neale, R., Hart, V., Leslie, D., Parsons, P., et.al. Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. Lancet, 1999. 354(9180): p. 723-9., https://www.ncbi.nlm.nih.gov/pubmed/10475183
377. Myung, S. K., Kim, Y., Ju, W., Choi, H. J., Bae, W. K., Effects of antioxidant supplements on cancer prevention: meta-analysis of randomized controlled trials. Ann Oncol, 2010. 21(1): p. 166-79., https://www.ncbi.nlm.nih.gov/pubmed/19622597
378. Miura, K., Hughes, M. C., Green, A. C., van der Pols, J. C., Caffeine intake and risk of basal cell and squamous cell carcinomas of the skin in an 11-year prospective study. Eur J Nutr, 2014. 53(2): p. 511-20., https://www.ncbi.nlm.nih.gov/pubmed/23824258
379. Lukic, M., Jareid, M., Weiderpass, E., Braaten, T., Coffee consumption and the risk of malignant melanoma in the Norwegian Women and Cancer (NOWAC) Study. BMC Cancer, 2016. 16: p. 562., https://www.ncbi.nlm.nih.gov/pubmed/27473841
380. Liu, J., Shen, B., Shi, M., Cai, J., Higher Caffeinated Coffee Intake Is Associated with Reduced Malignant Melanoma Risk: A Meta-Analysis Study. PLoS One, 2016. 11(1): p. e0147056., https://www.ncbi.nlm.nih.gov/pubmed/26816289
381. Rollison, D. E., Iannacone, M. R., Messina, J. L., Glass, L. F., Giuliano, A. R., Roetzheim, R. G., et.al. Case-control study of smoking and non-melanoma skin cancer. Cancer Causes Control, 2012. 23(2): p. 245-54., https://www.ncbi.nlm.nih.gov/pubmed/22101452
382. Kubo, J. T., Henderson, M. T., Desai, M., Wactawski-Wende, J., Stefanick, M. L., Tang, J. Y., Alcohol consumption and risk of melanoma and non-melanoma skin cancer in the Women's Health Initiative. Cancer Causes Control, 2014. 25(1): p. 1-10., https://www.ncbi.nlm.nih.gov/pubmed/24173533
383. Jiang, A. J., Rambhatla, P. V., Eide, M. J., Socioeconomic and lifestyle factors and melanoma: a systematic review. Br J Dermatol, 2015. 172(4): p. 885-915., https://www.ncbi.nlm.nih.gov/pubmed/25354495
384. Leitlinienprogramm Onkologie, S3 Leitlinie Aktinische Keratose und Plattenepithelkarzinom der Haut, 2019., https://www.leitlinienprogramm-onkologie.de/fileadmin/user_upload/Downloads/Leitlinien/Aktinische_Keratosen_und_PEK/LL_Aktinische_Keratose_und_PEK_Langversion_1.0.pdf

385. Lang, B., Balermpas, P., Bauer, A., Blum, A., Brölsch, G.,, Dirschka, T., Follmann, M., et.al. S2k-Leitlinie Basalzellkarzinom der Hau, 2018., https://www.awmf.org/uploads/tx_szleitlinien/032-021l_S2k_Basalzellkarzinom-der-Haut_2018-09_01.pdf
386. Buller, D. B., Andersen, P. A., Walkosz, B. J., Scott, M. D., Cutter, G. R., Dignan, M. B., et.al. Randomized trial testing a worksite sun protection program in an outdoor recreation industry. Health Educ Behav, 2005. 32(4): p. 514-35., https://www.ncbi.nlm.nih.gov/pubmed/16009748
387. Loescher, L. J., Emerson, J., Taylor, A., Christensen, D. H., McKinney, M., Educating preschoolers about sun safety. Am J Public Health, 1995. 85(7): p. 939-43., https://www.ncbi.nlm.nih.gov/pubmed/7604917
388. Mermelstein, R., Weeks, K., Turner, L., Cobb, J., When tailored feedback backfires: A skin cancer prevention intervention for adolescents. Cancer Research Therapy and Control, 1999. p. 8(1-2)(pp 69-79), 1999.
389. Norman, G. J., Adams, M. A., Calfas, K. J., Covin, J., Sallis, J. F., Rossi, J. S., et.al. A randomized trial of a multicomponent intervention for adolescent sun protection behaviors. Arch Pediatr Adolesc Med, 2007. 161(2): p. 146-52., https://www.ncbi.nlm.nih.gov/pubmed/17283299
390. Gallagher, R. P., Rivers, J. K., Lee, T. K., Bajdik, C. D., McLean, D. I., Coldman, A. J., Broad-spectrum sunscreen use and the development of new nevi in white children: A randomized controlled trial. JAMA, 2000. 283(22): p. 2955-60., https://www.ncbi.nlm.nih.gov/pubmed/10865273
391. de Maleissye, M. F., Beauchet, A., Saiag, P., Correa, M., Godin-Beeckmann, S., Haeffelin, M., et.al. Sunscreen use and melanocytic nevi in children: a systematic review. Pediatr Dermatol, 2013. 30(1): p. 51-9., https://www.ncbi.nlm.nih.gov/pubmed/22994908
392. Ulrich, C., Jurgensen, J. S., Degen, A., Hackethal, M., Ulrich, M., Patel, M. J., et.al. Prevention of non-melanoma skin cancer in organ transplant patients by regular use of a sunscreen: a 24 months, prospective, case-control study. Br J Dermatol, 2009. 161 Suppl 3: p. 78-84., https://www.ncbi.nlm.nih.gov/pubmed/19775361
393. Türk, T. R., Witzke, O., Zeier, M., KDIGO-Leitlinien zur Betreuung von Nierentransplantatempfängern. Der Nephrologe, 2010. 5(2): p. 94-107.
394. Schwalfenberg, G., Not enough vitamin D: Health consequences for Canadians. Canadian Family Physician, 2007. p. 53(5)(pp 841-854), 2007., https://www.ncbi.nlm.nih.gov/pubmed/17872747
395. Srikanth, V., Fryer, J., Venn, A., Blizzard, L., Newman, L., Cooley, H., et.al. The association between non-melanoma skin cancer and osteoporotic fractures—a population-based record linkage study. Osteoporos Int, 2007. 18(5): p. 687-92., https://www.ncbi.nlm.nih.gov/pubmed/17211531
396. Bonilla, C., Ness, A. R., Wills, A. K., Lawlor, D. A., Lewis, S. J., Davey Smith, G., Skin pigmentation, sun exposure and vitamin D levels in children of the Avon Longitudinal Study of Parents and Children. BMC Public Health, 2014. 14: p. 597., https://www.ncbi.nlm.nih.gov/pubmed/24924479
397. Lindqvist, P. G., Epstein, E., Landin-Olsson, M., Ingvar, C., Nielsen, K., Stenbeck, M., et.al. Avoidance of sun exposure is a risk factor for all-cause mortality: results from the Melanoma in Southern Sweden cohort. J Intern Med, 2014. 276(1): p. 77-86., https://www.ncbi.nlm.nih.gov/pubmed/24697969
398. Lindqvist, P. G., Epstein, E., Nielsen, K., Landin-Olsson, M., Ingvar, C., Olsson, H., Avoidance of sun exposure as a risk factor for major causes of death: a competing risk analysis of the Melanoma in Southern Sweden cohort. J Intern Med, 2016. 280(4): p. 375-87., https://www.ncbi.nlm.nih.gov/pubmed/26992108
399. UV-Schutz-Bündnis, Bundesamt für Strahlenschutz, Vorbeugung gesundheitlicher Schäden durch die Sonne – Verhältnisprävention in der Stadt und auf dem Land: Grundsatzpapier des UV-Schutz-Bündnisses. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, 2017. 60(10):1153–1160.:

400. van der Rhee, H. J., de Vries, E., Coebergh, J. W., Does sunlight prevent cancer? A systematic review. Eur J Cancer, 2006. 42(14): p. 2222-32., https://www.ncbi.nlm.nih.gov/pubmed/16904314
401. Tuohimaa, P., Pukkala, E., Scelo, G., Olsen, J. H., Brewster, D. H., Hemminki, K., et.al. Does solar exposure, as indicated by the non-melanoma skin cancers, protect from solid cancers: vitamin D as a possible explanation. Eur J Cancer, 2007. 43(11): p. 1701-12., https://www.ncbi.nlm.nih.gov/pubmed/17540555
402. Krause, R., Matulla-Nolte, B., Essers, M., Brown, A., Hopfenmuller, W., UV radiation and cancer prevention: what is the evidence?. Anticancer Res, 2006. 26(4A): p. 2723-7., https://www.ncbi.nlm.nih.gov/pubmed/16886683
403. Antonov, D., Hollunder, M., Schliemann, S., Elsner, P., Ultraviolet Exposure and Protection Behavior in the General Population: A Structured Interview Survey. Dermatology, 2016. 232(1): p. 11-6., https://www.ncbi.nlm.nih.gov/pubmed/26619287
404. Gavin, A., Boyle, R., Donnelly, D., Donnelly, C., Gordon, S., McElwee, G., et.al. Trends in skin cancer knowledge, sun protection practices and behaviours in the Northern Ireland population. Eur J Public Health, 2012. 22(3): p. 408-12., https://www.ncbi.nlm.nih.gov/pubmed/22094579
405. Haluza, D., Simic, S., Holtge, J., Cervinka, R., Moshammer, H., Gender aspects of recreational sun-protective behavior: results of a representative, population-based survey among Austrian residents. Photodermatol Photoimmunol Photomed, 2016. 32(1): p. 11-21., https://www.ncbi.nlm.nih.gov/pubmed/26431724
406. Ghiasvand, R., Lund, E., Edvardsen, K., Weiderpass, E., Veierod, M. B., Prevalence and trends of sunscreen use and sunburn among Norwegian women. Br J Dermatol, 2015. 172(2): p. 475-83., https://www.ncbi.nlm.nih.gov/pubmed/25279754
407. Falk, M., Faresjo, A., Faresjo, T., Sun exposure habits and health risk-related behaviours among individuals with previous history of skin cancer. Anticancer Res, 2013. 33(2): p. 631-8., https://www.ncbi.nlm.nih.gov/pubmed/23393359
408. Blashill, A. J., Safren, S. A., Skin cancer risk behaviors among US men: the role of sexual orientation. Am J Public Health, 2014. 104(9): p. 1640-1., https://www.ncbi.nlm.nih.gov/pubmed/25033138
409. Ackermann, S., Vuadens, A., Levi, F., Bulliard, J. L., Sun protective behaviour and sunburn prevalence in primary and secondary schoolchildren in western Switzerland. Swiss Med Wkly, 2016. 146: p. w14370., https://www.ncbi.nlm.nih.gov/pubmed/27878788
410. McNoe, B. M., Reeder, A. I., Adolescent sun protection at secondary school athletic sporting events - a misnomer. Aust N Z J Public Health, 2016. 40(4): p. 313-5., https://www.ncbi.nlm.nih.gov/pubmed/27028302
411. Basch, C. H., Basch, C. E., Rajan, S., Ruggles, K. V., Use of sunscreen and indoor tanning devices among a nationally representative sample of high school students, 2001-2011. Prev Chronic Dis, 2014. 11: p. E144., https://www.ncbi.nlm.nih.gov/pubmed/25144679
412. Dobbinson, S., Wakefield, M., Hill, D., Girgis, A., Aitken, J. F., Beckmann, K., et.al. Children's sun exposure and sun protection: prevalence in Australia and related parental factors. J Am Acad Dermatol, 2012. 66(6): p. 938-47., https://www.ncbi.nlm.nih.gov/pubmed/21890234
413. Dusza, S. W., Halpern, A. C., Satagopan, J. M., Oliveria, S. A., Weinstock, M. A., Scope, A., et.al. Prospective study of sunburn and sun behavior patterns during adolescence. Pediatrics, 2012. 129(2): p. 309-17., https://www.ncbi.nlm.nih.gov/pubmed/22271688
414. Reinau, D., Meier, C., Gerber, N., Hofbauer, G. F., Surber, C., Sun protective behaviour of primary and secondary school students in North-Western Switzerland. Swiss Med Wkly, 2012. 142: p. w13520., https://www.ncbi.nlm.nih.gov/pubmed/22367965
415. Tuncer Vural, A., Karatas Togral, A., Kirnap, M., Gulec, A. T., Haberal, M., Skin Cancer Risk Awareness and Sun-Protective Behavior Among Solid-Organ Transplant Recipients. Exp Clin Transplant, 2018. 16 Suppl 1(Suppl 1): p. 203-207., https://www.ncbi.nlm.nih.gov/pubmed/29528028

416. Heerfordt, I. M., Philipsen, P. A., Wulf, H. C., Sun behaviour on the beach monitored by webcam photos. Public Health, 2018. 155: p. 88-90., https://www.ncbi.nlm.nih.gov/pubmed/29328978
417. Cercato, M. C., Ramazzotti, V., Sperduti, I., Asensio-Pascual, A., Ribes, I., Guillen, C., et.al. Sun protection among Spanish beachgoers: knowledge, attitude and behaviour. J Cancer Educ, 2015. 30(1): p. 4-11., https://www.ncbi.nlm.nih.gov/pubmed/24890922
418. Diehl, K., Göring, T., Greinert, R., Breitbart, E.W., Schneider, S., Trends in Tanning Bed Use, Motivation, and Risk Awareness: Findings from four waves of the National Cancer Aid Monitoring (NCAM). International Journal of Environmental Research and Public Health, 2019. 16(20): p. 3913.
419. Gambla, W. C., Fernandez, A. M., Gassman, N. R., Tan, M. C. B., Daniel, C. L., College tanning behaviors, attitudes, beliefs, and intentions: A systematic review of the literature. Prev Med, 2017. 105: p. 77-87., https://www.ncbi.nlm.nih.gov/pubmed/28867504
420. Petersen, B., Triguero-Mas, M., Maier, B., Thieden, E., Philipsen, P. A., Heydenreich, J., et.al. Sun behaviour and personal UVR exposure among Europeans on short term holidays. J Photochem Photobiol B, 2015. 151: p. 264-9., https://www.ncbi.nlm.nih.gov/pubmed/26332747
421. Borner, F., Greinert, R., Schutz, H., Wiedemann, P., [UV risk perception by the general public: results of a representative questionnaire in Germany]. Gesundheitswesen, 2010. 72(12): p. e89-97., https://www.ncbi.nlm.nih.gov/pubmed/20049688
422. Eichhorn, C., Seibold, C., Loss, J., Steinmann, A., Nagel, E., [Knowledge about UV-radiation and sun protection: survey of adolescents and young adults in Bavaria]. Hautarzt, 2008. 59(10): p. 821-7., https://www.ncbi.nlm.nih.gov/pubmed/18810371
423. Rutten, L. F., Hesse, B. W., Moser, R. P., McCaul, K. D., Rothman, A. J., Public perceptions of cancer prevention, screening, and survival: comparison with state-of-science evidence for colon, skin, and lung cancer. J Cancer Educ, 2009. 24(1): p. 40-8., https://www.ncbi.nlm.nih.gov/pubmed/19259865
424. Hajdarevic, S., Hvidberg, L., Lin, Y., Donnelly, C., Gavin, A., Lagerlund, M., et.al. Awareness of sunburn in childhood, use of sunbeds and change of moles in Denmark, Northern Ireland, Norway and Sweden. Eur J Public Health, 2016. 26(1): p. 29-35., https://www.ncbi.nlm.nih.gov/pubmed/26082445
425. Boynton, A., Oxlad, M., Melanoma and its relationship with solarium use: health knowledge, attitudes and behaviour of young women. J Health Psychol, 2011. 16(6): p. 969-79., https://www.ncbi.nlm.nih.gov/pubmed/21444729
426. Gordon, M., Rodriguez, V. M., Shuk, E., Schoenhammer, M., Halpern, A. C., Geller, A. C., et.al. Teen Daughters and Their Mothers in Conversation: Identifying Opportunities for Enhancing Awareness of Risky Tanning Behaviors. J Adolesc Health, 2016. 58(5): p. 579-81., https://www.ncbi.nlm.nih.gov/pubmed/27107911
427. Keeney, S., McKenna, H., Fleming, P., McIlfatrick, S., Attitudes, knowledge and behaviours with regard to skin cancer: a literature review. Eur J Oncol Nurs, 2009. 13(1): p. 29-35., https://www.ncbi.nlm.nih.gov/pubmed/19153059
428. Butler, D. P., Lloyd-Lavery, A., Archer, C. M., Turner, R., Awareness of and attitudes towards skin-cancer prevention: a survey of patients in the UK presenting to their general practice. Clin Exp Dermatol, 2013. 38(4): p. 338-43., https://www.ncbi.nlm.nih.gov/pubmed/23530554
429. Kyle, R. G., Nicoll, A., Forbat, L., Hubbard, G., Adolescents' awareness of cancer risk factors and associations with health-related behaviours. Health Educ Res, 2013. 28(5): p. 816-27., https://www.ncbi.nlm.nih.gov/pubmed/23648385
430. Gefeller, O., Uter, W., Pfahlberg, A. B., Long-term development of parental knowledge about skin cancer risks in Germany: Has it changed for the better?. Prev Med, 2016. 89: p. 31-36., https://www.ncbi.nlm.nih.gov/pubmed/27211108
431. Hamilton, K., Cleary, C., White, K. M., Hawkes, A. L., Keeping kids sun safe: exploring parents' beliefs about their young child's sun-protective behaviours. Psychooncology, 2016. 25(2): p. 158-63., https://www.ncbi.nlm.nih.gov/pubmed/26101815

432. Day, A. K., Wilson, C. J., Hutchinson, A. D., Roberts, R. M., The role of skin cancer knowledge in sun-related behaviours: a systematic review. J Health Psychol, 2014. 19(9): p. 1143-62., https://www.ncbi.nlm.nih.gov/pubmed/23682066
433. Ruppert, L., Koster, B., Siegert, A. M., Cop, C., Boyers, L., Karimkhani, C., et.al. YouTube as a source of health information: Analysis of sun protection and skin cancer prevention related issues. Dermatol Online J, 2017. 23(1):, https://www.ncbi.nlm.nih.gov/pubmed/28329465
434. Buller, M. K., Kane, I. L., Martin, R. C., Giese, A. J., Cutter, G. R., Saba, L. M., et.al. Randomized trial evaluating computer-based sun safety education for children in elementary school. Journal of cancer education : the official journal of the American Association for Cancer Education, 2008. 23(2): p. 74-9.
435. Bränström, R., Ullén, H., Brandberg, Y., A randomised population-based intervention to examine the effects of the ultraviolet index on tanning behaviour. European Journal of Cancer, 2003. 39(7): p. 968-974.
436. Gritz, E. R., Tripp, M. K., James, A. S., Harrist, R. B., Mueller, N. H., Chamberlain, R. M., et.al. Effects of a preschool staff intervention on children's sun protection: outcomes of sun protection is fun!. Health Educ Behav, 2007. 34(4): p. 562-77., https://www.ncbi.nlm.nih.gov/pubmed/16740505
437. Reding, D. J., Fischer, V., Gunderson, P., Lappe, K., Anderson, H., Calvert, G., Teens teach skin cancer prevention. J Rural Health, 1996. 12(4 Suppl): p. 265-72., https://www.ncbi.nlm.nih.gov/pubmed/10162857
438. Bastuji-Garin, S., Grob, J. J., Grognard, C., Grosjean, F., Guillaume, J. C., Melanoma prevention: evaluation of a health education campaign for primary schools. Arch Dermatol, 1999. 135(8): p. 936-40., https://www.ncbi.nlm.nih.gov/pubmed/10456342
439. Bundeszentrale für politische Bildung, Medienkompetenz. Herausforderung für Politik, politische Bildung und Medienbildung., 2017., http://www.bpb.de/system/files/document_pdf/10111_Medienkompetenz_ba.pdf
440. Buller, D. B., Reynolds, K. D., Berteletti, J., Massie, K., Ashley, J., Buller, M. K., et.al. Accuracy of Principal and Teacher Knowledge of School District Policies on Sun Protection in California Elementary Schools. Prev Chronic Dis, 2018. 15: p. E07., https://www.ncbi.nlm.nih.gov/pubmed/29346065
441. Buller, D. B., Borland, R., Skin Cancer Prevention for Children: A Critical Review. Health Education & Behavior, 1999. 26(3): p. 317-343.
442. Dietrich, A. J., Olson, A. L., Sox, C. H., Tosteson, T. D., Grant-Petersson, J., Persistent increase in children's sun protection in a randomized controlled community trial. Prev Med, 2000. 31(5): p. 569-74., https://www.ncbi.nlm.nih.gov/pubmed/11071838
443. Hart, K. M., Demarco, R. F., Primary prevention of skin cancer in children and adolescents: a review of the literature. J Pediatr Oncol Nurs, 2008. 25(2): p. 67-78., https://www.ncbi.nlm.nih.gov/pubmed/18272782
444. Weinstock, M. A., Rossi, J. S., Redding, C. A., Maddock, J. E., Randomized controlled community trial of the efficacy of a multicomponent stage-matched intervention to increase sun protection among beachgoers. Prev Med, 2002. 35(6): p. 584-92., https://www.ncbi.nlm.nih.gov/pubmed/12460526
445. Milne, E., English, D. R., Cross, D., Corti, B., Costa, C., Johnston, R., Evaluation of an intervention to reduce sun exposure in children: design and baseline results. Am J Epidemiol, 1999. 150(2): p. 164-73., https://www.ncbi.nlm.nih.gov/pubmed/10412961
446. Bauer, J., Buttner, P., Wiecker, T. S., Luther, H., Garbe, C., Interventional study in 1,232 young German children to prevent the development of melanocytic nevi failed to change sun exposure and sun protective behavior. Int J Cancer, 2005. 116(5): p. 755-61., https://www.ncbi.nlm.nih.gov/pubmed/15849749
447. Mayer, J. A., Slymen, D. J., Eckhardt, L., Johnston, M. R., Elder, J. P., Sallis, J. F., et.al. Reducing ultraviolet radiation exposure in children. Prev Med, 1997. 26(4): p. 516-22., https://www.ncbi.nlm.nih.gov/pubmed/9245674

448. White, K. M., Starfelt, L. C., Young, R. M., Hawkes, A. L., Cleary, C., Leske, S., et.al. A randomised controlled trial of an online theory-based intervention to improve adult Australians' sun-protective behaviours. Prev Med, 2015. 72: p. 19-22., https://www.ncbi.nlm.nih.gov/pubmed/25572618
449. Garside, R., Pearson, M., Moxham, T., What influences the uptake of information to prevent skin cancer? A systematic review and synthesis of qualitative research. Health Educ Res, 2010. 25(1): p. 162-82., https://www.ncbi.nlm.nih.gov/pubmed/19858077
450. Loescher, L. J., Buller, M. K., Buller, D. B., Emerson, J., Taylor, A. M., Public education projects in skin cancer. The evolution of skin cancer prevention education for children at a comprehensive cancer center. Cancer, 1995. 75(2 Suppl): p. 651-6., https://www.ncbi.nlm.nih.gov/pubmed/7804990
451. Glanz, K., Schoenfeld, E. R., Steffen, A., A randomized trial of tailored skin cancer prevention messages for adults: Project SCAPE. American journal of public health, 2010. 100(4): p. 735-41.
452. Adams, M. A., Norman, G. J., Hovell, M. F., Sallis, J. F., Patrick, K., Reconceptualizing decisional balance in an adolescent sun protection intervention: mediating effects and theoretical interpretations. Health Psychol, 2009. 28(2): p. 217-25.
453. Hornung, R. L., Lennon, P. A., Garrett, J. M., DeVellis, R. F., Weinberg, P. D., Strecher, V. J., Interactive computer technology for skin cancer prevention targeting children. Am J Prev Med, 2000. 18(1): p. 69-76.
454. Gritz, E. R., Tripp, M. K., James, A. S., Carvajal, S. C., Harrist, R. B., Mueller, N. H., et.al. An intervention for parents to promote preschool children's sun protection: effects of Sun Protection is Fun!. Preventive medicine, 2005. 41(2): p. 357-66.
455. Kiekbusch, S., Hannich, H. J., Isacsson, A., Johannisson, A., Lindholm, L. H., Sager, E., et.al. Impact of a cancer education multimedia device on public knowledge, attitudes, and behaviors: a controlled intervention study in Southern Sweden. Journal of cancer education : the official journal of the American Association for Cancer Education, 2000. 15(4): p. 232-6.
456. Boer, H., Ter Huurne, E., Taal, E., Effects of pictures and textual arguments in sun protection public service announcements. Cancer detection and prevention, 2006. 30(5): p. 432-8.
457. Walkosz, B., Voeks, J., Andersen, P., Scott, M., Buller, D., Cutter, G., et.al. Randomized trial on sun safety education at ski and snowboard schools in western North America. Pediatr Dermatol, 2007. 24(3): p. 222-9.
458. Glazebrook, C., Garrud, P., Avery, A., Coupland, C., Williams, H., Impact of a multimedia intervention „Skinsafe" on patients' knowledge and protective behaviors. Preventive medicine, 2006. 42(6): p. 449-54.
459. Idriss, N. Z., Alikhan, A., Baba, K., Armstrong, A. W., Online, video-based patient education improves melanoma awareness: a randomized controlled trial. Telemed J E Health, 2009. 15(10): p. 992-7.
460. Hanrahan, P. F., Hersey, P., Watson, A. B., Callaghan, T. M., The effect of an educational brochure on knowledge and early detection of melanoma. Aust J Public Health, 1995. 19(3): p. 270-4.
461. Girardi, S., Gaudy, C., Gouvernet, J., Teston, J., Richard, M. A., Grob, J. J., Superiority of a cognitive education with photographs over ABCD criteria in the education of the general population to the early detection of melanoma: a randomized study. International journal of cancer. Journal international du cancer, 2006. 118(9): p. 2276-80.
462. Janda, M., Baade, P. D., Youl, P. H., Aitken, J. F., Whiteman, D. C., Gordon, L., et.al. The skin awareness study: promoting thorough skin self-examination for skin cancer among men 50 years or older. Contemporary clinical trials, 2010. 31(1): p. 119-30.
463. Glanz, K., Steffen, A. D., Schoenfeld, E., Tappe, K. A., Randomized trial of tailored skin cancer prevention for children: the Project SCAPE family study. J Health Commun, 2013. 18(11): p. 1368-83., https://www.ncbi.nlm.nih.gov/pubmed/23806094
464. Glanz, K., Volpicelli, K., Jepson, C., Ming, M. E., Schuchter, L. M., Armstrong, K., Effects of tailored risk communications for skin cancer prevention and detection: the PennSCAPE randomized

trial. Cancer Epidemiol Biomarkers Prev, 2015. 24(2): p. 415-21., https://www.ncbi.nlm.nih.gov/pubmed/25432953
465. Heckman, C. J., Darlow, S. D., Ritterband, L. M., Handorf, E. A., Manne, S. L., Efficacy of an Intervention to Alter Skin Cancer Risk Behaviors in Young Adults. Am J Prev Med, 2016. 51(1): p. 1-11., https://www.ncbi.nlm.nih.gov/pubmed/26810358
466. Crane, L. A., Asdigian, N. L., Baron, A. E., Aalborg, J., Marcus, A. C., Mokrohisky, S. T., et.al. Mailed intervention to promote sun protection of children: a randomized controlled trial. Am J Prev Med, 2012. 43(4): p. 399-410., https://www.ncbi.nlm.nih.gov/pubmed/22992358
467. Finch, Linda, Janda, Monika, Loescher, Lois J., Hacker, Elke, Can skin cancer prevention be improved through mobile technology interventions? A systematic review. Preventive Medicine: An International Journal Devoted to Practice and Theory, 2016. 90: p. 121-132., http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc13a&AN=2016-43790-019, http://sfx.gbv.de/sfx_subhh?sid=OVID:psycdb&id=pmid:&id=doi:10.1016%2Fj.ypmed.2016.06.037&issn=0091-7435&isbn=&volume=90&issue=&spage=121&pages=121-132&date=2016&title=Preventive+Medicine%3A+An+International+Journal+Devoted+to+Practice+and+Theory&atitle=Can+skin+cancer+prevention+be+improved+through+mobile+technology+interventions%3F+A+systematic+review.&aulast=Finch
468. Austoker, J., Bankhead, C., Forbes, L. J., Atkins, L., Martin, F., Robb, K., et.al. Interventions to promote cancer awareness and early presentation: systematic review. Br J Cancer, 2009. 101 Suppl 2: p. S31-9., https://www.ncbi.nlm.nih.gov/pubmed/19956160
469. Kahn, J. A., Huang, B., Ding, L., Geller, A., Frazier, A. L., Impact of maternal communication about skin, cervical, and lung cancer prevention on adolescent prevention behaviors. J Adolesc Health, 2011. 49(1): p. 93-6., https://www.ncbi.nlm.nih.gov/pubmed/21700165
470. Real, K., Rimal, R. N., Friends talk to friends about drinking: exploring the role of peer communication in the theory of normative social behavior. Health Commun, 2007. 22(2): p. 169-80.
471. Geulen, D, Sozialisation, in Lehrbuch der Soziologie, Joas, H , Editor. 2007, Campus Verlag: Frankfurt, New York. 3: p. 137-159.
472. Hillhouse, J., Turrisi, R., Scaglione, N. M., Cleveland, M. J., Baker, K., Florence, L. C., A Web-Based Intervention to Reduce Indoor Tanning Motivations in Adolescents: a Randomized Controlled Trial. Prev Sci, 2017. 18(2): p. 131-140., https://www.ncbi.nlm.nih.gov/pubmed/27549602
473. Falzone, A. E., Brindis, C. D., Chren, M. M., Junn, A., Pagoto, S., Wehner, M., et.al. Teens, Tweets, and Tanning Beds: Rethinking the Use of Social Media for Skin Cancer Prevention. Am J Prev Med, 2017. 53(3S1): p. S86-S94., https://www.ncbi.nlm.nih.gov/pubmed/28818251
474. Hill, S. E., Durante, K. M., Courtship, competition, and the pursuit of attractiveness: mating goals facilitate health-related risk taking and strategic risk suppression in women. Pers Soc Psychol Bull, 2011. 37(3): p. 383-94., https://www.ncbi.nlm.nih.gov/pubmed/21252381
475. Reifegerste, Doreen, Rössler, Patrick, Soziale Appelle in der Gesundheitskommunikation. Motivkategorien als Grundlage für die theoretische Integration und die Systematisierung empirischer Befunde. Medien & Kommunikationswissenschaft, 2014. 62(4): p. 606-634., https://doi.org/10.5771/1615-634x-2014-4-606
476. Williams, A. L., Grogan, S., Clark-Carter, D., Buckley, E., Appearance-based interventions to reduce ultraviolet exposure and/or increase sun protection intentions and behaviours: a systematic review and meta-analyses. Br J Health Psychol, 2013. 18(1): p. 182-217., https://www.ncbi.nlm.nih.gov/pubmed/22989352
477. Robinson, J. K., Turrisi, R., Stapleton, J., Efficacy of a partner assistance intervention designed to increase skin self-examination performance. Arch Dermatol, 2007. 143(1): p. 37-41.
478. Robinson, J. K., Turrisi, R., Stapleton, J., Examination of mediating variables in a partner assistance intervention designed to increase performance of skin self-examination. J Am Acad Dermatol, 2007. 56(3): p. 391-7., https://www.ncbi.nlm.nih.gov/pubmed/17147966
479. Heckman, C. J., Zhu, F., Manne, S. L., Kloss, J. D., Collins, B. N., Bass, S. B., et.al. Process and outcomes of a skin protection intervention for young adults. J Health Psychol, 2013. 18(4): p. 561-73., https://www.ncbi.nlm.nih.gov/pubmed/22843632

480. Blashill, A. J., Rooney, B. M., Luberto, C. M., Gonzales, M. th, Grogan, S., A brief facial morphing intervention to reduce skin cancer risk behaviors: Results from a randomized controlled trial. Body Image, 2018. 25: p. 177-185., https://www.ncbi.nlm.nih.gov/pubmed/29698824
481. Hollands, G. J., Hankins, M., Marteau, T. M., Visual feedback of individuals' medical imaging results for changing health behaviourJohn Wiley & Sons, Ltd. Cochrane Database of Systematic Reviews, 2010., http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD007434/frame.html
482. Hillhouse, J., Turrisi, R., Stapleton, J., Robinson, J., A randomized controlled trial of an appearance-focused intervention to prevent skin cancer. Cancer, 2008. 113(11): p. 3257-66., https://www.ncbi.nlm.nih.gov/pubmed/18937268
483. Hillhouse, J., Turrisi, R., Stapleton, J., Robinson, J., Effect of seasonal affective disorder and pathological tanning motives on efficacy of an appearance-focused intervention to prevent skin cancer. Arch Dermatol, 2010. 146(5): p. 485-91., https://www.ncbi.nlm.nih.gov/pubmed/20479295
484. Mahler, H. I., Kulik, J. A., Harrell, J., Correa, A., Gibbons, F. X., Gerrard, M., Effects of UV photographs, photoaging information, and use of sunless tanning lotion on sun protection behaviors. Arch Dermatol, 2005. 141(3): p. 373-80., https://www.ncbi.nlm.nih.gov/pubmed/15781679
485. Stock, M. L., Gerrard, M., Gibbons, F. X., Dykstra, J. L., Weng, C. Y., Mahler, H. I., et.al. Sun protection intervention for highway workers: long-term efficacy of UV photography and skin cancer information on men's protective cognitions and behavior. Ann Behav Med, 2009. 38(3): p. 225-36., https://www.ncbi.nlm.nih.gov/pubmed/20049658
486. Robinson, J. K., Turrisi, R., Stapleton, J., Efficacy of a partner assistance intervention designed to increase skin self-examination performance. Arch Dermatol, 2007. 143(1): p. 37-41., https://www.ncbi.nlm.nih.gov/pubmed/17224540
487. Rosenbrock, R., Hartung, S., Public Health Action Cycle / Gesundheitspolitischer Aktionszyklus, in Leitbegriffe der Gesundheitsförderung, Bundeszentrale für Gesundheitliche Auflärung (BZgA) , Editor. 2015, Bundeszentrale für gesundheitliche Aufklärung (BZgA)., https://www.leitbegriffe.bzga.de/?uid=6c2ee36daf9c988ea50649d69fb32afe&id=angebote&idx=163
488. Weltgesundheitsorganisation, Ottawa-Charta zur Gesundheitsförderung, 1986.
489. Crane, L. A., Deas, A., Mokrohisky, S. T., Ehrsam, G., Jones, R. H., Dellavalle, R., et.al. A randomized intervention study of sun protection promotion in well-child care. Prev Med, 2006. 42(3): p. 162-70., https://www.ncbi.nlm.nih.gov/pubmed/16376977
490. Milne, E., English, D. R., Johnston, R., Cross, D., Borland, R., Costa, C., et.al. Improved sun protection behaviour in children after two years of the Kidskin intervention. Aust N Z J Public Health, 2000. 24(5): p. 481-7., https://www.ncbi.nlm.nih.gov/pubmed/11109684
491. Milne, E., Johnston, R., Cross, D., Giles-Corti, B., English, D. R., Effect of a school-based sun-protection intervention on the development of melanocytic nevi in children. Am J Epidemiol, 2002. 155(8): p. 739-45., https://www.ncbi.nlm.nih.gov/pubmed/11943692
492. English, D. R., Milne, E., Jacoby, P., Giles-Corti, B., Cross, D., Johnston, R., The effect of a school-based sun protection intervention on the development of melanocytic nevi in children: 6-year follow-up. Cancer Epidemiol Biomarkers Prev, 2005. 14(4): p. 977-80., https://www.ncbi.nlm.nih.gov/pubmed/15824173
493. Naldi, L., Chatenoud, L., Bertuccio, P., Zinetti, C., Di Landro, A., Scotti, L., et.al. Improving sun-protection behavior among children: results of a cluster-randomized trial in Italian elementary schools. The „SoleSi SoleNo-GISED" Project. J Invest Dermatol, 2007. 127(8): p. 1871-7., https://www.ncbi.nlm.nih.gov/pubmed/17460732
494. Rat, C., Quereux, G., Riviere, C., Clouet, S., Senand, R., Volteau, C., et.al. Targeted melanoma prevention intervention: a cluster randomized controlled trial. Ann Fam Med, 2014. 12(1): p. 21-8., https://www.ncbi.nlm.nih.gov/pubmed/24445100
495. Falk, M., Magnusson, H., Sun protection advice mediated by the general practitioner: an effective way to achieve long-term change of behaviour and attitudes related to sun exposure?. Scand J Prim Health Care, 2011. 29(3): p. 135-43., https://www.ncbi.nlm.nih.gov/pubmed/21682578

496. Mayer, J. A., Slymen, D. J., Eckhardt, L., Rosenberg, C., Stepanski, B. M., Creech, L., et.al. Skin cancer prevention counseling by pharmacists: specific outcomes of an intervention trial. Cancer Detect Prev, 1998. 22(4): p. 367-75., https://www.ncbi.nlm.nih.gov/pubmed/9674880
497. Livingston, P. M., White, V., Hayman, J., Dobbinson, S., Australian adolescents' sun protection behavior: who are we kidding?. Prev Med, 2007. 44(6): p. 508-12., https://www.ncbi.nlm.nih.gov/pubmed/17400286
498. Shibuya, K., Ciecierski, C., Guindon, E., Bettcher, D. W., Evans, D. B., Murray, C. J., et.al. WHO Framework Convention on Tobacco Control: development of an evidence based global public health treaty. BMJ, 2003. 327(7407): p. 154-7., https://www.ncbi.nlm.nih.gov/pubmed/12869461
499. Dobbinson, S. J., White, V., Wakefield, M. A., Jamsen, K. M., White, V., Livingston, P. M., et.al. Adolescents' use of purpose built shade in secondary schools: cluster randomised controlled trial. BMJ, 2009. 338(feb17 1): p. b95., https://www.ncbi.nlm.nih.gov/pubmed/19223344
500. Buller, M. K., Goldberg, G., Buller, D. B., Sun Smart Day: a pilot program for photoprotection education. Pediatr Dermatol, 1997. 14(4): p. 257-63., https://www.ncbi.nlm.nih.gov/pubmed/9263304
501. Quereux, G., Nguyen, J. M., Volteau, C., Dreno, B., Prospective trial on a school-based skin cancer prevention project. Eur J Cancer Prev, 2009. 18(2): p. 133-44., https://www.ncbi.nlm.nih.gov/pubmed/19337061
502. Allinson, Sarah, Asmuss, Monika, Baldermann, Cornelia, Bentzen, Joan, Buller, David, Gerber, Nathalie, et.al. Validity and Use of the UV Index: Report from the UVI Working Group, Schloss Hohenkammer, Germany, 5–7 December 2011. Health Physics, 2012. 103(3): p. 301-306 10.1097/HP0b013e31825b581e., http://journals.lww.com/health-physics/Fulltext/2012/09000/Validity_and_Use_of_the_UV_Index___Report_from_the.9.aspx
503. Klimmt, C., Maurer, M. & Baumann, E., Prozessevaluation der Kampagnenfortsetzung 2011-2012 „Runter vom Gas!" (ID - 503, 2014.
504. Schnabel, P, Boedeker, M, GesundheitskommunikationBeltz Juventa, 2012.
505. Ajzen, I., The Theory of Planned Behavior. Organizational Behavior and Human Decision Processes, 1991. 50(2): p. 179-211.
506. Bonfadelli, H., Friemel, T. N., Kommunikationskampagnen im Gesundheitsbereich. Grundlagen und AnwendungenUVK-Verl.-Ges., 2010.
507. Rossmann, C., Strategic Health Communication: Theory- and Evidence-Based Campaign Development, in Routledge handbook of strategic communication, Holtzhausen, D. R. , Editor. 2015, Routledge: New York u.a.. p. 409–423.
508. Reifegerste, D., Baumann, E., Vielfalt und Herausforderungen der Evidenzbasierung in der strategischen Gesundheitskommunikation, in Evidenzbasierte und evidenzinformierte Gesundheitskommunikation, 2018, Nomos: Baden-Baden. p. 73-83.
509. Valente, T W, Evaluating Communication CampaignsSage Publications, Inc.. Public Communication Campaigns, 2001. 3: p. 105-124.
510. Janz, N. K., Becker, M. H., The Health Belief Model: a decade later. Health Educ Q, 1984. 11(1): p. 1-47., https://www.ncbi.nlm.nih.gov/pubmed/6392204
511. Prochaska, J. O., Velicer, W. F., Redding, C., Rossi, J. S., Goldstein, M., DePue, J., et.al. Stage-based expert systems to guide a population of primary care patients to quit smoking, eat healthier, prevent skin cancer, and receive regular mammograms. Prev Med, 2005. 41(2): p. 406-16., https://www.ncbi.nlm.nih.gov/pubmed/15896835
512. Del Mar, C. B., Green, A. C., Battistutta, D., Do public media campaigns designed to increase skin cancer awareness result in increased skin excision rates?. Aust N Z J Public Health, 1997. 21(7): p. 751-4., https://www.ncbi.nlm.nih.gov/pubmed/9489194
513. Oivanen, T., Kojo, K., Pylkkanen, L., Holli, K., Auvinen, A., Early detection of skin cancer as public health policy: comparison of campaign and routine activity. Prev Med, 2008. 46(2): p. 160-5., https://www.ncbi.nlm.nih.gov/pubmed/17919714

514. Intergovernmental Panel on Climate Change (IPCC), Fünfter Sachstandsbericht, Teilbericht 1 (Wissenschaftliche Grundlagen). Kernbotschaften (deutsche Zusammenfassung)., 2014.
515. European Environment Agency (EEA), Climate change, impacts and vulnerability in Europe 2016. An indicator-based report, 2017., https://www.eea.europa.eu/publications/climate-change-impacts-and-vulnerability-2016
516. Kyselý, Jan, Temporal fluctuations in heat waves at Prague-Klementinum, the Czech Republic, from 1901-97, and their relationships to atmospheric circulation. International Journal of Climatology, 2002. 22(1): p. 33-50.
517. Coumou, Dim, Robinson, Alexander, Historic and future increase in the global land area affected by monthly heat extremes. Environmental Research Letters, 2013. 8(3): p. 34018-6.
518. Schar, C., Jendritzky, G., Climate change: hot news from summer 2003. Nature, 2004. 432(7017): p. 559-60., https://www.ncbi.nlm.nih.gov/pubmed/15577890
519. Seneviratne, Sonia I., Donat, Markus G., Mueller, Brigitte, Alexander, Lisa V., No pause in the increase of hot temperature extremes. Nature Climate Change, 2014. 4(3): p. 161-163., https://www.nature.com/articles/nclimate2145#supplementary-information
520. Intergovernmental Panel on Climate Change (IPCC), Managing the risks of extreme events and disasters to advance climate change adaptation: special report of the Intergovernmental Panel on Climate Change, 2012.
521. Intergovernmental Panel on Climate Change (IPCC), Summary for Policymakers, 2013.
522. Coumou, Dim, Robinson, Alexander, Rahmstorf, Stefan, Global increase in record-breaking monthly-mean temperatures. Climatic Change, 2013. 118(3-4): p. 771-782., https://doi.org/10.1007/s10584-012-0668-1
523. Kandarr, J., Reckert, H., Mücke, G., Anpassung an die gesundheitlichen Risiken des Klimawandels als Aufgabe des umweltbezogenen Gesundheitsschutzes. Analyse einer bundesweiten Recherche und Erhebung des Umweltbundesamtes. Bundesgesundheitsblatt, Springer-Verlag Berlin Heidelberg, 2014.
524. Bais, A. F., Lucas, R. M., Bornman, J. F., Williamson, C. E., Sulzberger, B., Austin, A. T., et.al. Environmental effects of ozone depletion, UV radiation and interactions with climate change: UNEP Environmental Effects Assessment Panel, update 2017. Photochem Photobiol Sci, 2018. 17(2): p. 127-179., https://www.ncbi.nlm.nih.gov/pubmed/29404558
525. Norris, J. R., Allen, R. J., Evan, A. T., Zelinka, M. D., O'Dell, C. W., Klein, S. A., Evidence for climate change in the satellite cloud record. Nature, 2016. 536(7614): p. 72-5., https://www.ncbi.nlm.nih.gov/pubmed/27398619
526. Baldermann, C., Lorenz, Sebastian, UV-Strahlung in Deutschland: Einflüsse des Ozonabbaus und des Klimawandels sowie Maßnahmen zum Schutz der Bevölkerung. Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz, 2019. 62(5): p. 639-645.
527. Seckmeyer, G., Die genaue Messung und Simulation der solaren UV-Strahlung.Seiler, M., 1999.
528. Seckmeyer, G., Thiel, S., Blumthaler, M., Fabian, P., Gerber, S., Gugg-Helminger, A., et.al. Intercomparison of spectral-UV-radiation measurement systems. Appl Opt, 1994. 33(33): p. 7805-12., https://www.ncbi.nlm.nih.gov/pubmed/20962993
529. Baumann, S., Elsner, C., de Graaf, D., Hoffmann, G., Martens, K., Noack, C., et.al. 1987 – 2017: 30 Jahre Montrealer Protokoll. Vom Ausstieg aus den FCKW zum Ausstieg aus teilfluorierten Kohlenwasserstoffen, 2017.
530. Bais, A. F., McKenzie, R. L., Bernhard, G., Aucamp, P. J., Ilyas, M., Madronich, S., et.al. Ozone depletion and climate change: impacts on UV radiation. Photochem Photobiol Sci, 2015. 14(1): p. 19-52., https://www.ncbi.nlm.nih.gov/pubmed/25380284
531. Bais, A. F., Bernhard, G., McKenzie, R. L., Aucamp, P. J., Young, P. J., Ilyas, M., et.al. Ozone-climate interactions and effects on solar ultraviolet radiation. Photochem Photobiol Sci, 2019. 18(3): p. 602-640., https://www.ncbi.nlm.nih.gov/pubmed/30810565
532. Parsons, K., Human Thermal Environments: The Effects of Hot, Moderate, and Cold Environments on Human Health, Comfort and Performance, Second EditionCRC Press, 2002.

533. Menne, B., Matthies, F., Improving public health responses to extreme weather/heat-waves: EuroHEATWorld Health Organisation, 2009.
534. Zacharias, S., Koppe, C., Einfluss des Klimawandels auf die Biotropie des Wetters und die Gesundheit bzw. die Leistungsfähigkeit der Bevölkerung in DeutschlandDeutscher Wetterdienst. Umweltforschungsplan des Bundesministeriums für Umwelt, Naturschutz, Bau und Reaktorsicherheit, 2015.
535. Augustin, J., Kis, A., Sorbe, C., Schafer, I., Augustin, M., Epidemiology of skin cancer in the German population: impact of socioeconomic and geographic factors. J Eur Acad Dermatol Venereol, 2018. 32(11): p. 1906-1913., https://www.ncbi.nlm.nih.gov/pubmed/29633375
536. Augustin, J., Sauerborn, R., Burkart, K., Endlicher, W., Jochner, S., Koppe, C., et.al. Klimawandel in DeutschlandSpringer Verlag, 2017.
537. Martens, W. J., Climate change, thermal stress and mortality changes. Soc Sci Med, 1998. 46(3): p. 331-44., https://www.ncbi.nlm.nih.gov/pubmed/9460815
538. Michelozzi, P., Accetta, G., De Sario, M., D'Ippoliti, D., Marino, C., Baccini, M., et.al. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. Am J Respir Crit Care Med, 2009. 179(5): p. 383-9., https://www.ncbi.nlm.nih.gov/pubmed/19060232
539. Scherber, Katharina, Endlicher, Wilfried, Langner, Marcel, Klimawandel und Gesundheit in Berlin-Brandenburg, in Klimawandel und Gesundheit, 2013. p. 25-38.
540. Scherber, K., Langner, M., Endlicher, W., Spatial analysis of hospital admissions for respiratory diseases during summer months in Berlin taking bioclimatic and socio-economic aspects into account. Erde, 2013. 144: p. 217-237.
541. Koppe, C., Sari Kovats, R., Menne, B., Jendritzky, G., Organization, World Health, Europe, Regional Office for, Heat-waves : risks and responses, 2004.
542. van der Leun, J. C., Piacentini, R. D., de Gruijl, F. R., Climate change and human skin cancer. Photochem Photobiol Sci, 2008. 7(6): p. 730-3., https://www.ncbi.nlm.nih.gov/pubmed/18528559
543. Michal Freedman, D., Kitahara, C. M., Linet, M. S., Alexander, B. H., Neta, G., Little, M. P., et.al. Ambient temperature and risk of first primary basal cell carcinoma: A nationwide United States cohort study. J Photochem Photobiol B, 2015. 148: p. 284-289., https://www.ncbi.nlm.nih.gov/pubmed/25996074
544. D'Ippoliti, D., Michelozzi, P., Marino, C., de'Donato, F., Menne, B., Katsouyanni, K., et.al. The impact of heat waves on mortality in 9 European cities: results from the EuroHEAT project. Environ Health, 2010. 9: p. 37., https://www.ncbi.nlm.nih.gov/pubmed/20637065
545. Bouchama, A., Dehbi, M., Mohamed, G., Matthies, F., Shoukri, M., Menne, B., Prognostic factors in heat wave related deaths: a meta-analysis. Arch Intern Med, 2007. 167(20): p. 2170-6., https://www.ncbi.nlm.nih.gov/pubmed/17698676
546. Eis, Dieter, Helm, Dieter, Laußmann, Detlef, Stark, Klaus, Klimawandel und Gesundheit - ein SachstandsberichtRobert Koch-Institut, Epidemiologie und Gesundheitsberichterstattung, 2011.
547. Koppe, C., Gesundheitsrelevante Bewertungvon thermischer Belastungunter Berücksichtigung der kurzfristigen Anpassungder Bevölkerungan die lokalen WitterungsverhältnisseInaugural-Dissertation zurErlangung der Doktorwürdeder Fakultät für Forst- und Umweltwissenschaften derAlbert-Ludwigs-UniversitätFreiburg i. Brsg., 2005.
548. Heudorf, U., Meyer, C., [Health effects of extreme heat—an example of the heat wave and mortality in Frankfurt am Main in August 2003]. Gesundheitswesen, 2005. 67(5): p. 369-74., https://www.ncbi.nlm.nih.gov/pubmed/15918125
549. Schneider, A., Breitner, S., Wolf, K., Hampel, R., Peters, A., Wichmann, H.E., Ursachenspezifische Mortalität, Herzinfarkt und das Auftreten von Beschwerden bei Herzinfarktüberlebenden in Abhängigkeit von der Lufttemperatur in Bayern (MOHIT)Helmholtz Zentrum München – Deutsches Forschungszentrum für Gesundheit und Umwelt. Institut für Epidemiologie, 2009.

550. Muthers, S, aschewski, G, Matzarakis, A, The Summers 2003 and 2015 in South-West Germany: HeatWaves and Heat-Related Mortality in the Context of Climate Change. Atmosphere, 2017. 8: p. 224.
551. Hoffmann, B., Hertel, S., Boes, T., Weiland, D., Jockel, K. H., Increased cause-specific mortality associated with 2003 heat wave in Essen, Germany. J Toxicol Environ Health A, 2008. 71(11-12): p. 759-65., https://www.ncbi.nlm.nih.gov/pubmed/18569574
552. Gabriel, K. M., Endlicher, W. R., Urban and rural mortality rates during heat waves in Berlin and Brandenburg, Germany. Environ Pollut, 2011. 159(8-9): p. 2044-50., https://www.ncbi.nlm.nih.gov/pubmed/21295389
553. Burkart, K., Canario, P., Breitner, S., Schneider, A., Scherber, K., Andrade, H., et.al. Interactive short-term effects of equivalent temperature and air pollution on human mortality in Berlin and Lisbon. Environ Pollut, 2013. 183: p. 54-63., https://www.ncbi.nlm.nih.gov/pubmed/23941745
554. Ren, C., Williams, G. M., Tong, S., Does particulate matter modify the association between temperature and cardiorespiratory diseases?. Environ Health Perspect, 2006. 114(11): p. 1690-6., https://www.ncbi.nlm.nih.gov/pubmed/17107854
555. Ren, C., Williams, G. M., Morawska, L., Mengersen, K., Tong, S., Ozone modifies associations between temperature and cardiovascular mortality: analysis of the NMMAPS data. Occup Environ Med, 2008. 65(4): p. 255-60., https://www.ncbi.nlm.nih.gov/pubmed/17890300
556. Roberts, S., Interactions between particulate air pollution and temperature in air pollution mortality time series studies. Environ Res, 2004. 96(3): p. 328-37., https://www.ncbi.nlm.nih.gov/pubmed/15364601
557. Lucas, R. M., Yazar, S., Young, A. R., Norval, M., de Gruijl, F. R., Takizawa, Y., et.al. Human health in relation to exposure to solar ultraviolet radiation under changing stratospheric ozone and climate. Photochem Photobiol Sci, 2019. 18(3): p. 641-680., https://www.ncbi.nlm.nih.gov/pubmed/30810559
558. National Radiological Protection Board, Ultraviolet radiation (UVR): health effects from exposure, 2002. 13:, https://www.gov.uk/government/publications/ultraviolet-radiation-uvr-health-effects-from-exposure
559. Rizwan, M., Reddick, C. L., Bundy, C., Unsworth, R., Richards, H. L., Rhodes, L. E., Photodermatoses: environmentally induced conditions with high psychological impact. Photochem Photobiol Sci, 2013. 12(1): p. 182-9., https://www.ncbi.nlm.nih.gov/pubmed/22961505
560. Stafford, R., Farrar, M. D., Kift, R., Durkin, M. T., Berry, J. L., Webb, A. R., et.al. The impact of photosensitivity disorders on aspects of lifestyle. Br J Dermatol, 2010. 163(4): p. 817-22., https://www.ncbi.nlm.nih.gov/pubmed/20545692
561. Rhodes, L. E., Bock, M., Janssens, A. S., Ling, T. C., Anastasopoulou, L., Antoniou, C., et.al. Polymorphic light eruption occurs in 18% of Europeans and does not show higher prevalence with increasing latitude: multicenter survey of 6,895 individuals residing from the Mediterranean to Scandinavia. J Invest Dermatol, 2010. 130(2): p. 626-8., https://www.ncbi.nlm.nih.gov/pubmed/19693026
562. World Meteorological Organization (WMO), National Oceanic and Atmospheric, Administration (United States), United Nations Environment Programme, National Aeronautics and Space Administration (United States), European Commission, Scientific Assessment of Ozone Depletion: 2006: report of the Montreal Protocol Scientific Assessment Pane, 2007.
563. Manney, G. L., Santee, M. L., Rex, M., Livesey, N. J., Pitts, M. C., Veefkind, P., et.al. Unprecedented Arctic ozone loss in 2011. Nature, 2011. 478(7370): p. 469-75., https://www.ncbi.nlm.nih.gov/pubmed/21964337
564. Siani, Anna Maria, Investigation on a low ozone episode at the end of November 2000 and its effect on ultraviolet radiation. Optical Engineering, 2002. 41(12): p. 3082-3089.
565. Mangold, A., Grooß, J. U., De Backer, H., Kirner, O., Ruhnke, R., Müller, R., A model study of the January 2006 low total ozone episode over Western Europe and comparison with ozone sonde data. Atmospheric Chemistry and Physics, 2009. 9(17): p. 6429-6451.

566. Werner, R., Valev, D., Atanassov, At., Kostadinov, I., Petkov, B., Giovanelli, G., et.al. Ozone mini-hole observation over the Balkan Peninsula in March 2005. Advances in Space Research, Volume 43, Numero 2, p.195-200, 2009.
567. Dobson, G.M.B., Harrison, D.N., Lawrence, J., Measurements of the amount of ozone in the E-arth's atmosphere and its relation to other geophysical conditions, 1929., https://doi.org/10.1098/rspa.1929.0034
568. Molina, Mario J., Rowland, F. S., Stratospheric sink for chlorofluoromethanes: chlorine atom-catalysed destruction of ozone. Nature, 1974. 249(5460): p. 810-812., https://doi.org/10.1038/249810a0
569. Crutzen, Paul J., Arnold, Frank, Nitric acid cloud formation in the cold Antarctic stratosphere: a major cause for the springtime 'ozone hole'. Nature, 1986. 324(6098): p. 651-655., https://doi.org/10.1038/324651a0
570. World Meteorological Organization (WMO), Scientific Assessment of Ozone Depletion: 2010. World Meteorological Organization Report No. 52, 2010.
571. Hauchecorne, Alain, Quantification of the transport of chemical constituents from the polar vortex to midlatitudes in the lower stratosphere using the high-resolution advection model MI-MOSA and effective diffusivity. Journal of Geophysical Research, 2002. 107(D20):
572. Koch, G., Wernli, H., Buss, S., Staehelin, J., Peter, T., Liniger, M. A., et.al. Quantification of the impact in mid-latitudes of chemical ozone depletion in the 1999/2000 Arctic polar vortex prior to the vortex breakup. Atmospheric Chemistry and Physics Discussions, 2004. 4(2): p. 1911-1940., https://www.atmos-chem-phys-discuss.net/4/1911/2004
573. Rösevall, J.D., Murtagh, D.P., Urban, J., Feng, W., Eriksson, P., Brohede, S., A study of ozone depletion in the 2004/2005 Arctic winter based on data from Odin/SMR and Aura/MLS. Journal of Geophysical Research: Atmospheres, 2008. Volume 113, Issue D13:, https://doi.org/10.1029/2007JD009560
574. Arnone, E., Castelli, E., Papandrea, E., Carlotti, M., Dinelli, B. M., Extreme ozone depletion in the 2010–2011 Arctic winter stratosphere as observed by MIPAS/ENVISAT using a 2-D tomographic approach. Atmospheric Chemistry and Physics, 2012. 12(19): p. 9149-9165., https://www.atmos-chem-phys.net/12/9149/2012
575. von Hobe, M., Bekki, S., Borrmann, S., Cairo, F., Amato, F.D., Di Donfrancesco, G., et.al. Reconciliation of essential process parameters for an enhancedpredictability of Arctic stratospheric ozone loss and its climateinteractions (RECONCILE): activities and results. Atmospheric Chemistry and Physics, 2013.
576. RECONCILE, Through dedicated laboratory and field measurements, RECONCILE has improved model representations of key processes dominating chemistry, microphysics and dynamics of Arctic stratospheric ozone loss, 2013., https://www.fp7-reconcile.eu
577. Stick, C., Krüger, K., Schade, N. H., Sandmann, H., Macke, A., Episode of unusual high solar ultraviolet radiation over central Europe due to dynamical reduced total ozone in May 2005. Atmospheric Chemistry and Physics, 2006. 6(7): p. 1771-1776.
578. Brönnimann, S., Hood, L.L., Low total ozone events over northwestern Europe in the 1950s and 1990s.. Ozone. Proceedings of the XX Quadrennial Ozone Symposium, 1-8 June 2004, Kos, Greece (Ed. C. Zerefos), 1, 302-303, 2004.
579. Reid, S. J., Tuck, A. F., Kiladis, G., On the changing abundance of ozone minima at northern midlatitudes. Journal of Geophysical Research: Atmospheres, 2000. 105(D10): p. 12169-12180.
580. Stenke, A., Grewe, V., Impact of ozone mini-holes on the heterogeneous destruction of stratospheric ozone. Chemosphere, 2003. 50(2): p. 177-90., https://www.ncbi.nlm.nih.gov/pubmed/12653290
581. Gesetz zur Stärkung der Gesundheitsförderung und der Prävention, 2015.
582. Bund/Lander Ad-hoc Arbeitsgruppe Gesundheitliche Anpassung an die Folgen des, Klimawandels, Handlungsempfehlungen fur die Erstellung von Hitzeaktionsplanen zum Schutz der menschlichen Gesundheit.. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, 2017. 60(6): p. 662-672., https://www.ncbi.nlm.nih.gov/pubmed/28492969

583. Staiger, H., Laschewski, G., Gratz, A., The perceived temperature - a versatile index for the assessment of the human thermal environment. Part A: scientific basics. Int J Biometeorol, 2012. 56(1): p. 165-76., https://www.ncbi.nlm.nih.gov/pubmed/21336880
584. Stewart, A. E., Kimlin, M. G., The Dislike of Hot Thermal Conditions and Its Relationship with Sun (Ultraviolet Radiation) Exposure in the Southeastern United States. Int J Environ Res Public Health, 2018. 15(10):, https://www.ncbi.nlm.nih.gov/pubmed/30275387
585. Arana, P., Cabezudo, S., Peñalba, M., Influence of weather conditions on transit ridership: A statistical study using data from Smartcards. Transportation Research Part A: Policy and Practice, 2014. 59: p. 1-12., http://www.sciencedirect.com/science/article/pii/S0965856413002073
586. Belanger, M., Gray-Donald, K., O'Loughlin, J., Paradis, G., Hanley, J., Influence of weather conditions and season on physical activity in adolescents. Ann Epidemiol, 2009. 19(3): p. 180-6., https://www.ncbi.nlm.nih.gov/pubmed/19217000
587. Eisinga, R., Franses, P. H., Vergeer, M., Weather conditions and daily television use in the Netherlands, 1996-2005. Int J Biometeorol, 2011. 55(4): p. 555-64., https://www.ncbi.nlm.nih.gov/pubmed/20978912
588. Knuschke, P., Kurpiers, M., Koch, R., Kuhlisch, W., Wittke, K, Mittlere UV-Exposition der Bevölkerung. Schlussbericht des BMBF-Vorhabens 07UV-B54C/3., 2004.
589. Spinney, J. E., Millward, H., Weather impacts on leisure activities in Halifax, Nova Scotia. Int J Biometeorol, 2011. 55(2): p. 133-45., https://www.ncbi.nlm.nih.gov/pubmed/20499254
590. Yang, Bin, Olofsson, Thomas, Nair, Gireesh, Kabanshi, Alan, Outdoor thermal comfort under subarctic climate of north Sweden – A pilot study in Umeå. Sustainable Cities and Society, 2017. 28: p. 387-397., http://www.sciencedirect.com/science/article/pii/S2210670716302554
591. Banwell, C., Dixon, J., Bambrick, H., Edwards, F., Kjellstrom, T., Socio-cultural reflections on heat in Australia with implications for health and climate change adaptation. Glob Health Action, 2012. 5:, https://www.ncbi.nlm.nih.gov/pubmed/23078748
592. Liu, Y., Kostakos, V., Li, H., Climatic effects on planning behavior. PLoS One, 2015. 10(5): p. e0126205., https://www.ncbi.nlm.nih.gov/pubmed/25993567
593. Becker, Stefan, Potchter, Oded, Yaakov, Yaron, Calculated and observed human thermal sensation in an extremely hot and dry climate. Energy and Buildings, 2003. 35(8): p. 747-756.
594. Knuschke P., Unverricht I., Ott G., Janßen M., Personenbezogene Messung der UV-Exposition von Arbeitnehmern im Freien. Abschlussbericht Projekt F 1777, 2007.
595. Godar, D. E., UV doses worldwide. Photochem Photobiol, 2005. 81(4): p. 736-49., https://www.ncbi.nlm.nih.gov/pubmed/15819599
596. Godar, D. E., Urbach, F., Gasparro, F. P., van der Leun, J. C., UV doses of young adults. Photochem Photobiol, 2003. 77(4): p. 453-7., https://www.ncbi.nlm.nih.gov/pubmed/12733658
597. Gies, P., Roy, C., Toomey, S., Tomlinson, D., Ambient solar UVR, personal exposure and protection. J Epidemiol, 1999. 9(6 Suppl): p. S115-22., https://www.ncbi.nlm.nih.gov/pubmed/10709359
598. Kift, R., Berry, J. L., Vail, A., Durkin, M. T., Rhodes, L. E., Webb, A. R., Lifestyle factors including less cutaneous sun exposure contribute to starkly lower vitamin D levels in U.K. South Asians compared with the white population. Br J Dermatol, 2013. 169(6): p. 1272-8., https://www.ncbi.nlm.nih.gov/pubmed/23855783
599. Piacentini, R. D., Della Ceca, L. S., Ipina, A., Climate change and its relationship with non-melanoma skin cancers. Photochem Photobiol Sci, 2018. 17(12): p. 1913-1917., https://www.ncbi.nlm.nih.gov/pubmed/30334034
600. Gies, P., Mackay, C., Measurements of the solar UVR protection provided by shade structures in New Zealand primary schools. Photochem Photobiol, 2004. 80(2): p. 334-9., https://www.ncbi.nlm.nih.gov/pubmed/15264956
601. Kabisch, N., van den Bosch, M., Lafortezza, R., The health benefits of nature-based solutions to urbanization challenges for children and the elderly - A systematic review. Environ Res, 2017. 159: p. 362-373., https://www.ncbi.nlm.nih.gov/pubmed/28843167

602. Middel, A., Selover, N., Hagen, B., Chhetri, N., Impact of shade on outdoor thermal comfort-a seasonal field study in Tempe, Arizona. Int J Biometeorol, 2016. 60(12): p. 1849-1861., https://www.ncbi.nlm.nih.gov/pubmed/27192997
603. Antoniadis, D., Katsoulas, N., Papanastasiou, D., Christidou, V., Kittas, C., Evaluation of thermal perception in schoolyards under Mediterranean climate conditions. Int J Biometeorol, 2016. 60(3): p. 319-34., https://www.ncbi.nlm.nih.gov/pubmed/26190284
604. Buller, D. B., English, D. R., Buller, M. K., Simmons, J., Chamberlain, J. A., Wakefield, M., et.al. Shade Sails and Passive Recreation in Public Parks of Melbourne and Denver: A Randomized Intervention. Am J Public Health, 2017. 107(12): p. 1869-1875., https://www.ncbi.nlm.nih.gov/pubmed/29048958
605. Mahe, E., Correa, M. P., Godin-Beekmann, S., Haeffelin, M., Jegou, F., Saiag, P., et.al. Evaluation of tourists' UV exposure in Paris. J Eur Acad Dermatol Venereol, 2013. 27(3): p. e294-304., https://www.ncbi.nlm.nih.gov/pubmed/22775064
606. Sliney, D. H., Physical factors in cataractogenesis: ambient ultraviolet radiation and temperature. Invest Ophthalmol Vis Sci, 1986. 27(5): p. 781-90., https://www.ncbi.nlm.nih.gov/pubmed/3700027
607. Victoria, Cancer Council, Shade Guidelines, 2015.
608. Parisi, A. V., Turnbull, D. J., Shade provision for UV minimization: a review. Photochem Photobiol, 2014. 90(3): p. 479-90., https://www.ncbi.nlm.nih.gov/pubmed/24417678
609. Streiling, S., Matzarakis, A., Streiling, S., A. Matzarakis, (2003). Influence of singular trees and small clusters of trees on the bioclimate of a city – a case study. Journal of Arboriculture 29, 309-316. Journal of Arboriculture, 2003. 20: p. 309-316.
610. Gies, P., Elix, R., Lawry, D., Gardner, J., Hancock, T., Cockerell, S., et.al. Assessment of the UVR protection provided by different tree species. Photochem Photobiol, 2007. 83(6): p. 1465-70., https://www.ncbi.nlm.nih.gov/pubmed/18028222
611. Buller, D. B., Dobbinson, S., English, D. R., Wakefield, M., Buller, M. K., Rationale, design, and baseline data of a cross-national randomized trial on the effect of built shade in public parks for sun protection. Contemp Clin Trials, 2017. 55: p. 47-55., https://www.ncbi.nlm.nih.gov/pubmed/28185996
612. Knieling, J., Fröhlich, J., Greiving, S., Kannen, A., Morgenstern, N., Moss, T., et.al. PlanerischorganisatorischeAnpassungspotenziale an den Klimawandel, 2011.
613. Deutsche Gesetzliche Unfallversicherung (DGUV) e.V., Prävention - Sonnenschutz, https://www.dguv.de/de/praevention/themen-a-z/sonne/index.jsp
614. Deutsche Gesetzliche Unfallversicherung (DGUV) e.V., DGUV-Arbeitshilfe „Hautkrebs durch UV-Strahlung", 2013., https://www.dguv.de/medien/inhalt/versicherung/berufskrankheiten/hauterkrankungen/hautkrebs/dguv_arbeitshilfe_hautkrebs.pdf
615. Bundesrepublik Deutschland, Beschluss des Bundesrates: Zweite Verordnung zur Änderung der Verordnung zur arbeitsmedizinischen Vorsorge, 2019. Bundesdrucksache 237/19, 1-21:, https://www.bmas.de/SharedDocs/Downloads/DE/PDF-Gesetze/Regierungsentwuerfe/reg-zweite-verordnung-aenderung-verordnung-zur-arbeitsmedizinischen-vorsorge.pdf;jsessionid=5343C9B39F76571E42C10149A20324A9?__blob=publicationFile&v=3
616. Knuschke, P., Unverricht, I., Ott, G., Janßen, M., Personenbezogene Messungder UV-Exposition vonArbeitnehmern im Freien, 2007. ForschungProjekt F 1777:
617. Holman, C.D.J., Gibson, I.M., Stephenson, M., Armstrong, B.K., Ultraviolet irradiation of human body sites in relation to occupation and outdoor activity: field studies using personal UVR dosimeters, 1983.
618. Diffey, B., Personal ultraviolet radiation dosimetry with polysulphone film badges. Photodermatol, 1984. 1(3): p. 151-7., https://www.ncbi.nlm.nih.gov/pubmed/6527960
619. Knuschke, P., Krins, A., UV-Personendosimetrie Teil B: Mit Verwendung des Polysulfonfilms als UV-Sensor; Schlussbericht BMBF-Vorhaben 07UVB54B, 2000.

620. Thieden, E., Agren, M. S., Wulf, H. C., The wrist is a reliable body site for personal dosimetry of ultraviolet radiation. Photodermatol Photoimmunol Photomed, 2000. 16(2): p. 57-61., https://www.ncbi.nlm.nih.gov/pubmed/10823313
621. Thieden, E., Agren, M. S., Wulf, H. C., Solar UVR exposures of indoor workers in a Working and a Holiday Period assessed by personal dosimeters and sun exposure diaries. Photodermatol Photoimmunol Photomed, 2001. 17(6): p. 249-55., https://www.ncbi.nlm.nih.gov/pubmed/11722749
622. Wittlich, M., Westerhausen, S., Kleinespel, P., Rifer, G., Stoppelmann, W., An approximation of occupational lifetime UVR exposure: algorithm for retrospective assessment and current measurements. J Eur Acad Dermatol Venereol, 2016. 30 Suppl 3: p. 27-33., https://www.ncbi.nlm.nih.gov/pubmed/26995020
623. Serrano, M. A., Canada, J., Moreno, J. C., Solar Radiation, Group, Erythemal ultraviolet exposure in two groups of outdoor workers in Valencia, Spain. Photochem Photobiol, 2009. 85(6): p. 1468-73., https://www.ncbi.nlm.nih.gov/pubmed/19709385
624. Serrano, M. A., Canada, J., Moreno, J. C., Gurrea, G., Members of the Valencia Solar Radiation Research, Group, Occupational UV exposure of environmental agents in Valencia, Spain. Photochem Photobiol, 2014. 90(4): p. 911-8., https://www.ncbi.nlm.nih.gov/pubmed/24494834
625. Wittlich, M., John, S. M., Tiplica, G. S., Salavastru, C. M., Butacu, A. I., Modenese, A., et.al. Personal solar ultraviolet radiation dosimetry in an occupational setting across Europe. J Eur Acad Dermatol Venereol, 2020. n/a(n/a):, https://www.ncbi.nlm.nih.gov/pubmed/32080895
626. Kovacic, Personal ultraviolet radiation dosimetry and its relationship with environmental data: a longitudinal pilot study in Croatian construction workers, in Review.
627. Bundesamt für Justiz, Arbeitsschutzgesetz - ArbSchG, zuletzt geändert am 31.08.2015., https://www.gesetze-im-internet.de/arbschg/__12.html
628. Deutsche Gesetzliche Unfallversicherung e.V. (DGUV), DGUV Information 203-085: Arbeiten unter der Sonne, 2016., https://publikationen.dguv.de/dguv/udt_dguv_main.aspx?FDOCUID=26486
629. Ruppert L., Ofenloch R., Surber C., Diepgen T.L., Wirksamkeit beruflicher Hautkrebspräventionsmaßnahmen - Eine randomisierte Clusterumfrage unter Berufsschülern beschäftigt an Outdoor-Arbeitsplätzen in Deutschland. Dermatologie in Beruf und Umwelt, Jahrgang 66, Nr. 4/2018, 2018. p. 159-174.
630. Kearney, G. D., Xu, X., Balanay, J. A., Becker, A. J., Sun safety among farmers and farmworkers: a review. J Agromedicine, 2014. 19(1): p. 53-65., https://www.ncbi.nlm.nih.gov/pubmed/24417532
631. Mayer, J. A., Slymen, D. J., Clapp, E. J., Pichon, L. C., Eckhardt, L., Eichenfield, L. F., et.al. Promoting sun safety among US Postal Service letter carriers: impact of a 2-year intervention. Am J Public Health, 2007. 97(3): p. 559-65., https://www.ncbi.nlm.nih.gov/pubmed/17267715
632. Stock, M. L., Gerrard, M., Gibbons, F. X., Dykstra, J. L., Weng, C. Y., Mahler, H. I., et.al. Sun protection intervention for highway workers: long-term efficacy of UV photography and skin cancer information on men's protective cognitions and behavior. Ann Behav Med, 2009. 38(3): p. 225-36., https://www.ncbi.nlm.nih.gov/pubmed/20049658
633. Andersen, Peter A., Buller, David B., Voeks, Jenifer H., Walkosz, Barbara J., Scott, Michael D., Cutter, Gary R., et.al. Testing the long-term effects of the Go Sun Smart worksite health communication campaign: A group-randomized experimental study. Journal of Communication, 2008. 58(3): p. 447-471., http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc6&AN=2008-12578-003, http://sfx.gbv.de/sfx_subhh?sid=OVID:psycdb&id=pmid:&id=doi:10.1111%2Fj.1460-2466.2008.00394.x&issn=0021-9916&isbn=&volume=58&issue=3&spage=447&pages=447-471&date=2008&title=Journal+of+Communication&atitle=Testing+the+long-term+effects+of+the+Go+Sun+Smart+worksite+health+communication+campaign%3A+A+group-randomized+experimental+study.&aulast=Andersen, http://dx.doi.org/10.1111/j.1460-2466.2008.00394.x

634. Houdmont, J., Madgwick, P., Randall, R., Sun safety in construction: a U.K. intervention study. Occup Med (Lond), 2016. 66(1): p. 20-6., https://www.ncbi.nlm.nih.gov/pubmed/26409050
635. Thieden, E., Collins, S. M., Philipsen, P. A., Murphy, G. M., Wulf, H. C., Ultraviolet exposure patterns of Irish and Danish gardeners during work and leisure. Br J Dermatol, 2005. 153(4): p. 795-801., https://www.ncbi.nlm.nih.gov/pubmed/16181463
636. Bundesministerium für Arbeit und Soziales (BMAS), Zweite Verordnung zur Änderung der Verordnung zur arbeitsmedizinischen Vorsorge, 2019. Bundesdrucksache 237/19, 1-21:
637. Deutsche Gesetzliche Unfallversicherung (DGUV) e.V., Honorare in der Berufsdermatologie – Ein Leitfaden für die Abrechnung von A bis Z, 2019. Stand 10/2019:, https://publikationen.dguv.de/versicherungleistungen/berufskrankheiten/3207/honorare-in-der-berufsdermatologie-ein-leitfaden-fuer-die-abrechnung-von-a-bis-z
638. Beaglehole, R., Bonita, R., Kjellström, T., Einführung in die EpidemiologieHogrefe, Hans Huber, 1997.
639. Giersiepen, K., Hense, H., Klug, S., Antes, G., Zeeb, H., Entwicklung, Durchführung und Evaluation von Programmen zur Krebsfrüherkennung. Ein Positionspapier. Zeitschrift für ärztliche Fortbildung und Qualität im Gesundheitswesen, 2007. 101(1): p. 43-49.
640. Brantsch, K. D., Meisner, C., Schonfisch, B., Trilling, B., Wehner-Caroli, J., Rocken, M., et.al. Analysis of risk factors determining prognosis of cutaneous squamous-cell carcinoma: a prospective study. Lancet Oncol, 2008. 9(8): p. 713-20., https://www.ncbi.nlm.nih.gov/pubmed/18617440
641. Wilson, J.M.G., Jungner, G., Principles and Practice of Screening for DiseaseWorld Health Organization, 1968.
642. Spix, C., Blettner, M., Screening: part 19 of a series on evaluation of scientific publications. Dtsch Arztebl Int, 2012. 109(21): p. 385-90., https://www.ncbi.nlm.nih.gov/pubmed/22690254
643. Schwartz. F. W., Holstein, H., Brecht, J. G., Ergebnisse der gesetzlichen Frükerkennung unter Effektivitätsgesichtspunkten, in Probleme einer systematischen Früherkennung, van Eimeren, W. and Neiß, A., Editors. 1979, Springer: Berlin, Heidelberg, New York. p. 62-63.
644. Morrison, A.S., Screening in chronic diseaseUniversity Press, 1992.
645. Andermann, A., Blancquaert, I., Beauchamp, S., Dery, V., Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years. Bull World Health Organ, 2008. 86(4): p. 317-9., https://www.ncbi.nlm.nih.gov/pubmed/18438522
646. Gemeinsamer Bundesausschuss, Richtlinie des Gemeinsamen Bundesausschusses über die Früherkennung von Krebserkrankungen (Krebsfrüherkennungs-Richtlinie / KFE-RL). Bundesanzeiger, 2009. Nr. 148a:
647. Gordis, L., EpidemiologyElsevier / Saunders, 2009.
648. Gordis, L., EpidemiologyElsevier / Saunders, 2009.
649. Schmitt, J., Seidler, A., Heinisch, G., Sebastian, G., Effectiveness of skin cancer screening for individuals age 14 to 34 years. J Dtsch Dermatol Ges, 2011. 9(8): p. 608-16., https://www.ncbi.nlm.nih.gov/pubmed/21501381
650. Engelberg, D., Gallagher, R. P., Rivers, J. K., Follow-up and evaluation of skin cancer screening in British Columbia. J Am Acad Dermatol, 1999. 41(1): p. 37-42., https://www.ncbi.nlm.nih.gov/pubmed/10411408
651. Guther, S., Ramrath, K., Dyall-Smith, D., Landthaler, M., Stolz, W., Development of a targeted risk-group model for skin cancer screening based on more than 100,000 total skin examinations. J Eur Acad Dermatol Venereol, 2012. 26(1): p. 86-94., https://www.ncbi.nlm.nih.gov/pubmed/21371132
652. U.S. Preventive Services Task Force, Screening for Skin Cancer- Recommendations and Rationale. Am J Prev Med, 2001. 20:
653. Wolff, T., Tai, E., Miller, T., Screening for skin cancer: an update of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med, 2009. 150(3): p. 194-8., https://www.ncbi.nlm.nih.gov/pubmed/19189909

654. Australian Cancer Network Melanoma Guidelines Revision Working Party, Clinical Practice Guidelines for the Management of Melanoma in Australia and New ZealandThe Cancer Council Australia and Australian Cancer Network, Sydney and New Zealand Guidelines Group, 2008.
655. Osborne, J. E., Chave, T. A., Hutchinson, P. E., Comparison of diagnostic accuracy for cutaneous malignant melanoma between general dermatology, plastic surgery and pigmented lesion clinics. Br J Dermatol, 2003. 148(2): p. 252-8., https://www.ncbi.nlm.nih.gov/pubmed/12588376
656. Pacifico, M. D., Pearl, R. A., Grover, R., The UK Government two-week rule and its impact on melanoma prognosis: an evidence-based study. Ann R Coll Surg Engl, 2007. 89(6): p. 609-15., https://www.ncbi.nlm.nih.gov/pubmed/18201477
657. U.S. Preventive Services Task Force, Screening for Skin Cancer- Recommendations and Rationale. Am J Prev Med, 2001. 20:, https://www.ncbi.nlm.nih.gov/pubmed/11306231
658. Scottish Intercollegiate Guidelines Network, SIGN 72: Cutaneous Melanoma - A national clinical guidelineScottish Intercollegiate Guidelines Network, 2003., www.sign.ac.uk
659. Titus, L. J., Clough-Gorr, K., Mackenzie, T. A., Perry, A., Spencer, S. K., Weiss, J., et.al. Recent skin self-examination and doctor visits in relation to melanoma risk and tumour depth. Br J Dermatol, 2013. 168(3): p. 571-6., https://www.ncbi.nlm.nih.gov/pubmed/22897437
660. Paddock, L. E., Lu, S. E., Bandera, E. V., Rhoads, G. G., Fine, J., Paine, S., et.al. Skin self-examination and long-term melanoma survival. Melanoma Res, 2016. 26(4): p. 401-8., https://www.ncbi.nlm.nih.gov/pubmed/26990272
661. Chiu, V., Won, E., Malik, M., Weinstock, M. A., The use of mole-mapping diagrams to increase skin self-examination accuracy. J Am Acad Dermatol, 2006. 55(2): p. 245-50., https://www.ncbi.nlm.nih.gov/pubmed/16844506
662. Hanrahan, P. F., D'Este, C. A., Menzies, S. W., Plummer, T., Hersey, P., A randomised trial of skin photography as an aid to screening skin lesions in older males. J Med Screen, 2002. 9(3): p. 128-32., https://www.ncbi.nlm.nih.gov/pubmed/12370325
663. Oliveria, S. A., Chau, D., Christos, P. J., Charles, C. A., Mushlin, A. I., Halpern, A. C., Diagnostic accuracy of patients in performing skin self-examination and the impact of photography. Arch Dermatol, 2004. 140(1): p. 57-62., https://www.ncbi.nlm.nih.gov/pubmed/14732661
664. Muhn, C. Y., From, L., Glied, M., Detection of artificial changes in mole size by skin self-examination. J Am Acad Dermatol, 2000. 42(5 Pt 1): p. 754-9., https://www.ncbi.nlm.nih.gov/pubmed/10775850
665. Mogensen, M., Jemec, G. B., Diagnosis of nonmelanoma skin cancer/keratinocyte carcinoma: a review of diagnostic accuracy of nonmelanoma skin cancer diagnostic tests and technologies. Dermatol Surg, 2007. 33(10): p. 1158-74., https://www.ncbi.nlm.nih.gov/pubmed/17903149
666. Moffatt, C. R., Green, A. C., Whiteman, D. C., Diagnostic accuracy in skin cancer clinics: the Australian experience. Int J Dermatol, 2006. 45(6): p. 656-60., https://www.ncbi.nlm.nih.gov/pubmed/16796621
667. Katris, P., Donovan, R. J., Gray, B. N., Nurses screening for skin cancer: an observation study. Aust N Z J Public Health, 1998. 22(3 Suppl): p. 381-3., https://www.ncbi.nlm.nih.gov/pubmed/9629826
668. Kai, Y., Ishikawa, K., Goto, M., Sakai, T., Ito, A., Shono, T., et.al. Results of second-stage screening for skin cancers in Oita Prefecture, Japan. J Dermatol, 2015. 42(12): p. 1160-4., https://www.ncbi.nlm.nih.gov/pubmed/26177589
669. Burton, R. C., Howe, C., Adamson, L., Reid, A. L., Hersey, P., Watson, A., et.al. General practitioner screening for melanoma: sensitivity, specificity, and effect of training. J Med Screen, 1998. 5(3): p. 156-61., https://www.ncbi.nlm.nih.gov/pubmed/9795877
670. Bono, A., Bartoli, C., Cascinelli, N., Lualdi, M., Maurichi, A., Moglia, D., et.al. Melanoma detection. A prospective study comparing diagnosis with the naked eye, dermatoscopy and telespectrophotometry. Dermatology, 2002. 205(4): p. 362-6., https://www.ncbi.nlm.nih.gov/pubmed/12444332

671. Chen, S. C., Bravata, D. M., Weil, E., Olkin, I., A comparison of dermatologists' and primary care physicians' accuracy in diagnosing melanoma: a systematic review. Arch Dermatol, 2001. 137(12): p. 1627-34., https://www.ncbi.nlm.nih.gov/pubmed/11735713
672. Ferris, L. K., Saul, M. I., Lin, Y., Ding, F., Weinstock, M. A., Geller, A. C., et.al. A Large Skin Cancer Screening Quality Initiative: Description and First-Year Outcomes. JAMA Oncol, 2017. 3(8): p. 1112-1115., https://www.ncbi.nlm.nih.gov/pubmed/28241191
673. Cristofolini, M., Boi, S., Cattoni, D., Sicher, M. C., Decarli, A., Micciolo, R., A 10-Year Follow-Up Study of Subjects Recruited in a Health Campaign for the Early Diagnosis of Cutaneous Melanoma: Suggestions for the Screening Timetable. Dermatology, 2015. 231(4): p. 345-52., https://www.ncbi.nlm.nih.gov/pubmed/26278413
674. Aitken, J. F., Elwood, M., Baade, P. D., Youl, P., English, D., Clinical whole-body skin examination reduces the incidence of thick melanomas. Int J Cancer, 2010. 126(2): p. 450-8., https://www.ncbi.nlm.nih.gov/pubmed/19609948
675. Melia, J., Moss, S., Coleman, D., Frost, T., Graham-Brown, R., Hunter, J. A., et.al. The relation between mortality from malignant melanoma and early detection in the Cancer Research Campaign Mole Watcher Study. Br J Cancer, 2001. 85(6): p. 803-7., https://www.ncbi.nlm.nih.gov/pubmed/11556828
676. Helfand, M., Mahon, S. M., Eden, K. B., Frame, P. S., Orleans, C. T., Screening for skin cancer. Am J Prev Med, 2001. 20(3 Suppl): p. 47-58., https://www.ncbi.nlm.nih.gov/pubmed/11306232
677. Aitken, J. F., Youl, P. H., Janda, M., Lowe, J. B., Ring, I. T., Elwood, M., Increase in skin cancer screening during a community-based randomized intervention trial. Int J Cancer, 2006. 118(4): p. 1010-6., https://www.ncbi.nlm.nih.gov/pubmed/16152577
678. Aitken, J. F., Elwood, J. M., Lowe, J. B., Firman, D. W., Balanda, K. P., Ring, I. T., A randomised trial of population screening for melanoma. J Med Screen, 2002. 9(1): p. 33-7., https://www.ncbi.nlm.nih.gov/pubmed/11943795
679. Janda, M., Lowe, J. B., Elwood, M., Ring, I. T., Youl, P. H., Aitken, J. F., Do centralised skin screening clinics increase participation in melanoma screening (Australia)?. Cancer Causes Control, 2006. 17(2): p. 161-8., https://www.ncbi.nlm.nih.gov/pubmed/16425094
680. Watts, C. G., Dieng, M., Morton, R. L., Mann, G. J., Menzies, S. W., Cust, A. E., Clinical practice guidelines for identification, screening and follow-up of individuals at high risk of primary cutaneous melanoma: a systematic review. Br J Dermatol, 2015. 172(1): p. 33-47., https://www.ncbi.nlm.nih.gov/pubmed/25204572
681. Oliveria, S. A., Dusza, S. W., Phelan, D. L., Ostroff, J. S., Berwick, M., Halpern, A. C., Patient adherence to skin self-examination. effect of nurse intervention with photographs. Am J Prev Med, 2004. 26(2): p. 152-5., https://www.ncbi.nlm.nih.gov/pubmed/14751328
682. Fortes, C., Commentary: Reproductibility of skin characteristic measurments and reported sun exposure history. International Journal of Epidemiology, 2002. 31(2): p. 446-8.
683. Carli, P., Chiarugi, A., De Giorgi, V., Examination of lesions (including dermoscopy) without contact with the patient is associated with improper management in about 30% of equivocal melanomas. Dermatol Surg, 2005. 31(2): p. 169-72., https://www.ncbi.nlm.nih.gov/pubmed/15762209
684. Kaiser, M., Schiller, J., Schreckenberger, C., The effectiveness of a population-based skin cancer screening program: evidence from Germany. Eur J Health Econ, 2018. 19(3): p. 355-367., https://www.ncbi.nlm.nih.gov/pubmed/28353004
685. Eisemann, N., Waldmann, A., Geller, A. C., Weinstock, M. A., Volkmer, B., Greinert, R., et.al. Non-melanoma skin cancer incidence and impact of skin cancer screening on incidence. J Invest Dermatol, 2014. 134(1): p. 43-50., https://www.ncbi.nlm.nih.gov/pubmed/23877569
686. Eisemann, N., Waldmann, A., Katalinic, A., [Incidence of melanoma and changes in stage-specific incidence after implementation of skin cancer screening in Schleswig-Holstein]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, 2014. 57(1): p. 77-83., https://www.ncbi.nlm.nih.gov/pubmed/24357176

687. Stang, A., Jöckel, K. H., Heidinger, O., Skin cancer rates in North Rhine-Westphalia, Germany before and after the introduction of the nationwide skin cancer screening program (2000–2015). European Journal of Epidemiology, 2018. 33: p. 303-312.
688. Trautmann, F., Meier, F., Seidler, A., Schmitt, J., Effects of the German skin cancer screening programme on melanoma incidence and indicators of disease severity. Br J Dermatol, 2016. 175(5): p. 912-919., https://www.ncbi.nlm.nih.gov/pubmed/27203791
689. Hubner, J., Waldmann, A., Geller, A. C., Weinstock, M. A., Eisemann, N., Noftz, M., et.al. Interval cancers after skin cancer screening: incidence, tumour characteristics and risk factors for cutaneous melanoma. Br J Cancer, 2017. 116(2): p. 253-259., https://www.ncbi.nlm.nih.gov/pubmed/27898656
690. Boniol, M., Autier, P., Gandini, S., Melanoma mortality following skin cancer screening in Germany. BMJ Open, 2015. 5(9): p. e008158., https://www.ncbi.nlm.nih.gov/pubmed/26373399
691. Stang, A., Jockel, K. H., Does skin cancer screening save lives? A detailed analysis of mortality time trends in Schleswig-Holstein and Germany. Cancer, 2016. 122(3): p. 432-7., https://www.ncbi.nlm.nih.gov/pubmed/26480048
692. Schubert, A., [Malignant melanoma of the skin: does screening for cancer influence the incidence and mortality?]. Gesundheitswesen, 2012. 74(3): p. 154-9., https://www.ncbi.nlm.nih.gov/pubmed/21305450
693. Lüken, F., Batz, D., Kutschmann, M., Evaluation der Screeninguntersuchungen auf Hautkrebs gemäß Krebsfrüherkennungs-Richtlinie des Gemeinsamen Bundesauschusses. Abschlussbericht der Jahre 2011-2013.BQS Institut für Qualität & Patientensicherheit, 2016.
694. Arbeitsgemeinschaft Dermatologische Prävention, Abschlussbericht zur Phase III („Pilotphase“) des Projektes Weiterentwicklung der Hautkrebsfrüherkennung im Rahmen der gesetzlichen Krebsfrüherkennungsuntersuchung (KFU) als Vorbereitung für die flächendeckende Einführung-Gemeinsamer Bundesausschuss (German Joint Federal Committee), 2005., http://www.g-ba.de/downloads/40-268-1748/2007-11-15_HKS-Abschlussbericht_2004.pdf
695. Kommission Hautkrebs-Screening Deutschland, Fortbildungsprogramm Hautkrebs-Screening-Deutscher Ärzte-Verlag, 2008.
696. Gemeinsamer Bundesausschuss, Richtlinie des Gemeinsamen Bundesausschusses über die Früherkennung von Krebserkrankungen (Krebsfrüherkennungs-Richtlinie / KFE-RL). Bundesanzeiger, 2018. Nr. 148a:, https://www.g-ba.de/downloads/39-261-3203/2018-01-18_KFE-RL_Anpassung-Doku-Hautkrebsscreening_BAnz.pdf?
697. Anders, M. P., Fengler, S., Volkmer, B., Greinert, R., Breitbart, E. W., Nationwide skin cancer screening in Germany: Evaluation of the training program. Int J Dermatol, 2017. 56(10): p. 1046-1051., https://www.ncbi.nlm.nih.gov/pubmed/28832980
698. Choudhury, K., Unveröffentlichter Abschlussbericht SCSES, 2019.
699. Markova, A., Weinstock, M. A., Risica, P., Kirtania, U., Shaikh, W., Ombao, H., et.al. Effect of a web-based curriculum on primary care practice: basic skin cancer triage trial. Fam Med, 2013. 45(8): p. 558-68., https://www.ncbi.nlm.nih.gov/pubmed/24129868
700. Bedlow, A. J., Cliff, S., Melia, J., Moss, S. M., Seyan, R., Harland, C. C., Impact of skin cancer education on general practitioners‘ diagnostic skills. Clin Exp Dermatol, 2000. 25(2): p. 115-8., https://www.ncbi.nlm.nih.gov/pubmed/10733633
701. Benvenuto-Andrade, C., Dusza, S. W., Hay, J. L., Agero, A. L., Halpern, A. C., Kopf, A. W., et.al. Level of confidence in diagnosis: clinical examination versus dermoscopy examination. Dermatol Surg, 2006. 32(5): p. 738-44., https://www.ncbi.nlm.nih.gov/pubmed/16706773
702. Cliff, S., Bedlow, A. J., Melia, J., Moss, S., Harland, C. C., Impact of skin cancer education on medical students‘ diagnostic skills. Clin Exp Dermatol, 2003. 28(2): p. 214-7., https://www.ncbi.nlm.nih.gov/pubmed/12653717
703. de Gannes, G. C., Ip, J. L., Martinka, M., Crawford, R. I., Rivers, J. K., Early detection of skin cancer by family physicians: a pilot project. J Cutan Med Surg, 2004. 8(2): p. 103-9., https://www.ncbi.nlm.nih.gov/pubmed/15037942

704. Dolev, J. C., O'Sullivan, P., Berger, T., The eDerm online curriculum: a randomized study of effective skin cancer teaching to medical students. J Am Acad Dermatol, 2011. 65(6): p. e165-71., https://www.ncbi.nlm.nih.gov/pubmed/21112668
705. Gerbert, B., Bronstone, A., Maurer, T., Berger, T., McPhee, S. J., Caspers, N., The effectiveness of an Internet-based tutorial in improving primary care physicians' skin cancer triage skills. J Cancer Educ, 2002. 17(1): p. 7-11., https://www.ncbi.nlm.nih.gov/pubmed/12000111
706. Girgis, A., Sanson-Fisher, R. W., Howe, C., Raffan, B., A skin cancer training programme: evaluation of a postgraduate training for family doctors. Med Educ, 1995. 29(5): p. 364-71., https://www.ncbi.nlm.nih.gov/pubmed/8699975
707. Goulart, J. M., Quigley, E. A., Dusza, S., Jewell, S. T., Alexander, G., Asgari, M. M., et.al. Skin cancer education for primary care physicians: a systematic review of published evaluated interventions. J Gen Intern Med, 2011. 26(9): p. 1027-35., https://www.ncbi.nlm.nih.gov/pubmed/21472502
708. McCormick, L. K., Masse, L. C., Cummings, S. S., Burke, C., Evaluation of a skin cancer prevention module for nurses: change in knowledge, self-efficacy, and attitudes. Am J Health Promot, 1999. 13(5): p. 282-9., https://www.ncbi.nlm.nih.gov/pubmed/10538643
709. Mikkilineni, R., Weinstock, M. A., Goldstein, M. G., Dube, C. E., Rossi, J. S., The impact of the basic skin cancer triage curriculum on provider's skin cancer control practices. J Gen Intern Med, 2001. 16(5): p. 302-7., https://www.ncbi.nlm.nih.gov/pubmed/11359548
710. Gerbert, B., Bronstone, A., Wolff, M., Maurer, T., Berger, T., Pantilat, S., et.al. Improving primary care residents' proficiency in the diagnosis of skin cancer. J Gen Intern Med, 1998. 13(2): p. 91-7., https://www.ncbi.nlm.nih.gov/pubmed/9502368
711. Chen, J. G., Fleischer, A. B., Jr., Smith, E. D., Kancler, C., Goldman, N. D., Williford, P. M., et.al. Cost of nonmelanoma skin cancer treatment in the United States. Dermatol Surg, 2001. 27(12): p. 1035-8., https://www.ncbi.nlm.nih.gov/pubmed/11849266
712. Perry, N., Broeders, M., Wolf, C. de, Toernberg, S., Holland, R., Karsa, L. von, et.al. European guidelines for quality assurance in breast cancer screening and diagnosis (4th edition)Office for Official Publications of the European Communities, 2006. Fourth Edition:, https://www.ncbi.nlm.nih.gov/pubmed/18024988
713. Kassenärztliche Bundesvereinigung, IT in der Arztpraxis: Anforderungskatalog Hautkrebs-Screening (eHKS), 2012.
714. Hentschel, Stefan, Katalinic, Alexander, Das Manual der epidemiologischen Krebsregistrierung-Zuckschwerdt, 2011. 1. Auflage:
715. Gemeinsamer Bundesausschuss, Richtlinie des Gemeinsamen Bundesausschusses über die Früherkennung von Krebserkrankungen (Krebsfrüherkennungs-Richtlinie / KFE-RL). Bundesanzeiger, 2009. Nr. 148a:
716. Schmidtmann, Irene, Hammer, Gaël, Sariyar, Murat, Gerhold-Ay, Aslihan, Evaluation des Krebsregisters NRW: Schwerpunkt Record Linkage (Abschlussbericht 11.06.2009), 2009., www.krebsregister.nrw.de/fileadmin/user_upload/dokumente/Evaluation/EKR_NRW_Evaluation_Abschlussbericht_2009-06-11.pdf
717. Augustin, Matthias, Stadler, Rudolf, Reusch, Michael, Schäfer, Ines, Kornek, Thomas, Luger, Thomas, Gesetzliches Hautkrebsscreening in Deutschland: Wahrnehmung in der Oeffentlichkeit. Skin cancer screening in Germany - perception by the public. Journal der Deutschen Dermatologischen Gesellschaft, 2012. 10(ger):, http://www.zbmed.de/ccmedimages/2012/ZBMED-20121115153-3.pdf
718. Eissing, L., Schafer, I., Stromer, K., Kaufmann, R., Enk, A., Reusch, M., et.al. [Perception of statutory skin cancer screening in the general population : Current findings on participation, knowledge and evaluation]. Hautarzt, 2017. 68(5): p. 371-376., https://www.ncbi.nlm.nih.gov/pubmed/28246676
719. Sullivan, H. W., Rutten, L. J., Hesse, B. W., Moser, R. P., Rothman, A. J., McCaul, K. D., Lay representations of cancer prevention and early detection: associations with prevention behaviors. Prev Chronic Dis, 2010. 7(1): p. A14., https://www.ncbi.nlm.nih.gov/pubmed/20040229

720. Davis, J. L., Buchanan, K. L., Katz, R. V., Green, B. L., Gender differences in cancer screening beliefs, behaviors, and willingness to participate: implications for health promotion. Am J Mens Health, 2012. 6(3): p. 211-7., https://www.ncbi.nlm.nih.gov/pubmed/22071507
721. Janda, M., Youl, P. H., Lowe, J. B., Baade, P. D., Elwood, M., Ring, I. T., et.al. What motivates men age > or =50 years to participate in a screening program for melanoma?. Cancer, 2006. 107(4): p. 815-23., https://www.ncbi.nlm.nih.gov/pubmed/16832794
722. Starker, A., Sass, A. C., [Participation in cancer screening in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz, 2013. 56(5-6): p. 858-67., https://www.ncbi.nlm.nih.gov/pubmed/23703507
723. Bundesministerium für Gesundheit, „Inanspruchnahme Krebsfrüherkennung“, Handlungsfeld 1 „Weiterentwicklung der Krebsfrüherkennung“ des Nationalen Krebsplans, 2017., http://www.bmg.bund.de/fileadmin/dateien/Downloads/N/Nationaler_Krebsplan/Ziel_1_Inanspruchnahme_der_Krebsfrueherkennung.pdf
724. Rimer, B. K., Briss, P. A., Zeller, P. K., Chan, E. C., Woolf, S. H., Informed decision making: what is its role in cancer screening?. Cancer, 2004. 101(5 Suppl): p. 1214-28., https://www.ncbi.nlm.nih.gov/pubmed/15316908
725. Bundesministerium für Gesundheit, „Inanspruchnahme Krebsfrüherkennung“, Handlungsfeld 1 „Weiterentwicklung der Krebsfrüherkennung“ des Nationalen Krebsplans, 2010., http://www.bmg.bund.de/fileadmin/dateien/Downloads/N/Nationaler_Krebsplan/Ziel_1_Inanspruchnahme_der_Krebsfrueherkennung.pdf
726. Luhnen, J., Albrecht, M., Hanssen, K., Hildebrandt, J., Steckelberg, A., [Guideline for the Development of Evidence-based Patient Information: insights into the methods and implementation of evidence-based health information]. Z Evid Fortbild Qual Gesundhwes, 2015. 109(2): p. 159-65., https://www.ncbi.nlm.nih.gov/pubmed/26028454
727. Akl, E. A., Oxman, A. D., Herrin, J., Vist, G. E., Terrenato, I., Sperati, F., et.al. Using alternative statistical formats for presenting risks and risk reductions. Cochrane Database Syst Rev, 2011. p. CD006776., https://www.ncbi.nlm.nih.gov/pubmed/21412897
728. Schwartz, L. M., Woloshin, S., Black, W. C., Welch, H. G., The role of numeracy in understanding the benefit of screening mammography. Ann Intern Med, 1997. 127(11): p. 966-72., https://www.ncbi.nlm.nih.gov/pubmed/9412301
729. Reifegerste, D., Gesundheitskommunikation in der Prävention und Gesundheitsförderung für schwer erreichbare Zielgruppen, in Prävention und Gesundheitsförderung, 2019, Springer: Heidelberg.
730. Roski, R, Akteure, Ziele und Stakeholder im Gesundheitswesen - Business Marketing, Social Marketing und Zielgruppensegmentierung, in Zielgruppengerechte Gesundheitskommunikation, Roski, R , Editor. 2009, Springer VS: Wiesbaden. p. 3-31.
731. Geber, S., Baumann, E., Klimmt, C., Tailoring in risk communication by linking risk profiles and communication preferences: The case of speeding of young car drivers. Accid Anal Prev, 2016. 97: p. 315-325., https://www.ncbi.nlm.nih.gov/pubmed/26432690
732. Baumann, E, Auf der Suche nach der Zielgruppe - Das Informationsverhalten hinsichtlich Gesundheit und Krankheit als Grundlage erfolgreicher Gesundheitskommunikation, in Gesundheitsmonitor 2006. Gesundheitsversorgung und Gestaltungsoptionen aus der Perspektive von Bevölkerung und Ärzten, Böcken, JBraun, BAmhof, R and Schnee, M, Editors. 2006, Verlag Bertelsmann Stiftung: Gütersloh. p. 117-153.
733. Robinson, J. K., Stapleton, J., Turrisi, R., Relationship and partner moderator variables increase self-efficacy of performing skin self-examination. J Am Acad Dermatol, 2008. 58(5): p. 755-62., https://www.ncbi.nlm.nih.gov/pubmed/18258332
734. Geller, A. C., Emmons, K. M., Brooks, D. R., Powers, C., Zhang, Z., Koh, H. K., et.al. A randomized trial to improve early detection and prevention practices among siblings of melanoma patients. Cancer, 2006. 107(4): p. 806-14., https://www.ncbi.nlm.nih.gov/pubmed/16832795

735. Manne, S., Jacobsen, P. B., Ming, M. E., Winkel, G., Dessureault, S., Lessin, S. R., Tailored versus generic interventions for skin cancer risk reduction for family members of melanoma patients. Health Psychol, 2010. 29(6): p. 583-93., https://www.ncbi.nlm.nih.gov/pubmed/21090893
736. Mayer, J. A., Eckhardt, L., Stepanski, B. M., Sallis, J. F., Elder, J. P., Slymen, D. J., et.al. Promoting skin cancer prevention counseling by pharmacists. Am J Public Health, 1998. 88(7): p. 1096-9., https://www.ncbi.nlm.nih.gov/pubmed/9663162
737. Youl, P. H., Janda, M., Elwood, M., Lowe, J. B., Ring, I. T., Aitken, J. F., Who attends skin cancer clinics within a randomized melanoma screening program?. Cancer Detect Prev, 2006. 30(1): p. 44-51., https://www.ncbi.nlm.nih.gov/pubmed/16457967
738. King, A. J., Visual Exemplification and Skin Cancer: The Utility of Exemplars in Promoting Skin Self-Exams and Atypical Nevi Identification. J Health Commun, 2016. 21(7): p. 826-36., https://www.ncbi.nlm.nih.gov/pubmed/27337542
739. McWhirter, J. E., Hoffman-Goetz, L., Visual images for patient skin self-examination and melanoma detection: a systematic review of published studies. J Am Acad Dermatol, 2013. 69(1): p. 47-55., https://www.ncbi.nlm.nih.gov/pubmed/23474227
740. Edwards, A. G., Naik, G., Ahmed, H., Elwyn, G. J., Pickles, T., Hood, K., et.al. Personalised risk communication for informed decision making about taking screening tests. Cochrane Database Syst Rev, 2013. p. CD001865., https://www.ncbi.nlm.nih.gov/pubmed/23450534
741. Anders, M. P., Nolte, S., Waldmann, A., Capellaro, M., Volkmer, B., Greinert, R., et.al. The German SCREEN project—design and evaluation of the communication strategy. Eur J Public Health, 2015. 25(1): p. 150-5., https://www.ncbi.nlm.nih.gov/pubmed/24760725
742. Schnabel, P, Bödeker, M, GesundheitskommunikationBeltz Juventa, 2012.
743. Janis, Irving Lester, Mann, Leon, Decision making: A psychological analysis of conflict, choice and commitmentCassel & Collier Macmillian, 1977.
744. Mann, Leon, Use of a balance-sheet procedure to improve the quality of personal decision making: A field experiment with college applicants. Journal of Vocational Behavior, 1972. 2(3): p. 291-300.
745. Mullen, P D, Allen, J D, Glanz, K, Fernandez, M E, Bowen, D J, Pruitt, S L, et.al. Measures Used in Studies of Informed Decision Making About Cancer Screening: A Systematic Review. Annals of Behavioral Medicine, 2006. 32(3): p. 188-201., https://www.ncbi.nlm.nih.gov/pubmed/17107291
746. Eppstein, R. M., Street Jr., R., Patient-Centered Communication in Cancer Care: Promoting Healing and Reducing SufferingBethesda, 2007.
747. Bientzle, M., Fissler, T., Cress, U., Kimmerle, J., The impact of physicians‘ communication styles on evaluation of physicians and information processing: A randomized study with simulated video consultations on contraception with an intrauterine device. Health Expect, 2017. 20(5): p. 845-851., https://www.ncbi.nlm.nih.gov/pubmed/27860037
748. Eggly, S. S., Albrecht, T. L., Kelly, K., Prigerson, H. G., Sheldon, L. K., Studts, J., The role of the clinician in cancer clinical communication. J Health Commun, 2009. 14 Suppl 1(Suppl1): p. 66-75., https://www.ncbi.nlm.nih.gov/pubmed/19449270
749. Fox, S. A., Heritage, J., Stockdale, S. E., Asch, S. M., Duan, N., Reise, S. P., Cancer screening adherence: does physician-patient communication matter?. Patient Educ Couns, 2009. 75(2): p. 178-84., https://www.ncbi.nlm.nih.gov/pubmed/19250793
750. Riedl, D., Schussler, G., The Influence of Doctor-Patient Communication on Health Outcomes: A Systematic Review. Z Psychosom Med Psychother, 2017. 63(2): p. 131-150., https://www.ncbi.nlm.nih.gov/pubmed/28585507
751. Dillon, E. C., Stults, C. D., Wilson, C., Chuang, J., Meehan, A., Li, M., et.al. An evaluation of two interventions to enhance patient-physician communication using the observer OPTION(5) measure of shared decision making. Patient Educ Couns, 2017. 100(10): p. 1910-1917., https://www.ncbi.nlm.nih.gov/pubmed/28532861

752. Shay, L. A., Dumenci, L., Siminoff, L. A., Flocke, S. A., Lafata, J. E., Factors associated with patient reports of positive physician relational communication. Patient Educ Couns, 2012. 89(1): p. 96-101., https://www.ncbi.nlm.nih.gov/pubmed/22554386
753. Baker, Susan C., Watson, Bernadette M., How Patients Perceive Their Doctors' Communication. Journal of Language and Social Psychology, 2015. 34(6): p. 621-639., http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc13a&AN=2015-51535-003, http://sfx.gbv.de/sfx_subhh?sid=OVID:psycdb&id=pmid:&id=doi:10.1177%2F0261927X15587015&issn=0261-927X&isbn=&volume=34&issue=6&spage=621&pages=621-639&date=2015&title=Journal+of+Language+and+Social+Psychology&atitle=How+patients+perceive+their+doctors%27+communication%3A+Implications+for+patient+willingness+to+communicate.&aulast=Baker
754. Thomas, Marlyn, Hariharan, Meena, Rana, Suvashisa, Swain, Sunayana, Andrew, Asher, Medical Jargons as Hindrance in Doctor–Patient Communication. Psychological Studies, 2014. 59(4): p. 394-400., http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc11&AN=2014-26202-001, http://sfx.gbv.de/sfx_subhh?sid=OVID:psycdb&id=pmid:&id=doi:10.1007%2Fs12646-014-0262-x&issn=0033-2968&isbn=&volume=59&issue=4&spage=394&pages=394-400&date=2014&title=Psychological+Studies&atitle=Medical+jargons+as+hindrance+in+doctor-patient+communication.&aulast=Thomas
755. Jünger, Jana, Ärtzliche Kommunikation: Praxisbuch zum Masterplan Medizinstudium 2020Schattauer, 2018.
756. Schweickhardt, A., Fritzsche, K., Kursbuch ärztliche Kommunikation: Grundlagen und Fallbeispiele aus Klinik und PraxisDeutscher Ärzte-Verlag, 2009.
757. Bundesministerium fuer Gesundheit, „Inanspruchnahme Krebsfrüherkennung", Handlungsfeld 1 „Weiterentwicklung der Krebsfrüherkennung" des Nationalen Krebsplans, 2010.
758. Loescher, L. J., Crist, J. D., Cranmer, L., Curiel-Lewandrowski, C., Warneke, J. A., Melanoma high-risk families' perceived health care provider risk communication. J Cancer Educ, 2009. 24(4): p. 301-7., https://www.ncbi.nlm.nih.gov/pubmed/19838889
759. Loescher, L. J., Crist, J. D., Siaki, L. A., Perceived intrafamily melanoma risk communication. Cancer Nurs, 2009. 32(3): p. 203-10., https://www.ncbi.nlm.nih.gov/pubmed/19295423
760. Graves, J., Fleischman, M. H., Goldstein, G. D., Derm Access: a new triage system to rapidly identify suspicious skin lesions. Dermatol Surg, 2006. 32(12): p. 1486-90., https://www.ncbi.nlm.nih.gov/pubmed/17199657
761. Karri, V., Bragg, T. W., Jones, A., Soldin, M., Misch, K., Patient satisfaction with receiving skin cancer diagnosis by letter: comparison with face-to-face consultation. J Plast Reconstr Aesthet Surg, 2009. 62(8): p. 1059-62., https://www.ncbi.nlm.nih.gov/pubmed/18485851
762. Bahmer, J., Bahmer, F., Konfrontation mit der Diagnose „Melanom". Aktuelle Dermatologie, 2006. 32(6): p. 243-248.
763. Butow, P. N., Kazemi, J. N., Beeney, L. J., Griffin, A. M., Dunn, S. M., Tattersall, M. H., When the diagnosis is cancer: patient communication experiences and preferences. Cancer, 1996. 77(12): p. 2630-7., https://www.ncbi.nlm.nih.gov/pubmed/8640715
764. Baile, W. F., Buckman, R., Lenzi, R., Glober, G., Beale, E. A., Kudelka, A. P., SPIKES-A six-step protocol for delivering bad news: application to the patient with cancer. Oncologist, 2000. 5(4): p. 302-11., https://www.ncbi.nlm.nih.gov/pubmed/10964998
765. Australian Cancer Network Melanoma Guidelines Revision Working Party, Clinical Practice Guidelines for the Management of Melanoma in Australia and New ZealandThe Cancer Council Australia and Australian Cancer Network, Sydney and New Zealand Guidelines Group, 2008.
766. Bafounta, M. L., Beauchet, A., Aegerter, P., Saiag, P., Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. Arch Dermatol, 2001. 137(10): p. 1343-50., https://www.ncbi.nlm.nih.gov/pubmed/11594860
767. Kittler, H., Pehamberger, H., Wolff, K., Binder, M., Diagnostic accuracy of dermoscopy. Lancet Oncol, 2002. 3(3): p. 159-65., https://www.ncbi.nlm.nih.gov/pubmed/11902502

768. Dolianitis, C., Kelly, J., Wolfe, R., Simpson, P., Comparative performance of 4 dermoscopic algorithms by nonexperts for the diagnosis of melanocytic lesions. Arch Dermatol, 2005. 141(8): p. 1008-14., https://www.ncbi.nlm.nih.gov/pubmed/16103330
769. Westerhoff, K., McCarthy, W. H., Menzies, S. W., Increase in the sensitivity for melanoma diagnosis by primary care physicians using skin surface microscopy. Br J Dermatol, 2000. 143(5): p. 1016-20., https://www.ncbi.nlm.nih.gov/pubmed/11069512
770. Carli, P., de Giorgi, V., Chiarugi, A., Nardini, P., Weinstock, M. A., Crocetti, E., et.al. Addition of dermoscopy to conventional naked-eye examination in melanoma screening: a randomized study. J Am Acad Dermatol, 2004. 50(5): p. 683-9., https://www.ncbi.nlm.nih.gov/pubmed/15097950
771. van der Rhee, J. I., Bergman, W., Kukutsch, N. A., The impact of dermoscopy on the management of pigmented lesions in everyday clinical practice of general dermatologists: a prospective study. Br J Dermatol, 2010. 162(3): p. 563-7., https://www.ncbi.nlm.nih.gov/pubmed/19832836
772. Haenssle, H. A., Vente, C., Bertsch, H. P., Rupprecht, R., Abuzahra, F., Junghans, V., et.al. Results of a surveillance programme for patients at high risk of malignant melanoma using digital and conventional dermoscopy. Eur J Cancer Prev, 2004. 13(2): p. 133-8., https://www.ncbi.nlm.nih.gov/pubmed/15100580
773. Carli, P., De Giorgi, V., Argenziano, G., Palli, D., Giannotti, B., Pre-operative diagnosis of pigmented skin lesions: in vivo dermoscopy performs better than dermoscopy on photographic images. J Eur Acad Dermatol Venereol, 2002. 16(4): p. 339-46., https://www.ncbi.nlm.nih.gov/pubmed/12224689
774. Lorentzen, H. F., Eefsen, R. L., Weismann, K., Comparison of classical dermatoscopy and acrylic globe magnifier dermatoscopy. Acta Derm Venereol, 2008. 88(2): p. 139-42., https://www.ncbi.nlm.nih.gov/pubmed/18311441
775. Zalaudek, I., Kreusch, J., Giacomel, J., Ferrara, G., Catricala, C., Argenziano, G., How to diagnose nonpigmented skin tumors: a review of vascular structures seen with dermoscopy: part I. Melanocytic skin tumors. J Am Acad Dermatol, 2010. 63(3): p. 361-74; quiz 375-6., https://www.ncbi.nlm.nih.gov/pubmed/20708469
776. Carli, P., De Giorgi, V., Crocetti, E., Mannone, F., Massi, D., Chiarugi, A., et.al. Improvement of malignant/benign ratio in excised melanocytic lesions in the ‚dermoscopy era': a retrospective study 1997-2001. Br J Dermatol, 2004. 150(4): p. 687-92., https://www.ncbi.nlm.nih.gov/pubmed/15099364
777. Drugge, R. J., Nguyen, C., Drugge, E. D., Gliga, L., Broderick, P. A., McClain, S. A., et.al. Melanoma screening with serial whole body photographic change detection using Melanoscan technology. Dermatol Online J, 2009. 15(6): p. 1., https://www.ncbi.nlm.nih.gov/pubmed/19723475
778. Malvehy, J., Puig, S., Follow-up of melanocytic skin lesions with digital total-body photography and digital dermoscopy: a two-step method. Clin Dermatol, 2002. 20(3): p. 297-304., https://www.ncbi.nlm.nih.gov/pubmed/12074871
779. English, D. R., Burton, R. C., del Mar, C. B., Donovan, R. J., Ireland, P. D., Emery, G., Evaluation of aid to diagnosis of pigmented skin lesions in general practice: controlled trial randomised by practice. BMJ, 2003. 327(7411): p. 375., https://www.ncbi.nlm.nih.gov/pubmed/12919990
780. Del Mar, C. B., Green, A. C., Aid to diagnosis of melanoma in primary medical care. BMJ, 1995. 310(6978): p. 492-5., https://www.ncbi.nlm.nih.gov/pubmed/7888887
781. Guitera, P., Menzies, S. W., Longo, C., Cesinaro, A. M., Scolyer, R. A., Pellacani, G., In vivo confocal microscopy for diagnosis of melanoma and basal cell carcinoma using a two-step method: analysis of 710 consecutive clinically equivocal cases. J Invest Dermatol, 2012. 132(10): p. 2386-2394., https://www.ncbi.nlm.nih.gov/pubmed/22718115
782. Manousaki, A. G., Manios, A. G., Tsompanaki, E. I., Panayiotides, J. G., Tsiftsis, D. D., Kostaki, A. K., et.al. A simple digital image processing system to aid in melanoma diagnosis in an everyday melanocytic skin lesion unit: a preliminary report. Int J Dermatol, 2006. 45(4): p. 402-10., https://www.ncbi.nlm.nih.gov/pubmed/16650167

783. Haenssle, H. A., Krueger, U., Vente, C., Thoms, K. M., Bertsch, H. P., Zutt, M., et.al. Results from an observational trial: digital epiluminescence microscopy follow-up of atypical nevi increases the sensitivity and the chance of success of conventional dermoscopy in detecting melanoma. J Invest Dermatol, 2006. 126(5): p. 980-5., https://www.ncbi.nlm.nih.gov/pubmed/16514414
784. Haenssle, H. A., Mograby, N., Ngassa, A., Buhl, T., Emmert, S., Schon, M. P., et.al. Association of Patient Risk Factors and Frequency of Nevus-Associated Cutaneous Melanomas. JAMA Dermatol, 2016. 152(3): p. 291-8., https://www.ncbi.nlm.nih.gov/pubmed/26536613
785. Kittler, H., Guitera, P., Riedl, E., Avramidis, M., Teban, L., Fiebiger, M., et.al. Identification of clinically featureless incipient melanoma using sequential dermoscopy imaging. Arch Dermatol, 2006. 142(9): p. 1113-9., https://www.ncbi.nlm.nih.gov/pubmed/16982998
786. Menzies, S. W., A method for the diagnosis of primary cutaneous melanoma using surface microscopy. Dermatol Clin, 2001. 19(2): p. 299-305, viii., https://www.ncbi.nlm.nih.gov/pubmed/11556238
787. Robinson, J. K., Nickoloff, B. J., Digital epiluminescence microscopy monitoring of high-risk patients. Arch Dermatol, 2004. 140(1): p. 49-56., https://www.ncbi.nlm.nih.gov/pubmed/14732660
788. Menzies, S. W., Gutenev, A., Avramidis, M., Batrac, A., McCarthy, W. H., Short-term digital surface microscopic monitoring of atypical or changing melanocytic lesions. Arch Dermatol, 2001. 137(12): p. 1583-9., https://www.ncbi.nlm.nih.gov/pubmed/11735708
789. Leitlinienprogramm Onkologie, S3 Leitlinie Diagnostik, Therapie und Nachsorge des Melanoms, 2019., https://www.awmf.org/uploads/tx_szleitlinien/032-024OL_l_S3_Melanom-Diagnostik-Therapie-Nachsorge_2018-07_01.pdf
790. Menzies, S. W., Emery, J., Staples, M., Davies, S., McAvoy, B., Fletcher, J., et.al. Impact of dermoscopy and short-term sequential digital dermoscopy imaging for the management of pigmented lesions in primary care: a sequential intervention trial. Br J Dermatol, 2009. 161(6): p. 1270-7., https://www.ncbi.nlm.nih.gov/pubmed/19747359
791. Ferrandiz, L., Moreno-Ramirez, D., Nieto-Garcia, A., Carrasco, R., Moreno-Alvarez, P., Galdeano, R., et.al. Teledermatology-based presurgical management for nonmelanoma skin cancer: a pilot study. Dermatol Surg, 2007. 33(9): p. 1092-8., https://www.ncbi.nlm.nih.gov/pubmed/17760600
792. Moreno-Ramirez, D., Ferrandiz, L., Nieto-Garcia, A., Carrasco, R., Moreno-Alvarez, P., Galdeano, R., et.al. Store-and-forward teledermatology in skin cancer triage: experience and evaluation of 2009 teleconsultations. Arch Dermatol, 2007. 143(4): p. 479-84., https://www.ncbi.nlm.nih.gov/pubmed/17438180
793. May, C., Giles, L., Gupta, G., Prospective observational comparative study assessing the role of store and forward teledermatology triage in skin cancer. Clin Exp Dermatol, 2008. 33(6): p. 736-9., https://www.ncbi.nlm.nih.gov/pubmed/18681874
794. Jolliffe, V. M., Harris, D. W., Whittaker, S. J., Can we safely diagnose pigmented lesions from stored video images? A diagnostic comparison between clinical examination and stored video images of pigmented lesions removed for histology. Clin Exp Dermatol, 2001. 26(1): p. 84-7., https://www.ncbi.nlm.nih.gov/pubmed/11260186
795. Warshaw, E. M., Lederle, F. A., Grill, J. P., Gravely, A. A., Bangerter, A. K., Fortier, L. A., et.al. Accuracy of teledermatology for pigmented neoplasms. J Am Acad Dermatol, 2009. 61(5): p. 753-65., https://www.ncbi.nlm.nih.gov/pubmed/19679375
796. Kittler, H., Seltenheim, M., Pehamberger, H., Wolff, K., Binder, M., Diagnostic informativeness of compressed digital epiluminescence microscopy images of pigmented skin lesions compared with photographs. Melanoma Res, 1998. 8(3): p. 255-60., https://www.ncbi.nlm.nih.gov/pubmed/9664147
797. Bono, Aldo, Bartoli, Cesare, Cascinelli, Natale, Lualdi, Manuela, Maurichi, Andrea, Moglia, Daniele, et.al. Melanoma detection - A prospective study comparing diagnosis with the naked eye, dermatoscopy and telespectrophotometry. Dermatology, 2002. 205(4): p. 362-366.

798. Bono, A., Tomatis, S., Bartoli, C., Tragni, G., Radaelli, G., Maurichi, A., et.al. The ABCD system of melanoma detection: a spectrophotometric analysis of the Asymmetry, Border, Color, and Dimension. Cancer, 1999. 85(1): p. 72-7., https://www.ncbi.nlm.nih.gov/pubmed/9921976
799. Haniffa, M. A., Lloyd, J. J., Lawrence, C. M., The use of a spectrophotometric intracutaneous analysis device in the real-time diagnosis of melanoma in the setting of a melanoma screening clinic. Br J Dermatol, 2007. 156(6): p. 1350-2., https://www.ncbi.nlm.nih.gov/pubmed/17535234
800. McIntosh, L. M., Summers, R., Jackson, M., Mantsch, H. H., Mansfield, J. R., Howlett, M., et.al. Towards non-invasive screening of skin lesions by near-infrared spectroscopy. J Invest Dermatol, 2001. 116(1): p. 175-81., https://www.ncbi.nlm.nih.gov/pubmed/11168814
801. S1-Leitlinie Konfokale Lasermikroskopie in der Dermatologie, 2019.
802. Kadouch, D. J., Schram, M. E., Leeflang, M. M., Limpens, J., Spuls, P. I., de Rie, M. A., In vivo confocal microscopy of basal cell carcinoma: a systematic review of diagnostic accuracy. J Eur Acad Dermatol Venereol, 2015. 29(10): p. 1890-7., https://www.ncbi.nlm.nih.gov/pubmed/26290493
803. Edwards, S. J., Osei-Assibey, G., Patalay, R., Wakefield, V., Karner, C., Diagnostic accuracy of reflectance confocal microscopy using VivaScope for detecting and monitoring skin lesions: a systematic review. Clin Exp Dermatol, 2017. 42(3): p. 266-275., https://www.ncbi.nlm.nih.gov/pubmed/28218469
804. Lorber, A., Wiltgen, M., Hofmann-Wellenhof, R., Koller, S., Weger, W., Ahlgrimm-Siess, V., et.al. Correlation of image analysis features and visual morphology in melanocytic skin tumours using in vivo confocal laser scanning microscopy. Skin Res Technol, 2009. 15(2): p. 237-41., https://www.ncbi.nlm.nih.gov/pubmed/19622133
805. Guitera, P., Pellacani, G., Longo, C., Seidenari, S., Avramidis, M., Menzies, S. W., In vivo reflectance confocal microscopy enhances secondary evaluation of melanocytic lesions. J Invest Dermatol, 2009. 129(1): p. 131-8., https://www.ncbi.nlm.nih.gov/pubmed/18633444
806. Couzan, C., Cinotti, E., Labeille, B., Vercherin, P., Rubegni, P., Cambazard, F., et.al. Reflectance confocal microscopy identification of subclinical basal cell carcinomas during and after vismodegib treatment. J Eur Acad Dermatol Venereol, 2018. 32(5): p. 763-767., https://www.ncbi.nlm.nih.gov/pubmed/29055164
807. Stevenson, A. D., Mickan, S., Mallett, S., Ayya, M., Systematic review of diagnostic accuracy of reflectance confocal microscopy for melanoma diagnosis in patients with clinically equivocal skin lesions. Dermatol Pract Concept, 2013. 3(4): p. 19-27., https://www.ncbi.nlm.nih.gov/pubmed/24282659
808. Xiong, Y. D., Ma, S., Li, X., Zhong, X., Duan, C., Chen, Q., A meta-analysis of reflectance confocal microscopy for the diagnosis of malignant skin tumours. J Eur Acad Dermatol Venereol, 2016. 30(8): p. 1295-302., https://www.ncbi.nlm.nih.gov/pubmed/27230832
809. Alarcon, I., Carrera, C., Palou, J., Alos, L., Malvehy, J., Puig, S., Impact of in vivo reflectance confocal microscopy on the number needed to treat melanoma in doubtful lesions. Br J Dermatol, 2014. 170(4): p. 802-8., https://www.ncbi.nlm.nih.gov/pubmed/24124911
810. Pellacani, G., Pepe, P., Casari, A., Longo, C., Reflectance confocal microscopy as a second-level examination in skin oncology improves diagnostic accuracy and saves unnecessary excisions: a longitudinal prospective study. Br J Dermatol, 2014. 171(5): p. 1044-51., https://www.ncbi.nlm.nih.gov/pubmed/24891083
811. Pellacani, G., Witkowski, A., Cesinaro, A. M., Losi, A., Colombo, G. L., Campagna, A., et.al. Cost-benefit of reflectance confocal microscopy in the diagnostic performance of melanoma. J Eur Acad Dermatol Venereol, 2016. 30(3): p. 413-9., https://www.ncbi.nlm.nih.gov/pubmed/26446299
812. Seidenari, S., Arginelli, F., Dunsby, C., French, P. M., Konig, K., Magnoni, C., et.al. Multiphoton laser tomography and fluorescence lifetime imaging of melanoma: morphologic features and quantitative data for sensitive and specific non-invasive diagnostics. PLoS One, 2013. 8(7): p. e70682., https://www.ncbi.nlm.nih.gov/pubmed/23923016

813. Balu, M., Kelly, K. M., Zachary, C. B., Harris, R. M., Krasieva, T. B., Konig, K., et.al. Distinguishing between benign and malignant melanocytic nevi by in vivo multiphoton microscopy. Cancer Res, 2014. 74(10): p. 2688-97., https://www.ncbi.nlm.nih.gov/pubmed/24686168
814. Cheng, H. M., Lo, S., Scolyer, R., Meekings, A., Carlos, G., Guitera, P., Accuracy of optical coherence tomography for the diagnosis of superficial basal cell carcinoma: a prospective, consecutive, cohort study of 168 cases. Br J Dermatol, 2016. 175(6): p. 1290-1300., https://www.ncbi.nlm.nih.gov/pubmed/27146027
815. Cheng, H. M., Guitera, P., Systematic review of optical coherence tomography usage in the diagnosis and management of basal cell carcinoma. Br J Dermatol, 2015. 173(6): p. 1371-80., https://www.ncbi.nlm.nih.gov/pubmed/26211438
816. Coleman, A. J., Richardson, T. J., Orchard, G., Uddin, A., Choi, M. J., Lacy, K. E., Histological correlates of optical coherence tomography in non-melanoma skin cancer. Skin Res Technol, 2013. 19(1): p. 10-9., https://www.ncbi.nlm.nih.gov/pubmed/22738357
817. Hussain, A. A., Themstrup, L., Jemec, G. B., Optical coherence tomography in the diagnosis of basal cell carcinoma. Arch Dermatol Res, 2015. 307(1): p. 1-10., https://www.ncbi.nlm.nih.gov/pubmed/25223745
818. Markowitz, O., Schwartz, M., Feldman, E., Bienenfeld, A., Bieber, A. K., Ellis, J., et.al. Evaluation of Optical Coherence Tomography as a Means of Identifying Earlier Stage Basal Cell Carcinomas while Reducing the Use of Diagnostic Biopsy. J Clin Aesthet Dermatol, 2015. 8(10): p. 14-20., https://www.ncbi.nlm.nih.gov/pubmed/26557214
819. Olsen, J., Themstrup, L., De Carvalho, N., Mogensen, M., Pellacani, G., Jemec, G. B., Diagnostic accuracy of optical coherence tomography in actinic keratosis and basal cell carcinoma. Photodiagnosis Photodyn Ther, 2016. 16: p. 44-49., https://www.ncbi.nlm.nih.gov/pubmed/27519350
820. Ulrich, M., von Braunmuehl, T., Kurzen, H., Dirschka, T., Kellner, C., Sattler, E., et.al. The sensitivity and specificity of optical coherence tomography for the assisted diagnosis of nonpigmented basal cell carcinoma: an observational study. Br J Dermatol, 2015. 173(2): p. 428-35., https://www.ncbi.nlm.nih.gov/pubmed/25904111
821. Gambichler, T., Schmid-Wendtner, M. H., Plura, I., Kampilafkos, P., Stucker, M., Berking, C., et.al. A multicentre pilot study investigating high-definition optical coherence tomography in the differentiation of cutaneous melanoma and melanocytic naevi. J Eur Acad Dermatol Venereol, 2015. 29(3): p. 537-41., https://www.ncbi.nlm.nih.gov/pubmed/25073788
822. Malvehy, J., Hauschild, A., Curiel-Lewandrowski, C., Mohr, P., Hofmann-Wellenhof, R., Motley, R., et.al. Clinical performance of the Nevisense system in cutaneous melanoma detection: an international, multicentre, prospective and blinded clinical trial on efficacy and safety. Br J Dermatol, 2014. 171(5): p. 1099-107., https://www.ncbi.nlm.nih.gov/pubmed/24841846
823. Lassau, N., Spatz, A., Avril, M. F., Tardivon, A., Margulis, A., Mamelle, G., et.al. Value of high-frequency US for preoperative assessment of skin tumors. Radiographics, 1997. 17(6): p. 1559-65., https://www.ncbi.nlm.nih.gov/pubmed/9397463
824. Krahn, G., Gottlober, P., Sander, C., Peter, R. U., Dermatoscopy and high frequency sonography: two useful non-invasive methods to increase preoperative diagnostic accuracy in pigmented skin lesions. Pigment Cell Res, 1998. 11(3): p. 151-4., https://www.ncbi.nlm.nih.gov/pubmed/9730322
825. Wortsman, X., Wortsman, J., Clinical usefulness of variable-frequency ultrasound in localized lesions of the skin. J Am Acad Dermatol, 2010. 62(2): p. 247-56., https://www.ncbi.nlm.nih.gov/pubmed/19962214
826. Elbaum, M., Kopf, A. W., Rabinovitz, H. S., Langley, R. G., Kamino, H., Mihm, M. C., Jr., et.al. Automatic differentiation of melanoma from melanocytic nevi with multispectral digital dermoscopy: a feasibility study. J Am Acad Dermatol, 2001. 44(2): p. 207-18., https://www.ncbi.nlm.nih.gov/pubmed/11174377
827. Monheit, G., Cognetta, A. B., Ferris, L., Rabinovitz, H., Gross, K., Martini, M., et.al. The performance of MelaFind: a prospective multicenter study. Arch Dermatol, 2011. 147(2): p. 188-94., https://www.ncbi.nlm.nih.gov/pubmed/20956633

828. Hauschild, A., Chen, S. C., Weichenthal, M., Blum, A., King, H. C., Goldsmith, J., et.al. To excise or not: impact of MelaFind on German dermatologists' decisions to biopsy atypical lesions. J Dtsch Dermatol Ges, 2014. 12(7): p. 606-14., https://www.ncbi.nlm.nih.gov/pubmed/24944011
829. Lim, L., Nichols, B., Migden, M. R., Rajaram, N., Reichenberg, J. S., Markey, M. K., et.al. Clinical study of noninvasive in vivo melanoma and nonmelanoma skin cancers using multimodal spectral diagnosis. J Biomed Opt, 2014. 19(11): p. 117003., https://www.ncbi.nlm.nih.gov/pubmed/25375350
830. Philipsen, P. A., Knudsen, L., Gniadecka, M., Ravnbak, M. H., Wulf, H. C., Diagnosis of malignant melanoma and basal cell carcinoma by in vivo NIR-FT Raman spectroscopy is independent of skin pigmentation. Photochem Photobiol Sci, 2013. 12(5): p. 770-6., https://www.ncbi.nlm.nih.gov/pubmed/23348560
831. Kassenärztliche Bundesvereinigung, Bekanntmachungen Vereinbarung von Qualitätssicherungsmaßnahmen nach § 135 Abs. 2 SGB V zur histopathologischen Untersuchung im Rahmen des Hautkrebs-Screenings (Qualitätssicherungsvereinbarung Histopathologie Hautkrebs-Screening). Dtsch Arztebl, 2009. 106(39): p. A-1924 / B-1652 / C-1620.
832. Manstein, M. E., Manstein, C. H., Smith, R., How accurate is frozen section for skin cancers?. Ann Plast Surg, 2003. 50(6): p. 607-9., https://www.ncbi.nlm.nih.gov/pubmed/12783011
833. Tran, Kien T., Wright, Natalie A., Cockerell, Clay J., Biopsy of the pigmented lesion—When and how. Journal of the American Academy of Dermatology, 2008. 59(5): p. 852-871., http://linkinghub.elsevier.com/retrieve/pii/S0190962208006579?showall=true
834. Martin, R. C., 2nd, Scoggins, C. R., Ross, M. I., Reintgen, D. S., Noyes, R. D., Edwards, M. J., et.al. Is incisional biopsy of melanoma harmful?. Am J Surg, 2005. 190(6): p. 913-7., https://www.ncbi.nlm.nih.gov/pubmed/16307945
835. Zager, J. S., Hochwald, S. N., Marzban, S. S., Francois, R., Law, K. M., Davis, A. H., et.al. Shave biopsy is a safe and accurate method for the initial evaluation of melanoma. J Am Coll Surg, 2011. 212(4): p. 454-60; discussion 460-2., https://www.ncbi.nlm.nih.gov/pubmed/21463767
836. Kassenärztliche, Bundesvereinigung, IT in der Arztpraxis: Anforderungskatalog Hautkrebs-Screening (eHKS), 2012.
837. Messina, M. C. D. L., Valente, N. Y. S., Castroe, L. G. M., Is incisional biopsy helpful in the histopathological classification of basal cell carcinoma?. Anais Brasileiros de Dermatologia, 2006. p. 81(5)(pp 443-448), 2006.
838. Fawzy, N. W., A psychoeducational nursing intervention to enhance coping and affective state in newly diagnosed malignant melanoma patients. Cancer Nurs, 1995. 18(6): p. 427-38., https://www.ncbi.nlm.nih.gov/pubmed/8564938
839. Trask, P. C., Paterson, A. G., Griffith, K. A., Riba, M. B., Schwartz, J. L., Cognitive-behavioral intervention for distress in patients with melanoma: comparison with standard medical care and impact on quality of life. Cancer, 2003. 98(4): p. 854-64., https://www.ncbi.nlm.nih.gov/pubmed/12910531
840. Loquai, C., Schmidtmann, I., Beutel, M., Sunderkotter, C., Grabbe, S., Schiller, M., et.al. Quality of life in melanoma patients during adjuvant treatment with pegylated interferon-alpha2b: patients' and doctors' views. Eur J Dermatol, 2011. 21(6): p. 976-84., https://www.ncbi.nlm.nih.gov/pubmed/21896421
841. Dunn, J., Watson, M., Aitken, J. F., Hyde, M. K., Systematic review of psychosocial outcomes for patients with advanced melanoma. Psychooncology, 2017. 26(11): p. 1722-1731., https://www.ncbi.nlm.nih.gov/pubmed/27696578
842. Gjorup, C. A., Groenvold, M., Hendel, H. W., Dahlstroem, K., Drzewiecki, K. T., Klausen, T. W., et.al. Health-related quality of life in melanoma patients: Impact of melanoma-related limb lymphoedema. Eur J Cancer, 2017. 85: p. 122-132., https://www.ncbi.nlm.nih.gov/pubmed/28918186
843. Waalboer-Spuij, R., Nijsten, T. E., A review on quality of life in keratinocyte carcinoma patients. G Ital Dermatol Venereol, 2013. 148(3): p. 249-54., https://www.ncbi.nlm.nih.gov/pubmed/23670061

844. Tennvall, G. R., Norlin, J. M., Malmberg, I., Erlendsson, A. M., Haedersdal, M., Health related quality of life in patients with actinic keratosis—an observational study of patients treated in dermatology specialist care in Denmark. Health Qual Life Outcomes, 2015. 13: p. 111., https://www.ncbi.nlm.nih.gov/pubmed/26220553
845. Guy, G. P., Jr., Zhang, Y., Ekwueme, D. U., Rim, S. H., Watson, M., The potential impact of reducing indoor tanning on melanoma prevention and treatment costs in the United States: An economic analysis. J Am Acad Dermatol, 2017. 76(2): p. 226-233., https://www.ncbi.nlm.nih.gov/pubmed/27939556
846. Hirst, N., Gordon, L., Gies, P., Green, A. C., Estimation of avoidable skin cancers and cost-savings to government associated with regulation of the solarium industry in Australia. Health Policy, 2009. 89(3): p. 303-11., https://www.ncbi.nlm.nih.gov/pubmed/18760857
847. Waters, Hugh R., Adamson, Adewole, The health and economic implications of the use of tanning devices. Journal of Cancer Policy, 2018. 17: p. 45-50., http://www.sciencedirect.com/science/article/pii/S2213538316300340
848. Pil, L., Hoorens, I., Vossaert, K., Kruse, V., Tromme, I., Speybroeck, N., et.al. Burden of skin cancer in Belgium and cost-effectiveness of primary prevention by reducing ultraviolet exposure. Prev Med, 2016. 93: p. 177-182., https://www.ncbi.nlm.nih.gov/pubmed/27713103
849. Kyle, J. W., Hammitt, J. K., Lim, H. W., Geller, A. C., Hall-Jordan, L. H., Maibach, E. W., et.al. Economic evaluation of the US Environmental Protection Agency's SunWise program: sun protection education for young children. Pediatrics, 2008. 121(5): p. e1074-84., https://www.ncbi.nlm.nih.gov/pubmed/18450850
850. Shih, S. T., Carter, R., Sinclair, C., Mihalopoulos, C., Vos, T., Economic evaluation of skin cancer prevention in Australia. Prev Med, 2009. 49(5): p. 449-53., https://www.ncbi.nlm.nih.gov/pubmed/19747936
851. Shih, S. T., Carter, R., Heward, S., Sinclair, C., Economic evaluation of future skin cancer prevention in Australia. Prev Med, 2017. 99: p. 7-12., https://www.ncbi.nlm.nih.gov/pubmed/28131778
852. Gordon, L. G., Rowell, D., Health system costs of skin cancer and cost-effectiveness of skin cancer prevention and screening: a systematic review. Eur J Cancer Prev, 2015. 24(2): p. 141-9., https://www.ncbi.nlm.nih.gov/pubmed/25089375
853. Gordon, L. G., Brynes, J., Baade, P. D., Neale, R. E., Whiteman, D. C., Youl, P. H., et.al. Cost-Effectiveness Analysis of a Skin Awareness Intervention for Early Detection of Skin Cancer Targeting Men Older Than 50 Years. Value Health, 2017. 20(4): p. 593-601., https://www.ncbi.nlm.nih.gov/pubmed/28408001
854. Hirst, N. G., Gordon, L. G., Scuffham, P. A., Green, A. C., Lifetime cost-effectiveness of skin cancer prevention through promotion of daily sunscreen use. Value Health, 2012. 15(2): p. 261-8., https://www.ncbi.nlm.nih.gov/pubmed/22433757
855. Anderson, A. J. M., Ferris, L. K., Binion, D. G., Smith, K. J., Cost-Effectiveness of Melanoma Screening in Inflammatory Bowel Disease. Dig Dis Sci, 2018. 63(10): p. 2564-2572., https://www.ncbi.nlm.nih.gov/pubmed/29948569
856. Wilson, E. C. F., Usher-Smith, J. A., Emery, J., Corrie, P., Walter, F. M., A Modeling Study of the Cost-Effectiveness of a Risk-Stratified Surveillance Program for Melanoma in the United Kingdom. Value Health, 2018. 21(6): p. 658-668., https://www.ncbi.nlm.nih.gov/pubmed/29909870
857. Watts, C. G., Cust, A. E., Menzies, S. W., Mann, G. J., Morton, R. L., Cost-Effectiveness of Skin Surveillance Through a Specialized Clinic for Patients at High Risk of Melanoma. J Clin Oncol, 2017. 35(1): p. 63-71., https://www.ncbi.nlm.nih.gov/pubmed/28034073
858. Okafor, P. N., Stallwood, C. G., Nguyen, L., Sahni, D., Wasan, S. K., Farraye, F. A., et.al. Cost-effectiveness of nonmelanoma skin cancer screening in Crohn's disease patients. Inflamm Bowel Dis, 2013. 19(13): p. 2787-95., https://www.ncbi.nlm.nih.gov/pubmed/24193153
859. Losina, E., Walensky, R. P., Geller, A., Beddingfield, F. C., 3rd, Wolf, L. L., Gilchrest, B. A., et.al. Visual screening for malignant melanoma: a cost-effectiveness analysis. Arch Dermatol, 2007. 143(1): p. 21-8., https://www.ncbi.nlm.nih.gov/pubmed/17224538

860. Beddingfield, Iii, Melanoma: A Decision Analysis to Estimate the Effectiveness and Cost-Effectiveness of Screening and an Analysis of the Relevant Epidemiology of the Disease, 2002.
861. Freedberg, K. A., Geller, A. C., Miller, D. R., Lew, R. A., Koh, H. K., Screening for malignant melanoma: A cost-effectiveness analysis. J Am Acad Dermatol, 1999. 41(5 Pt 1): p. 738-45., https://www.ncbi.nlm.nih.gov/pubmed/10534637
862. Girgis, A., Clarke, P., Burton, R. C., Sanson-Fisher, R. W., Screening for melanoma by primary health care physicians: a cost-effectiveness analysis. J Med Screen, 1996. 3(1): p. 47-53., https://www.ncbi.nlm.nih.gov/pubmed/8861052
863. Siebert, U., When should decision-analytic modeling be used in the economic evaluation of health care? [Editorial]. European Journal of Health Economics, 2003. 4(3): p. 143-150., pdf, C:\!Fulltext\Siebert\Siebert_2003_Eur, J, Health, Econom_When, should, DA, modeling, be, used, in, econom, eval.pdf
864. Siebert, U., Transparente Entscheidungen in Public Health mittels systematischer Entscheidungsanalyse, in Public Health. Gesundheit und Gesundheitswesen, Schwartz, F. W.Walter, U.Siegrist, J.Kolip, P.Leidl, R.Dierks, M.-L.Busse, R. and Schneider, N., Editors. 2012, Urban & Fischer in Elsevier: München. p. 517-535., pdf
865. Siebert, U., Alagoz, O., Bayoumi, A.M., Jahn, B., Owens, D.K., Cohen, D.J., et.al. State-Transition Modeling: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force -3. Medical Decision Making, 2012. 32(5): p. 690-700., pdf
866. Lorenz, W., Ollenschläger, G., Geraedts, M., Gerlach, F., Gandjour, A., Helou, A., et.al. Das Leitlinien-Manual: Entwicklung und Implementierung von Leitlinien in der Medizin. Zeitschrift für ärztliche Fortbildung und Qualitätssicherung, 2001. 95(Suppl I): p. 1-84.
867. Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF), Erarbeitung von Leitlinien für Diagnostik und Therapie - Methodische Empfehlungen („Leitlinie für Leitlinien“, Stand Dez. 2004).Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF), 2004., http://www.awmf.org/fileadmin/user_upload/Leitlinien/Werkzeuge/Publikationen/methoden.pdf
868. Leidl, R., von der Schulenburg, J.M., Wasem, J., Ansätze und Methoden der ökonomischen Evaluation - eine internationale Perspektive Health Technology AssessmentNomos, 1999.
869. IQWiG, Allgemeine Methoden (Version 4.2)Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG), 2015.