German Guideline Program in Oncology (GGPO)

Evidenced-based Guideline: Palliative care for patients with incurable cancer

Short version 1.1 – May 2015

AWMF-Registration number: 128/001OL

Guideline (Short Version)

DKG KREBSGESELLSCHAFT

Deutsche Krebshilfe HELFEN. FORSCHEN. INFORMIEREN.

AWMF

Table of contents

Preface

The goal of palliative care is to improve and maintain quality of life for both patients with life threatening illness and their families. This guideline aims at achieving the best possible treatment and care for patients with terminal cancer. The recommendations and background texts presented here are to support all the health care providers involved in the treatment of these patients. The guideline at hand serves as an aid for decision-making in practice and provides systematically developed treatment recommendations on the basis of the best possible evidence (scientific studies) and clinical experience of a large number of experts. It presents the current national and international state of knowledge and experience in the topics concerned and aims to offer orientation and assurance in the provision of palliative care. The recommendations are an aid for decision-making and not the decision itself – they will often require "translating" and if necessary adjusting in order to reflect the individual situation.

The term palliative care is used to describe all treatment and care options available for people with incurable, life-threatening cancer as well as other illnesses. It emphasises the special interdisciplinary and multi-professional character of this area of care. Palliative care and hospice care are understood as a joint approach.

The rapid development experienced by palliative care has been unlike that of almost any other area of healthcare. This area of medicine has received considerable sociopolitical support which is likely due to the epidemiological developments expected in our society. The consistent focus that palliative care affords to the needs of both patients and their families in such an existential situation has certainly also led to its rapid development.

Death is a natural part of life. This guideline is based on the views of the German Association for Palliative Medicine (DGP), as the leading specialist association for the guideline: "From its life-affirming approach, palliative care offers help while dying but not help to die" (Brochure "Ärztlich Assistierter Suizid – Reflexionen der DGP", 2014). Therefore, ending life prematurely does not belong to the fundamental principles of palliative care. This includes physician assisted suicide as well as euthanasia.

For the first time, there is now a guideline in Germany which complies with the highest quality standards (S3-level)[1] and which additionally integrates or refers to the expertise of national and international guidelines and standards (Palliative care treatment recommendations from the German Medical Association[2], recommendations and White Papers from the European Association for Palliative Care (EAPC) [1, 2] etc.) The guideline at hand refers explicitly to patients with cancer – the extent to which the recommendations can be used for patients with non-oncological diseases would have to be considered on an individual basis. Moreover, due to limited resources, the guideline focuses on seven topic areas (breathlessness, cancer pain, constipation, depression, communication, the dying phase, health care structures). The guideline thus only covers part of the entire area of palliative care, but an extension of the guideline will follow. This second part of the guideline addresses eight further topics: (1) malignant intestinal obstruction (MIO), (2) nausea/vomiting, (3) sleep disturbance/night agitation,

[1] The „S3-level" refers to the German classification scale of guidelines. The highest "S3-level" means that the guideline is evidenced and consensus-based and has been developed according to strict methodological criteria: systematical search of evidence, representative guideline-group, and structured process of consensus.

[2] Bundesärztekammer

(4) wound care (e.g. ulcerating malignant skin lesions), (5) fatigue, (6) anxiety, (7) treatment goal decision-making and (8) handling with the desire for hastened death. The development of this second guideline part should begin in 2016.

The guideline clearly shows how, in addition to decades of experience, there is now also a considerable amount of evidence from studies available in palliative care – approximately half of the recommendations are evidence based. However, the guideline also demonstrates that there is still a need for research in this field and for further efforts and investments in order to further improve palliative care (regarding this, please see the research agenda from the Leopoldina[3] [3]).

The presented guideline is a collaborative piece of work. In addition to many experts from various professional groups and different specialist medical disciplines, people from diverse sections of the society as well as representatives of patients and their families were closely involved in the development process. We would like to thank all those involved very much for their help, which was for the most part done gratuitously. A special thank you is directed to the Guideline Programme in Oncology (DKG, AWMF, DKH[4]) which made this guideline possible through their continual support and advice as well as by the financial support received from the German Cancer Aid.

Professor Dr Claudia Bausewein
Lead Coordinator

Professor Dr Raymond Voltz
Lead Coordinator

Dr Steffen Simon
Project Leader

Professor Dr Lukas Radbruch
DGP President

[3] The Leopoldina was appointed as the German National Academy of Sciences in 2008. In this capacity, it represents the German scientific community in international committees and speaks out on social and political questions, providing a nonpartisan, factual framework for discussion. (http://www.leopoldina.org/en/about-us/about-the-leopoldina/leopoldina-mission-statement/)

[4] DKG – Deutsche Krebs Gesellschaft – German Cancer Society, AWMF - Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V. - The Association of the Scientific Medical Societies in Germany, DKH - Deutsche Krebshilfe e.V. - German Cancer Aid.

1. Information about this guideline

1.1. Editors

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

1.2. Leading professional society

German Association for Palliative Medicine
Aachener Straße 5
10713 Berlin

DEUTSCHE GESELLSCHAFT FÜR PALLIATIVMEDIZIN

1.3. Funding of the guideline

This guideline was funded by the German Cancer Aid (DKH) as part of the German Guideline Programme in Oncology.

1.4. Contact

Office Leitlinienprogramm Onkologie
c/o Deutsche Krebsgesellschaft e.V.
Kuno-Fischer-Straße 8
14057 Berlin

leitlinienprogramm@krebsgesellschaft.de
www.leitlinienprogramm-onkologie.de

1.5. Citation

German Guideline Programme in Oncology (German Cancer Society, German Cancer Aid, AWMF): Palliative care for patients with incurable cancer, short version 1.1, 2015 AWMF-registration number 128/001OL, http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html (cited: DD.MM.YYYY)

1.6. Amendment of version 1

July 2015, version 1.1: Some editorial amendments were carried out. Step 3 of the step-wise approach for the therapy of constipation was clarified (page 45).

1.7. Special notice

Due to the fact that medicine is subject to a process of continuous development, all information, in particular that on diagnostic and treatment procedures, is only in accordance with knowledge available at the time of printing. With regard to the recommendations provided for treatment and the choice and doses of medication, the highest possible care was taken. Nevertheless, users are asked to consult the package leaflet and summary of product characteristics from the manufacturer and when in doubt consult a specialist. In the question of general interest, please inform the editorial staff of any questionable irregularities.

The user is responsible for every diagnostic and therapeutic application, medication and dosing.

In this guideline, trademarks (registered trademarks) are not specifically identified. Therefore, a missing indication does not indicate that a trade name is unregistered.

1.8. Objectives of the German Guideline Programme in Oncology

With the German Guideline Programme in Oncology (GGPO), The Association of the Scientific Medical Societies in Germany (AWMF), The German Cancer Society (DKG) and the German Cancer Aid (DKH) set themselves the goal of collaboratively promoting and supporting the development, updating and application of scientifically founded, practicable guidelines in oncology. This programme is based on the medical-scientific knowledge of the specialist associations and the DKG, the consensus of medical specialists, users and patients, as well as on the regulations for the production of guidelines from the AWMF and the specialist and financial support by the German Cancer Aid. In order to reflect current medical knowledge and progress, guidelines need to be regularly checked and updated. The usage of the AWMF-regulations acts as a basis for developing high quality oncology guidelines. Guidelines provide an important instrument for quality assurance and management in oncology and should therefore be purposefully and sustainably implemented into the day-to-day provision of patient care. In this way, active implementation and evaluation programmes are an important element of promoting the German Guideline Programme in Oncology. The aim of the programme is to establish a professional basis and mid-term financial security for the development and provision of high quality guidelines. This is because these guidelines do not only allow for the structured transfer of knowledge but can also help in shaping health care structures. Worth mentioning here are evidence based guidelines as the basis for producing and updating disease management programmes or the usage of quality indicators from guidelines in the certification of tumour centres.

1.9. Further documents relating to this guideline

The content of this short version is based on the extended version of the S3-guideline for palliative care for patients with incurable cancer which is available on the following websites:

- www.awmf.org/leitlinien/aktuelle-leitlinien.html
- www.leitlinienprogramm-onkologie.de/OL/leitlinien.html
- www.krebsgesellschaft.de/wub_llevidenzbasiert,120884.html
- www.krebshilfe.de
- www.g-i-n.net (Guidelines International Network)
- www.dgpalliativmedizin.de

In addition to the short version there are the following supplementary documents:

- Full version
- Guideline methodology report for producing the guideline
- Evidence tables
- Patient guideline

All these documents are also available from the aforementioned websites.

1.10. Guideline group composition

1.10.1. Coordination and editing

Guideline coordination: Professor Dr Claudia Bausewein, Professor Dr Raymond Voltz, Dr Steffen Simon (Project management)

Guideline office: Verena Geffe M.A., Dr Anne Pralong

Editing: The coordination group and the leader of the working groups (steering group) were involved in editing the guideline.

1.10.2. Professional societies and authors involved

- Academy for Ethics in Medicine (AEM) - Dr Alfred Simon
- Conference of Oncology and Paediatric Oncology Nurses within the German Cancer Society** (KOK) - Ulrike Ritterbusch, Kerstin Paradies
- Department of Further Professions within the German Association for Palliative Medicine** - Dr Martin Fegg
- Department of Nursing within the German Association for Palliative Medicine** - Thomas Montag
- Dermatologic Cooperative Oncology Group (ADO) - Dr Katharina Kähler, Dr Carmen Loquai
- Evangelical Church in Germany (EKD) - Professor Dr Traugott Roser
- Frauenselbsthilfe nach Krebs e.V., a self-help association for cancer survivors (FSH) - Sabine Kirton
- German Association for Logopedics (DBL) - Ricki Nusser-Müller-Busch, Dr Ruth Nobis-Bosch
- German Association for Palliative Medicine (DGP) - Professor Dr Gerhild Becker
- German Association for Physiotherapy (ZVK) - Dr Beate Kranz-Opgen-Rhein, Andrea Heinks
- German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) - Professor Dr Vjera Holthoff
- German Association for Social Work in Health Care (DVSG) - Hans Nau, Franziska Hupke
- German Association of Hospice and Palliative Care** (DHPV) - Ursula Neumann
- German Association of Occupational Therapists (DVE) - Carsten Schulze
- German Association of Psychosocial Oncology (dapo) - Dr Thomas Schopperth
- German Care and Case Management Society (DGCC) - Dr Rudolf Pape
- German College of General Practitioners and Family Physicians (DEGAM) - Dr Peter Engeser, Professor Dr Nils Schneider
- German Interdisplinary Association for Pain Therapy (DIVS) (left the guideline development group in September 2011) - Professor Dr Heinz Laubenthal*
- German Pain Society - Professor Dr Winfried Meißner, Dr Stefan Wirz
- German Psychogeriatric Association (DGGPP) - Dr Klaus Maria Perrar
- German Respiratory Society (DGPB) - Professor Dr Helgo Magnussen
- German Society for Anaesthesiology and Intensive Care** (DGAI) - Professor Dr Christof Müller-Busch
- German Society for Dermatology** (DDG) - Dr Carmen Loquai
- German Society for General and Visceral Surgery (DGAV) - Professor Dr Pompiliu Piso, Professor Stefan Fichtner-Feigl

- German Society for Geriatric Medicine (DGG) and German Society for Gerontology and Geriatric Medicine** (DGGG) - Dr M. Pfisterer
- German Society for Gynecology and Obstetrics (DGGG) - Professor Dr Werner Meier, Professor Dr Christoph Thomssen
- German Society for Hematology and Medical Oncology (DGHO) - Dr Bernd-Oliver Maier, Dr Werner Freier
- German Society for Internal Medicine and Emergency Care** (DGIIN) - Professor Dr Uwe Janssens
- German Society for Psychological Pain Therapy and Research** (DGPSF) - Dipl.-Psych. Karin Kieseritzky
- German Society for Senology (DGS) - Professor Dr Ulrich Kleeberg
- German Society of Gastroenterology (DGVS) - Dr Martin H. Holtmann, Professor Dr Gerhard Werner Pott
- German Society of Internal Medicine (DGIM) - Professor Dr Norbert Frickhofen
- German Society of Neurology (DGN) - Professor Dr Raymond Voltz
- German Society of Neurosurgery (DGNC) - Professor Dr Roland Goldbrunner
- German Society of Oto-Rhino-Laryngology, Head and Neck Surgery (HNO) - Professor Dr Barbara Wollenberg, Professor Dr Jens Büntzel
- German Society of Radiation Oncology (DEGRO) - Dr Birgit van Oorschot, Professor Dr Dirk Rades
- German Society of Specialist Nursing and Allied Technical Assistants (DGFF) - Elke Goldhammer
- German Society of Surgery (DGCH) - Professor Dr Stefan Mönig, Professor Stefan Fichtner-Feigl
- German Society of Urology (DGU) - Dr Chris Protzel
- Hospice and Palliative Care Evaluation (HOPE) - core documentation for palliative care facilities within the German Association for Palliative Medicine (AG HOPE) - Professor Dr Lukas Radbruch
- The German Bishops' Conference (DBK) - Ulrich Fink
- The German Society of Hospital Pharmacists (ADKA) - Constanze Rémi, Dr Stefan Amann
- The German Society of Nursing Science (DGPflege) - Dr Margit Haas
- Women's Health Coalition e.V. (WHC) - Irmgard Nass-Griegoleit
- Working Group for Education and Training within the German Association for Palliative Medicine** (AG AFW) - Axel Doll
- Working Group for Ethics in Medicine within the German Association for Palliative Medicine (AG Ethik) - Professor Dr Martin Weber
- Working Group for Palliative Care within the German Cancer Society (AG PM) - Dr Bernd Alt-Epping, Professor Florian Lordick, Dr Joan Panke
- Working Group for Prevention and Integrative Oncology within the German Cancer Society (AG PriO) - Dr Christoph Stoll
- Working Group for Psycho-oncology within the German Cancer Society** (AG PSO) - Dr Pia Heußner, Dr Monika Keller, Professor Dr Joachim Weis
- Working Group for Research within the German Association for Palliative Medicine (AG Forschung) - Professor Dr Christoph Ostgathe
- Working Group for Urologic Oncology (AUO) within the German Cancer Society** - Dr Chris Protzel
- Working Group Guidelines within German Association for Palliative Medicine (AG Leitlinien) - Professor Dr Claudia Bausewein
- Working Group Medical Oncology (AIO) within the German Cancer Society (AIO) - Dr Ulrich Wedding

**own translation

In addition to the elected representatives there were 49 experts involved in the development of the guideline who had no voting rights:

Dr Elisabeth Albrecht, Dr Susanne Ditz, Professor Michael Ewers, Dr Steffen Eychmüller, Professor Thomas Frieling, Dr Sabine Gabrijel, Dr Jan Gärtner, Manfred Gaspar, Dr Christiane Gog, Jan Gramm, Dr Birgit Haberland, Dr David Heigener, Professor Peter Herschbach, Franziska Hupke, Dr Jürgen in der Schmitten, Stephanie Jeger, Dr Thomas Jehser, Dr Marianne Kloke, Dr Julia Köpp, Dr Tanja Krones, Norbert Krumm, Dr Stefan Lorenzl, Heiner Melching, Dr Elke Müller, Dr Gabriele Müller-Mundt, Professor Friedemann Nauck, Wiebke Nehls, Professor Günter Ollenschläger, Professor Gerhard Pott*, Dr Susanne Riha, Dr Roman Rolke, Dr Susanne Roller, Dr Justina Rozeboom, Professor Rainer Sabatowski, Dr Christian Scheurlen, Dr Jan Schildmann, Dr Christine Schiessl, Dr Christian Schulz, Dr Ulrike Stamer, Professor Michael Thomas, Dr Martin Steins, Dr Mariam Ujeyl*, Stefanie Volsek, Dr von Andreas Aretin, Professor Andreas von Leupoldt, Professor Maria Wasner, Professor Jürgen Wolf, Dr Birgit Weihrauch, Dr Heidi Wurst

(*withdrew during the course of the guideline preparation)

1.10.3. Patient involvement

The guideline was developed with the direct involvement of two patient representatives from the Frauenselbsthilfe nach Krebs e.V.[5] and the Women's Health Coaltion e.V.

1.10.4. Methodological support

Methodological support was received from the German Guideline Programme in Oncology with:

- Professor Ina Kopp (AWMF), Marburg,
- Dr Markus Follmann MPH MSc (DKG), Berlin, and
- Dr Monika Nothacker MPH (AWMF), Marburg

For further methodological support the following experts or institutions were consulted:

- ÄZQ (Agency for Quality in Medicine, Berlin)[6]
- Cicely Saunders Institute at King's College London (London/UK)
- German Cochrane Centre (Freiburg)[7], Cochrane Haematological Malignancies Group (CHMG, Köln)
- SIGN (Scottish Intercollegiate Guidelines Network, Edinburgh/UK)

1.11. Abbreviations used

Abbreviation	Explanation
ACP	Advance Care Planning
APV	Allgemeine PalliativVersorgung (Generalist palliative care)
ÄZQ	Ärztliches Zentrum für Qualität in der Medizin (Agency for Quality in Medicine)

[5] a self-help association for cancer survivors

[6] ÄZQ - Ärztliches Zentrum für Qualität in der Medizin – Agency for Quality in Medicine

[7] Das Deutsche Cochrane Zentrum – A Centre of the German Cochrane Collaboration

Abbreviation	Explanation
CCT	Controlled Clinical Trial
CHMG	Cochrane Haematological Malignancies Group
COPD	Chronic Obstructive Pulmonary Disease
CNS	Central Nervous System
DEGAM	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (German College of General Practitioners and Family Physicians)
DGP	Deutsche Gesellschaft für Palliativmedizin (German Society for Palliative Medicine)
DHPV	Deutscher Hospiz- und Palliativverband (German Association of Hospice and Palliative Care)
EAPC	European Association of Palliative Care
ECOG	Eastern Cooperative Oncology Group
EC	Expert Consensus
EORTC	European Organization for Research and Treatment of Cancer
ESAS	Edmonton Symptom Assessment System
ESAS-r	Edmonton Symptom Assessment System – revised Version
GFR	Glomerular Filtration Rate
GKV	Gesetzliche Krankenversicherung (Statutory health insurance)
GL	Guideline
GoR	Grade of Recommendation
HPS	Home care scale
i.v.	Intravenous
ICD	Implanted Cardioverter-Defibrillator
ICD-10	International Statistical Classification of Diseases
IPOS	Integrated Palliative care Outcome Scale
LoE	Level of Evidence
MIDOS	Minimales Dokumentationssystem (German version of the Edmonton Symptom Assessment Scale)
NaSSA	Noradrenergic and Specific Serotonergic Antidepressant
NDMG	National Disease Management Guideline (Nationale Versorgungsleitlinie)
NSAIDS	Nonsteroidal anti-inflammatory drugs
OTFC	Oral Transmucosal Fentanyl Citrate

Abbreviation	Explanation
p. o.	per os (oral administration)
PEG	Percutaneous Endoscopic Gastrostomy
POS	Palliative care Outcome Scale
PROs	Patient Reported Outcomes
QI	Quality indicator
QoL	Quality of Life
QUAL-E	Quality of Life at the End of Life Measure
RCT	Randomised Controlled Trial
s. c.	Subcutaneous
SAPV	Spezialisierte Ambulante Palliativversorgung (Specialised Home Palliative Care)
SGB	Sozialgesetzbuch (German social code book)
SIGN	Scottish Intercollegiate Guidelines Network
s. l.	Sublingual
SPV	Spezialisierte PalliativVersorgung (Specialist Palliative Care)
SSNRI	Selective Serotonin-Noradrenalin-Reuptake-Inhibitor
SSPV (SIPC)	Spezialisierte Stationäre Palliativversorgung (Specialist in-Patient Palliative Care)
SSRI	Selective Serotonin Reuptake Inhibitor
ST	Statement
TTS	Transdermal Therapeutic System
TCA	Tricyclic antidepressant
WHO	World Health Organization

2. Introduction

2.1. Scope and purpose

2.1.1. Objective and key questions

The main aim of this guideline is the improvement of symptom control in palliative care for patients with incurable cancer and their families. Improving the quality of care is to be achieved by:

- providing palliative care services in both a timely manner and in accordance with the affected persons' needs (chapter Palliative care services),
- treating the common symptoms according to current scientific evidence and clinical expertise (chapter Breathlessness, Pain, Depression, Constipation),
- enabling conversations with patients and their families to be held and treatment goals to be set together (chapter Communication)
- ensuring that support in the dying phase can be appropriately and optimally given (chapter The dying phase)

This palliative care guideline for patients with incurable cancer presents the fundamental principles of palliative care which, in organ specific guidelines, would be repetitive and/or not able to be dealt with in a comprehensive manner. It does not make statements about tumour specific measures (e.g. radiotherapy, operative procedures, drug-based tumour therapy), even when these could be adopted with the primary or secondary goal of symptom reduction, but rather refers to the organ specific guidelines, e.g. those from the German Guideline Programme in Oncology among others. With regard to psycho-oncological aspects, we also refer to the S3-guideline "Psychoonkologische Diagnostik, Beratung und Behandlung" (Psycho-oncological diagnosis, consultation and treatment) [4].

2.1.2. Addressees

Target patient group

The target patient group for this guideline is adult patients with incurable cancer for whom the primary treatment goal is improving quality of life. The recommendations for palliative care measures formulated in this guideline are independent from the implementation of tumour-specific therapies (e.g. radiotherapy, operative procedures, drug-based tumour therapy), therefore they can be used on their own or parallel to tumour specific measures.

Area of care

The palliative care guideline for patients with incurable cancer should be applicable to all areas of care. That includes both in and out-patient care as well as generalist and specialist palliative care.

User target group

This guideline is aimed at all physicians as well as any other professional group in health care that treats patients with terminal cancer. The guideline is additionally aimed at affected patients as well as their families. Moreover, it should act as an orientation for funding agencies and political decision-makers.

2.1.3. Period of validity and updating procedure

The S3-guideline is deemed valid until the next update. The next update is planned for in five years' time, in 2019. If there is an urgent need for changes, a new version can be produced earlier. Comments and information for the updating process are very welcome and can be addressed to:

Dr Steffen Simon (Project Management)
Uniklinik Köln
Zentrum für Palliativmedizin
Kerpener Str. 62
50924 Köln

S3-palliativ@uk-koeln.de

2.2. Basic methodology

The methodological approach for producing this guideline is presented in the guideline methodology report. This can be accessed free of cost on the internet e.g. on the website of the German Guideline Programme in Oncology (http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html) or on the website of the AWMF (http://www.awmf.org/)

2.2.1. SIGN evidence grading system

In order to assess the risk of bias in identified studies, the guideline uses the Scottish Intercollegiate Guidelines Network (SIGN) system, which is displayed in Table 1 (see www.sign.ac.uk/pdf/sign50.pdf).

According to SIGN, the evidence level represents a body of evidence which summarises all of the identified evidence. Therefore, the evidence level of a recommendation, which is based on a systematic review, is the body of evidence of all included primary studies. This body of evidence can differ from the evidence level of the systematic review (shown in the evidence tables). The systematic review could be of high quality while that of the included studies found in the body of evidence is low.

Table 1: SIGN evidence classification system

Level	Description
1++	High quality meta-analysis, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews or RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies or High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control studies or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytical studies, e.g. case reports, case series
4	Expert opinion

2.2.2. Recommendation grading system

The German Guideline Programme in Oncology methodology requires the guideline authors to allocate Grade of Recommendations (GoR) in accordance with a formal process of consensus. In accordance with this, structured consensus conferences were held by the AWMF [5]. In the course of these processes, elected representatives (see chapter 1.10.2) came to an agreement on the recommendation levels by voting.

In the guideline, the evidence level (see chapter 2.2.1) of the underlying studies is given for all evidence based statements and recommendations, for which the strength of the recommendation (Grade of Recommendation) is also provided. With regard to the strength of the recommendation, the guideline differentiates between three

ommendation levels (see Table 2) which are reflected in the wording of the recommendations.

Table 2: Recommendation levels grading system

Recommendation level	Description	Wording
A	Strong recommendation	must
B	Recommendation	should
0	Open recommendation	can

2.2.3. Statements

Statements are to be understood as explanations of specific facts and circumstances or questions without any direct call for action. They are adopted in accordance with the formal consensus procedure and can be based on either study results or expert opinions.

2.2.4. Expert consensus (EC)

Recommendations which are not based on a systematic appraisal of the literature, but were rather decided upon on the basis of expert consensus are indicated with “expert consensus = EC”. There was no symbol or letter used for the classification of expert consensus, therefore the strength of the consensus is implied by the wording used (must/should/can) in accordance with the levels in Table 2.

2.2.5. Independence and disclosure of possible conflicts of interest

The German Cancer Aid provided financial resources through the German Guideline Programme in Oncology (GGPO). The production of the guideline was editorially independent of the funding organisations and there were no additional sponsors.

The financial resources were used exclusively for staff costs, office materials, purchasing literature and consensus conferences (room hire, technology, catering, facilitator’s fees, travelling and accommodation expenses of participants).

All members of the guideline group provided a standardised written disclosure of possible conflicts of interest (AWMF form) which was verified and assessed by the coordinators. The relationships, facts and circumstances which were reported are presented in the guideline report. The conflicts of interest reported by the elected representatives (with voting rights) and experts (without voting rights) are shown in two tables.

The topic, conflicts of interest, was explained in the specific working groups, at the kick-off event of the compilation process and also numerous times at consensus conferences. In individual cases, where there was a potential conflict of interest, a consultation was held with the elected representative concerned. In no case, however, was it necessary to exclude anybody because of potential bias.

By the use of the formal consensus processes, as well as the interdisciplinary multi-occupational compilation and the possibility of a public assessment, further risk of confounding or bias could be reduced.

The elected representatives and experts are expressly thanked for their participation in an honorary capacity.

3. Glossary

The glossary is not intended to establish any new definitions, but rather to clarify for the reader how the terms used in this guideline are to be understood. The glossary is applicable to the entire guideline.

DIMENSIONS OF A PERSON, FOUR

Palliative care is a holistic approach in which the patient is considered in his/her four personal dimensions: physical, psychological, social and spiritual. The aforementioned dimensions tie in with the definition of health in the Ottawa Charta and the definition of palliative care from the WHO [6, 7]. Such an approach allows to provide an answer to the multi-dimensional suffering of people at the end of life – as expressed by Cicely Saunders with the term *total pain* [8]. The four dimensions are interrelated.

- **Physical dimension**: somatic components of a person.
- **Psychological dimension**: cognitive und emotional dimension of a person.
- **Social dimension**: relational dimension of a person which includes all interpersonal relationships. At the end of life, involving family carers in the palliative care of the patient is of particular importance.
- **Spiritual dimension**: dynamic dimension of human life which refers to how people (individually and in community) experience, express and/or look for purpose, meaning and transcendence and how they are connected to the moment, self, others, nature, to the significant and/or the sacred [9]. The spiritual dimension includes:
    - Existential questions (e.g. identity, meaning, suffering and death, guilt and shame, reconciliation and forgiveness, freedom and responsibility, hope and despair, love and joy)
    - Values and attitudes (that is, things which are most important to a person, such as relations to oneself, to family and friends, to work, material things, nature, art and culture, ethics and morals, and to life itself)
    - Religious aspects and principles (faith, beliefs and practices, relationship with God or with the transcendent).

DYING PHASE

The dying phase is used to describe the last days of life. For this guideline, the dying phase is defined as the last three to seven days of life – based on an international expert recommendation and the available evidence [10, 11].

FAMILY CARERS

(Synonym: relatives, loved ones)

People who have a close relationship to the patient through family or other ties e.g. children, parents, friends or neighbours.

INTERDISCIPLINARY APPROACH

The structured cooperation of representatives from different specialties (synonym: disciplines) within one profession (synonym: professional group) is understood as interdisciplinary work.

MULTI-PROFESSIONALISM

The structured cooperation of representatives from different professional groups (synonym: professions) within a team is understood as multi-professional work.

NEED AND REQUIREMENT

Need is the subjective, individual demand or desire of a person or group of persons, that is to say an experienced distressing condition connected with the desire for relief or satisfaction.

Normative need is the objectively recognisable and understandable distressing condition of a patient which cannot be alleviated by individual resources.

Resources "are on the one hand material means (time, money, work) which can be used for a specific goal. On the other hand, they describe the possibility of a person or group to deal with difficult experiences. In particular, social support has proven itself as a particularly important resource for health (www.gesundheitsfoerderung-zh.ch/fileadmin/user_upload/publikationen/Konzept/Leitfaden/Glossar.pdf)."

(Need – resource = normative need)

PALLIATIVE CANCER THERAPY

(Synonym: tumour-specific therapy, palliative therapy)

Palliative cancer therapies are drug-based or non-drug based measures with the primary aim of prolonging life and/or symptom control (e.g. radiotherapy, operative procedures, and drug-based tumour therapies). They are based on the tumour biology and are thus tumour-specific.

Therefore, palliative cancer therapy or palliative therapy is not a synonym for palliative care. The implementation of palliative cancer therapy does not exclude the possibility for a parallel indication for palliative care, but is rather complementary.

PALLIATIVE CARE

(Synonym: palliative medicine, hospice care)

The goal of palliative care is to improve and/or maintain quality of life for both patients with life threatening illnesses and their families. This is achieved by the means of prevention and alleviation of suffering by early identification and treatment of problems in the physical, psychological, social or spiritual dimension [12]. Palliative care is life affirming and sees dying as a natural process. It neither hastens nor delays death [1].

In this guideline, the term palliative care is used to describe all treatment and care options available for people with terminal, life threatening cancer as well as other illnesses. It emphasises the special interdisciplinary and multi-professional character of this area of care. In this sense, palliative care is not reduced to the medical contribution made by physicians but rather is a comprehensive approach in terms of the multi-professional care approach.

In spite of historically diverging developments in Germany, palliative and hospice care are to be understood as a joint approach. Hospice care is rooted in active citizenship.

Patients at the end of their life and their family carers are supported at home, in palliative care out-patient clinics and in in-patient wards. Professionals and volunteers work together in multi-professional teams in order to offer support which is geared towards individual needs and decisions where dignity, peace and calm are the aim [1].

Quality of life

The patient themself determines the most important components of quality of life and their prioritisation. Quality of life is constructed from all possible individual factors and goes beyond the experience of aspects connected to illness.

Health-related quality of life is the subjective assessment of individuals or groups with regard to satisfaction concerning physical, psychological, social and everyday aspects of well-being and functioning. It does not cover external factors that determine quality of life. There are psychometrically tested and standardised measurements to assess health-related quality of life.

Respite Care

Respite care makes it possible for family carers to recover and gain some relief from the prolonged strain of caring for their severely ill relative. Respite care does not only explicitly include care facilities (such as short-term care, substitute care or replacement care) but also all expenses and care measures, as well as aiding with coping, dealing with death and dying and family distress (for current legal regulations see §§ 39 und 42 SGB XI).

Supportive Care

Supportive care encompasses all measures used for the prevention and treatment of the side effects or cancer and its treatment. This refers to the management of physical and psychological symptoms or to side effects over the course of treatment and illness from diagnosis through tumour therapy to post-treatment care (from S3-guideline "Supportive Care for Cancer Patients" [currently in production], according to the definition from the international supportive organisation MASCC; www.mascc.org/about-mascc). Supportive care and palliative care are not synonyms. Whether "side effects of cancer" are part of supportive or palliative care is a question of debate.

Symptom

Ambiguous with different meanings:

On the one hand, symptom is used for objective, observable clinical signs, in terms of clinical findings (e.g. leading symptom) and on the other hand, it is used to describe subjective, individually felt distress or suffering.

In the context of this guideline, symptom is exclusively used to describe the subjective distress and signs to describe objective, observable clinical findings.

Team

A team is a group of people who work together and are responsible for a joint goal – here palliative care. The work is thus competence-based and it is structured in a parent manner. People from various hierarchical levels work together. The structure of

the team and a common attitude enable reliable care. Relationships governed by mutual respect and interaction between team members, team spirit and strong group cohesion are possible characteristics of a team [13, 14].

4. Principles of palliative care

No.	Recommendations/Statements	GoR	LoE	Sources
4.1.	In palliative care, the quality of life of the patient affected by incurable cancer and their family carers is of central importance.		ST (EC)	
4.2.	Palliative care is characterised by a multi-professional and interdisciplinary approach.		ST (EC)	
4.3.	The attitude of health care providers must be characterised by accepting and appreciating the patient as a person with her physical, psychological, social and spiritual dimensions, by including their family carers, by being truthful with the patient and by accepting dying and death as being a part of life.		EC	
4.4.	The following principles *must* be applied when providing palliative care for patients with incurable cancer: 1. Respect the needs of the patient in all four dimensions (physical, psychological, social and spiritual) and respond to them; 2. Respect patient preferences; 3. Determine realistic therapy goals; 4. Be informed about organisational forms of palliative care; 5. Create conditions which respect the patient's privacy.		EC	
4.5.	The following principles *must* be applied in palliative care symptom control in patients with incurable cancer: 1. Consider an appropriate differential diagnosis for the cause of the symptom to enable targeted therapy and the detection of potentially reversible causes; 2. Treat reversible causes when possible and appropriate; 3. Implement a symptomatic therapy on its own or parallel to a causal therapy; 4. Assess tumour specific measures (e.g. radiotherapy, operative procedures, drug-based cancer therapy) with the primary or sole therapy goal of relieving symptoms. A requirement for this is the interdisciplinary cooperation between the various specialities and palliative care; 5. Assess the benefit and risk of the aforementioned measures in an open and honest exchange with patients and, if necessary, their family carers.		EC	
4.6.	The following principles *must* be applied in palliative care of family carers of a patient with incurable cancer: 1. Respect the needs and distress of the family carers and respond to them; 2. Determine realistic goals;		EC	

No.	Recommendations/Statements	GoR	LoE	Sources
	3. Be informed about specific support offers for family carers.			
4.7.	The following principles *must* be applied in palliative care for health care providers who care for patients with incurable cancer: 1. Be prepared to deal with the possibilities and limitations of dying, death and grief and to reflect upon the finite nature of one's own life; 2. Use personal and provided possibilities of salutogenesis and self-care; 3. Be prepared to get more continuing education; 4. Create suitable basic conditions through people in leadership positions.		EC	
4.8.	Criteria for the quality of palliative care *must* include patient-reported outcomes (PRO).		EC	

5. Breathlessness

5.1. Introduction

Breathlessness is a common and distressing symptom for patients with cancer. The widespread and internationally recognised definition of breathlessness from the *American Thoracic Society* describes breathlessness as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity. The experience derives from interactions among multiple physiological, psychological, social and environmental factors, and may induce secondary, physiological and behavioural responses" [15, 16]. In the international context, breathlessness is described as "refractory breathlessness", if breathlessness persists despite optimal treatment of the underlying condition or likely cause, thus indicating the need for symptomatic treatment (e.g. persistent breathlessness in a patient with lung cancer despite optimal chemotherapy and radiotherapy) [17]. The recommendations in this chapter only refer to the **symptomatic treatment** of breathlessness.

Various terms are used to describe "breathlessness": dyspn(o)ea, difficult breathing, and shortness of breath among others.

Breathlessness can be subdivided into two main categories: continuous breathlessness and episodic breathlessness [18]. Patients with continuous breathlessness complain of uninterrupted distress due to breathlessness which, albeit, typically varies significantly in its intensity [19]. On the basis of an international consensus, episodic breathlessness is defined as follows: Episodic breathlessness is one form of breathlessness characterised by a severe worsening of breathlessness intensity or unpleasantness beyond usual fluctuations in the patient's perception. Episodes are time-limited (seconds to hours) and occur intermittently, with or without underlying continuous breathlessness. Episodes may be predictable or unpredictable, depending on whether any trigger(s) can be identified. There is a range of known triggers which can interact (e.g. exertion, emotions, comorbidities or external environment). One episode can be caused by one or more triggers [20, 21].

Breathlessness is a frequent symptom in patients with advanced cancer. A survey of 5,014 in-patients with cancer conducted in palliative and hospice care institutions in Germany in the years 2006-2008 revealed a prevalence of breathlessness of 53.4% [22]. The highest prevalence was shown in patients with lung cancer (74.3%). These results correlate with data from other countries [23-25]. Cancer patients with pulmonary, pleural or mediastinal affections suffer breathlessness both more frequently and more severely [24, 26]. Breathlessness will increase in its frequency and severity over the course of the illness [23, 27, 28].

Breathlessness is not only a distressing symptom for patients but also for their family carers [29, 30]. In comparison to other symptoms, breathlessness causes the highest levels of distress [31]. Patients often describe significant restrictions in their physical abilities which can lead to social isolation among other things [32]. Breathlessness is closely related to anxiety and panic [15, 16, 19, 33]. There appears to be a connection between anxiety/panic and breathlessness, in that breathlessness causes anxiety and in turn anxiety/panic worsens breathlessness [34]. Patients describe this as a *circulus vitiosus* which often leads to acute emergencies, hospital admissions and need of help [34, 35].

As well as statements on how to detect breathlessness, the following recommendations also contain non drug-based and drug-based treatment measures for the symptomatic relief of breathlessness. Procedures which are causal or tumour oriented are not dealt with here (e.g. radiotherapy, operations, bronchoscopy etc.; see also chapter 5.2).

5.2. Assessment

No.	Recommendations/Statements	GoR	LoE	Sources
5.1	Breathlessness *must* be assessed by the patient's subjective experience, e.g. as part of an evaluation of several symptoms.		EC	
5.2	When undertaking a comprehensive assessment of breathlessness, breathlessness *should* be evaluated in three dimensions: • Sensory experience: Intensity/severity level of breathlessness • Affective distress: unpleasant feeling due to breathlessness • Symptom impact: restriction in day to day life due to breathlessness		EC	
5.3	A repeated assessment of breathlessness before, during and following a symptomatic therapy *must* be part of the evaluation.		EC	
5.4	In incurable cancer patients with breathlessness and considerable cognitive or physical restrictions, the assessment of breathlessness *must* be carried out by others (family carers or staff).		EC	
5.5	Potentially treatable causes of breathlessness *must* be identified.		EC	
5.6	Where causal treatment of breathlessness is possible, it *must* be carried out before or parallel to a symptomatic treatment. In this case the following *must* be taken into consideration: • Consideration of medical indication • Burden and benefit for the patient • Patient's wishes		EC	

Optimal treatment of the underlying condition and excluding treatable causes must either precede a symptomatic treatment or occur simultaneously. This occurs by cooperating closely with relevant specialists (e.g. oncology, pulmonology, radiotherapy). In cancer patients, the following potentially reversible causes are often responsible for breathlessness (see Table 3).

Table 3: Examples of possible causes for breathlessness and their causal treatment option

Cause of breathlessness	Causal treatment
Anaemia	Transfusion
Airway obstruction, COPD as comorbidity	Anti-obstructive therapy, corticosteroids
Haemoptysis	Antifibrinolytic agents, bronchoscopy or operative interventions (stent, laser, argon beamer), radiotherapy
Infections, e.g. pneumonia	Antibiotics, antimycotics
Superior vena cava syndrome	Anticoagulants, vena cava stent, corticosteroids, radiotherapy
Airway obstruction due to tumour	Bronchoscopy or operative interventions (stent, laser, argon beamer), radiotherapy
Pericardial effusion	Pericardiocentesis, pericardiodesis
Pleural effusion	Thoracentesis, chest tube, pleurodesis
Pulmonary edema	Diuretics, other appropriate, drug-based treatments

5.3. Opioids

No.	Recommendations/Statements	GoR	LoE	Sources
5.7	In incurable cancer patients with breathlessness, oral[8] or parenteral opioids *must* be administered for the symptomatic relief of breathlessness.	A	1+	[36-47]
5.8	In cases of renal impairment with an increase in side effects the dose and/or the choice of opioid *should* be adjusted according to the clinical situation and severity of renal impairment.	B	3	[48]
5.9	There is no evidence that a correct treatment of breathlessness with opioids leads to clinically relevant respiratory depression.	ST	1+	[36-47]

With pre-existing renal impairment and opioid therapy increased vigilance is required (see Table 4) [49]. However, pre-existing renal impairment must not lead to a delayed administration of opioids for symptomatic treatment of breathlessness [48]. In accordance with the clinical picture (increased occurrence of side-effects?), patients with pre-existing renal impairment (especially severe renal impairment) should receive a lower dose, longer dosing intervals or another opioid which produces no/fewer active metabolites with renal excretion (see Table 5**Fehler! Verweisquelle konnte nicht gefunden werden.**). It is important to note that the current evidence on the usage of opioids for renal impairment (independent of the treated symptom – pain or breathlessness) is very limited and the recommendations are primarily based on pharmacokinetic rationale as well as clinical experience [48-51].

[8] Oral application includes enteral application (e.g. by PEG [Percutaneous endoscopic gastrostomy]).

Table 4: Using opioids depending on the severity level of renal impairment in newly presenting or increasing breathlessness (adapted from: King et al. 2011 and Twycross et al. 2011 [48, 49])

Level of renal insufficiency	Use of opioids
Mild to moderate renal impairment (GFR 30-89 ml/min)	All opioids, which can be used for the symptomatic treatment of breathlessness, can be administered after considering reducing the dose or the frequency Monitor for changes in renal function and consider a pre-emptive opioid switching in rapidly deteriorating renal function Assess for any possible reversible causes of renal impairment Be aware that estimations of GFR may be less accurate in the presence of cachexia, low serum protein states, edema or acute renal failure.
Severe renal impairment (GFR < 30 ml/min)	Opioid switching to quick releasing hydromorphone or fentanyl/buprenorphine if necessary Significantly increased caution, close observation and evaluation in order to quickly adjust the dose if necessary (dose amount or frequency) Transdermal applications and slow releasing drugs are to be administered with increased caution due to the delayed elimination and limited possibility of dose adjustment.
GFR = Glomerular filtration rate	

Table 5: Opioids with and without active metabolites with renal excretion and possibility of dialysis (haemodialysis) (adapted from: King et al. 2011, Twycross et al. 2011 and Murtagh et al. 2007 [48, 49, 51])

Opioid	Active metabolites with renal excretion	Removed by dialysis*?	Safe and effective use in dyalisis patients**?
Morphine	Yes	Yes	Avoid if possible
Hydromorphone	(Yes)	Yes	Yes, with caution
Oxycodone	Yes	(Yes)	Unclear (limited evidence)
Fentanyl	No	No	Yes, with caution
Buprenorphine	(Yes)	No	Yes, with caution

* Whether an opioid is cleared by dialysis or not is much more complicated than the yes/no classification used and it has to be additionally considered whether metabolites are also removed. The yes/no classification used here is to describe whether a significant effect of the drug or its metabolites are removed by dialysis.

** In dialysis patients with renal insufficiency, all opioids should be used with increased caution and additional evaluation and observation and if necessary a dose adjustment (amount, frequency) should occur. The classification used here, whether an opioid can be used in patients having dialysis is a generalization and can vary from patient to patient. The classification is based predominantly on case reports and clinical experience.

5.4. Other drugs

5.4.1. Benzodiazepines

No.	Recommendations/Statements	GoR	LoE	Sources
5.10	Benzodiazepines *can* be administered for the relief of breathlessness if treatment with opioids is not effective.	0	1+	[52, 53]
5.11	Benzodiazepines *can* be administered in combination with opioids for the relief of breathlessness, particularly in patients in an advanced stage of illness or in the dying phase.	0	1-	[46, 54]

5.4.2. Phenothiazines

No.	Recommendations	GoR	LoE	Sources
5.12	Patients with incurable cancer *should not* be administered phenothiazines for the relief of breathlessness.	B	1-	[55-58]

5.4.3. Antidepressants, buspirone

No.	Recommendations	GoR	LoE	Sources
5.13	Patients with incurable cancer *should not* be administered antidepressants or buspirone for the relief of breathlessness.	B	1-	[59-66]

5.4.4. Steroids (Glucocorticoids)

No.	Recommendations	GoR	LoE	Sources
5.14	Patients with incurable cancer *should not* be administered steroids for the relief of breathlessness, if lymphangiosis carcinomatosa or an airway obstruction due to a tumour does not additionally exist.	B	1-	[67-85]
5.15	Patients with incurable cancer who have lymphangiosis carcinomatosa or airway obstruction due to a tumour *can* be administered steroids for the relief of breathlessness.	0	4	-

5.5. Non-pharmacological therapy

No.	Recommendations	GoR	LoE	Sources
5.16	In patients with incurable cancer and breathlessness, non-pharmacological measures for the relief of breathlessness *must* be used, e.g. informing the patient about the symptom of breathlessness, calming or relaxation, breathing exercises or cooling of the face.		EC	
5.17	A cool air flow directed at the face (e.g. caused by a hand held fan) *should* be administered for the symptomatic relief of breathlessness in incurable cancer patients with breathlessness.	B	1-	[86-88]
5.18	A walker and other walking aids *should* be used for supporting mobility and for the relief of breathlessness in incurable cancer patients with breathlessness.	B	1-	[86]

5.6. Oxygen

No.	Recommendation	GoR	LoE	Sources
5.19	Oxygen *should not* be administered for the relief of breathlessness in non-hypoxaemic patients with incurable cancer.	B	1+	[17, 89-91]

5.7. Breathlessness in the dying phase[9]

See additionally chapter 10, the dying phase.

No.	Recommendations	GoR	LoE	Sources
5.20	In the dying phase of an incurable cancer patient who is no longer able for self-assessment of his or her breathlessness, the assessment, whether there is breathlessness and how intense it is, *must* be carried out by others (professional, family carers) on the basis of clinical signs (sweating, cyanosis, quick, flat breaths, physical restlessness, facial expressions of discomfort and distress).		EC	
5.21	Patients with breathlessness who are in the dying phase and who require pharmacological treatment for the relief of breathlessness *must* be administered opioids as the method of choice. In cases of symptoms of anxiety benzodiazepines *can* be given in addition to opioids.		EC	

[9] The "dying phase" refers to the final days of life (see chapter 10).

6. Cancer pain

6.1. Introduction

According to the definition of the International Association for the Study of Pain (IASP), pain is „an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [92]. In addition to the physical components (nociception) psychological, social and spiritual dimensions also play a role in cancer pain. In this sense Cicely Saunders coined the term "Total Pain" which denotes the inter-relational nature of the physical, psychological, social and spiritual components of pain [8].

For the S3-guideline „Palliative care for patients with incurable cancer", the 2012 published European EAPC/Caraceni-guideline for drug-based cancer pain therapy was translated and adapted for Germany [50]. All recommendations from the EAPC-publication are evidence based. In addition to these recommendations, further recommendations were developed for the purpose of this guideline. Therefore, a chapter on pain evaluation was written in order to maintain a consistent structure with other symptom related chapters in this guideline. The recommendations on pain assessment are based on expert opinions of the guideline group. Likewise, the evidence based recommendations on metamizole were newly developed with the goal of better reflecting the pain therapy practice in Germany (see chapter 6.9.1). Adjustments to the original guideline were made with regard to the particular features of German practice. In this way, statements concerning drugs which are not licenced for use in Germany (diamorphine, hydrocodone) were not adopted. Wherever such adjustments to the original text were made they were explained in the background texts of the long version. This adaptation process to the German context as well as the methodological application of the S3-guideline requirements explains why this English short version differs in some formulation and in its presentation from the original EAPC recommendations. We had particularly to adapt the two level grading system used in the EAPC guideline to determine the grade of recommendation (GRADE: weak – strong) to the three degree system of S3-guidelines (strong recommendation – recommendation – open recommendation, see chapter 2.2.2), using the corresponding S3 wording "must", "should" and "can" (for more information about this adaptation process, see Guideline methodology report).

The guideline at hand focuses exclusively on drug-based and symptomatic treatment options. Non-pharmacological measures (e.g. physiotherapy or psychotherapy [4]) will not be evaluated here. Additionally, tumour specific treatments (e.g. radiotherapy, operative measures, and drug-based tumour treatments) or invasive procedures will not be evaluated here, although they also play an important role in cancer pain therapy (for this see organ-specific guidelines from the German Guideline Programme in Oncology, www.leitlinienprogramm-onkologie.de)

Moderate to severe cancer pain is common and occurs in 70 – 80 % of patients in an advanced stage of cancer. According to the current knowledge, it is possible to relieve pain in almost all patients [93]. In spite of this, data from questionnaires and observational studies indicate that many patients still suffer from moderate to severe pain and do not receive appropriate treatment [94]. The recommendations for cancer pain refer to various levels of pain intensity which are described as mild, moderate or severe. The classification is based on the patient's subjective estimation and has deliberately not

been defined more clearly. It also has not been allocated a number between 0 - 10 on the pain scale.

Most opioid analgesics are subject to legal regulations. In everyday clinical practice the *Betäubungsmittelgesetz* (Narcotics Law) and *Betäubungsmittelverschreibungsverordnung* (BtMVV) (Narcotic Drugs Prescription Ordinance) are of particular importance. The BtMVV regulates, among other things

- Who is permitted to prescribe which narcotics in which amounts;
- The prescription itself (form and content of the prescription);
- The documentation of the entire narcotics prescription and distribution process
- The usage of narcotics in various healthcare facilities including hospices and specialised home care teams (SAPV)

The knowledge of these regulations is a requirement for appropriate opioid treatment.

A pharmacoeconomic evaluation was not conducted. In particular cases it can be difficult to assess the clinical benefit, which is the basis for the recommendation, against the higher costs of new medication in comparison to cheaper, older or less effective medication. This is the case for the fast-working opioids used for the treatment of breakthrough pain and for the opioid antagonists administered for treatment of opioid induced constipation. Although the possibility of bias in the included studies has been thoroughly considered in both the EAPC/Caraceni 2012 – guideline and for the newly developed sections for these recommendations by means of a quality evaluation, it naturally cannot be completely ruled out (also see Guideline methodology report).

As part of a diagnosis of pain the possibility of a treatable cause of the pain should be explored (including the indication for tumour-specific treatment). In general, a reduction in tumour size normally leads to a reduction in pain. The possibility of radiotherapy should be investigated for painful bone metastases in particular because an effective reduction in pain can be achieved [95-97]. However, a latency period in pain reduction is to be expected with tumour-specific treatment, hence indicating the need for a sufficient drug-based analgesia up until this point. The elimination of other causes e.g. the drainage of ascites or pleural effusions or the reduction of pain caused by liver capsule stretch or nerve compression can also contribute to the acute relief of pressure pain. Additionally, other forms of pressure relief e.g. the use of a venting PEG for a gastrointestinal obstruction can be useful. Likewise, the treatment of infections can be indicated if pain – e.g. from mucosal lesions - can be alleviated. In general, causal treatments in cancer pain therapy should be used. However, as a rule, these are not sufficiently effective on their own or have a delayed effect and should thus be combined with analgesia.

6.2. Pain assessment

No.	Recommendations	GoR	LoE	Sources
6.1.	Pain history and a pain related clinical examination *must* be part of every diagnosis of pain.		EC	
6.2.	Where possible the assessment of pain intensity *must* be made by the patient him/herself e.g. by the use of simple one dimensional pain scales as part of an assessment of several symptoms.		EC	
6.3.	In patients with incurable cancer and pain, as well as cognitive and physical impairment, the assessment of pain intensity *must* be made by family carers or staff.		EC	

6.3. Application of various opioids

6.3.1. WHO-Level-II-opioids

No.	Recommendations	GoR	LoE	Sources
6.4.	For patients with mild to moderate cancer pain, or whose pain is not adequately controlled by non-opioid analgesics given regularly by mouth, step II opioid given orally or low doses of a step III opioid *should* additionally be administered.	B	1-	[50, 98, 99]

6.3.2. WHO-level-III first-choice opioids

No.	Recommendations	GoR	LoE	Sources
6.5.	In patients with moderate to severe cancer pain step III opioids *must* be used.		EC	
6.6.	Morphine, oxycodone or hydromorphone *can* be used as the first choice step III opioid for moderate to severe cancer pain.	0	1-	[50, 100-103]

6.3.3. Levomethadone in cancer pain treatment

No.	Recommendations	GoR	LoE	Sources
6.7.	In patients with moderate to severe cancer pain, levomethadone *can* be used as a step III opioid of first or later choice.	0	1-	[50, 104]
6.8.	Levomethadone *must* be used only by experienced doctors due to a complex pharamacokinetic profile with an unpredictably long half-life.	A	1-	[50, 104]

In the original English guideline, the recommendations are based on methadone and not levomethadone. In Germany, methadone (as a racemate) is only administered for opioid replacement therapy in patients with opioid abuse. For treatment of pain, only levomethadone is available on the market as a ready-to-use pharmaceutical product and is therefore the topic of the aforementioned recommendations.

6.4. Opioid titration

No.	Recommendations	GoR	LoE	Sources
6.9.	In patients with cancer pain, immediate-release and slow release oral formulations of morphine, oxycodone and hyromophone *can* be used for dose titration.	0	1-	[50, 105]
6.10.	In patients with cancer pain, titration schedules for immediate- and slow-release formulations *should* be supplemented with oral[10] immediate-release opioids given as needed.	B	1-	[50, 105]

6.5. Routes of administration

6.5.1. The role of transdermal opioids

No.	Recommendations	GoR	LoE	Sources
6.11.	Transdermal fentanyl and burprenorphine *can* be alternatives to oral opioids as the preferred step III opioid for some patients with cancer pain.	0	1-	[50, 106]
6.12.	For patients with cancer pain unable to swallow, transdermal opioids *can* be given as an effective, non-invasive means of opioid delivery.	0	1-	[50, 106]

6.5.2. Alternative systematic routes of opioid administration

No.	Recommendations	GoR	LoE	Sources
6.13.	The subcutaneous route for administering morphine and hydromorphone *must* be the first choice alternative for patients unable to receive opioids by oral[11] or transdermal routes.	A	1+	[50, 107]

[10] Oral application includes enteral application (e.g. by PEG [Percutaneous endoscopic gastrostomy]). In patients with dysphasia, there are other application forms in addition to transdermal and parenteral methods available with the usage of the appropriate pharmaceutical form. For example, morphine can be administered as a fluid (fast releasing) or as slow-releasing granules through an enteral tube (feeding tube, PEG). The availability and suitability of the various forms can be enquired about at a pharmacy.

No.	Recommendations	GoR	LoE	Sources
6.14.	In patients with cancer pain, intravenous infusion must be considered when subcutaneous administration is contraindicated (e.g, because of peripheral oedema, coagulation disorders, poor peripheral circulation, and need for high volumes and doses)	A	1+	[50, 107]
6.15.	In patients with cancer pain, intravenous administration *must* be used for opioid titration when rapid pain control is needed.	A	1+	[50, 107]
6.16.	Intravenous and subcutaneous infusions *can* be used to achieve optimum pain control in patients unable to achieve adequate analgesia with oral and transdermal administration.	0	3	[50, 107]
6.17.	Techniques for patient-controlled analgesia can be adopted for subcutaneous and intravenous opioid infusions in patients.	0	3	[50, 107]
6.18.	When switching from oral[6] to subcutaneous and intravenous morphine administration, the relative analgesic potency *should* be between 3:1 and 2:1.	B	3	[50, 107]
6.19.	Rectal administration of opioids *should* only be used as a second choice, because appropriate formulations are often not readily available and for many patients are not acceptable.	B	3	[50, 107]

6.5.3. Spinal administration of opioids

No.	Recommendations	GoR	LoE	Sources
6.20.	Spinal (epidural or intrathecal) administration of opioid analgesics in combination with local anaesthetics or clonidine *can* be given for patients in whom analgesia is inadequate or who have intolerable adverse effects despite the optimal use of oral and parenteral opioids and non-opioid agents.	0	1-	[50, 108, 109]

6.6. Opioid switching

No.	Recommendation	GoR	LoE	Sources
6.21.	Patients receiving step III opioids who do not achieve adequate analgesia and have side-effects that are severe, unmanageable, or both, *can* be switched to an alternative opioid.	0	3	[50, 110, 111]

6.6.1. Relative opioid analgesic potencies

No.	Recommendations	GoR	LoE	Sources
6.22.	When switching from one opioid drug to another, dose conversion ratios *should* be used.	B	1-	[50, 112]
6.23.	When the opioid is switched because of unsatisfactory analgesia, excessive side-effects, or both, the starting dose *should* be lower than that calculated dose from published equianalgesic ratios. In all cases the dose needs to be titrated in accordance with clinical response.	B	1-	[50, 112]

Conversion ratios are shown in Table 6 together with the strength of the recommendation on the basis of current evidence.

Table 6: Relative analgesic ratios for opioid switching

	Relative analgesic ratio	Strength of the recommendation for use
Oral morpheme to oral oxycodone	1.5:1	strong
Oral oxycodone to oral hydromorphone	4:1	strong
Oral morphine to oral hydromorphone	5:1	weak
Oral morphine to TD buprenorphine*	75:1	weak
Oral morphine to TD fentanyl **	100:1	strong

TD = transdermal. *Example: 60 mg oral morphine to 35 µg/h TD buprenorphine (equal to 0.8 mg per 24 h). **Example: 60 mg oral morphine to 25 µg/h TD fentanyl (equal to 0.6 mg per 24 hours).

In the first three rows of the original table, the data for the conversion ratios was incorrectly mixed up. For this version this information was corrected. The data given here with regard to the conversion ratios is therefore correct.

6.7. Prophylaxis and treatment of side effects

6.7.1. Treatment of opioid-related nausea and emesis

No.	Recommendations	GoR	LoE	Sources
6.24.	Antidopaminergic drugs (e.g, haloperidol) and other drugs with antidopaminergic and additional modes of action (e.g, metoclopramide) *should* be used in patients with opioid-induced nausea and emesis.	B	1-	[50, 113]

6.7.2. Treatment of opioid-related constipation

See also paragraph 7.4.2. in the chapter "Opioid-related constipation"

No.	Recommendations	GoR	LoE	Sources
6.25.	Laxatives *must* be routinely prescribed for the management or prophylaxis of opioid-induced constipation.	A	1+	[50, 114]
6.26.	No evidence suggests that one laxative agent *should* be recommended over others.	State ment	1+	[50, 114]
6.27.	A combination of laxatives with different modes of action *can* be administered in resistant constipation.	0	1+	[50, 114]
6.28.	Subcutaneous methylnaltrexone *should* be considered in the treatment of opioid-related constipation when traditional laxatives are not effective.	A	1+	[50, 114]

6.7.3. Treatment of opioid-related CNS symptoms

No.	Recommendations	GoR	LoE	Sources
6.29.	Methylphenidate *can* be used to improve opioid-induced sedation but the threshold between desirable and undesirable effects is narrow.	0	1-	[50, 115]
6.30.	In patients with opioid-related neurotoxic effects (delirium, hallucinations, myoclonus and hyperalgesia), dose reduction or opioid switching *can* be performed.	0	1-	[50, 115]

6.8. Use of opioids in patients with renal failure

No.	Recommendations	GoR	LoE	Sources
6.31.	In patients with severe impairment of renal function (glomerular filtration rate < 30 mL/min) opioids *should* be used with caution.	B	3	[48, 50]
6.32.	In patients with severe impairment of renal function (glomerular filtration rate < 30 mL/min), the opioid of first choice *should* be fentanyl or buprenorphine administered at low starting doses and with subsequent careful titration.	B	3	[48, 50]
6.33.	In patients with severe impairment of renal function (glomerular filtration rate < 30 mL/min), alternative strategies, for instance reductions in dose or frequency of administration of morphine, *can* be adequate short-term strategies.	0	3	[48, 50]

6.9. Non-opioids

6.9.1. Metamizole

No.	Recommendation	GoR	LoE	Sources
6.34.	Metamizole *can* be administered as a monotherapy in cases of mild pain and as a combination therapy with opioids in cases of moderate and severe cancer pain as an alternative to NSAIDs and paracetamol.	0	1-	[116-119]

6.9.2. NSAIDs and paracetamol as supplement to level-III-opioids

No.	Recommendations	GoR	LoE	Sources
6.35.	NSAIDs *can* be added to step III opioids to improve analgesia or reduce the opioid dose required to achieve analgesia.	0	1-	[50, 120]
6.36.	The use of NSAIDs *should* be restricted because of the risk of serious adverse effects, in particular in elderly patients and those with renal, hepatic, or cardiac failure.	B	1-	[50, 120]
6.37.	Metamizole or paracetamol *can* be preferred to NSAIDs in combination with step III opioids because of a more favourable side-effect profile, but its efficacy is not well documented.	0	1-	[50, 120]

6.10. Role of adjuvant drugs for neuropathic pain (antidepressants and anticonvulsants)

No.	Recommendation	GoR	LoE	Sources
6.38.	Amitriptyline, gabapentin or pregabalin *must* be considered for patients with neuropathic cancer pain that is only partially responsive to opioid analgesia. The combination of an opioid with these drugs is likely to cause more CNS adverse events unless careful titration of both drugs is undertaken.	A	1+	[50, 121, 122]

6.11. Opioids for pain exacerbation and breakthrough pain

No.	Recommendations	GoR	LoE	Sources
6.39.	Pain exacerbations resulting from uncontrolled background cancer pain *must* be treated with additional doses of immediate-release oral[12] opioids.	A	1+	[50, 123, 124]
6.40.	In cases of pain exacerbations resulting from uncontrolled background cancer pain an appropriate titration of around-the-clock opioid therapy *must* always precede the recourse to potent rescue opioid analgesics.	A	1+	[50, 123]
6.41.	In patients with cancer, breakthrough pain (e.g. incident pain) *must* be managed with oral[4], immediate-release opioids or with tranmucosal[13] fentanyl preparations.	A	1+	[50, 123, 124]
6.42.	In some cases of breaththrough pain, the tranmucosal fentanyl preparations *should* be favoured over immediate-release oral opioids because of more-rapid onset of action and shorter duration of effect.	B	1-	[50, 123, 124]
6.43.	In patients with cancer, immediate-release formulations of opioids with short half-lives *should* be used to treat pre-emptively predictable episodes of breakthrough pain in the 20–30 min preceding the provoking manoeuvre.	B	1+	[50, 123, 124]

[12] Oral application includes enteral application (e.g. by PEG [Percutaneous endoscopic gastrostomy]). Each medicinal product must be specifically assessed to ascertain whether it is suitable for usage in this way.

[13] The „transmucosal" pharmaceutical form includes the following administration routes: buccal, sublingual or intranasal.

7. Constipation

7.1. Introduction

While constipation has traditionally rather been seen as a problem of discomfort, it is increasingly being regarded by professional medical bodies as a medical problem in its own right and considered as a diagnosis. This applies in particular to chronic constipation [125].

This guideline refers explicitly to palliative care patients with incurable cancer. The specific circumstances in the palliative care situation do not justify a differentiation between temporary and chronic constipation or rather between a discomfort problem and a diagnosis. The Rome criteria for the definition of constipation and the clinical subtypes only hold limited significance [126].

The prevalence of constipation in a palliative care situation is stated in the literature as being between 32 – 82 % depending on the definition used and the patient population examined [127, 128]. Approximately half of all patients complain about constipation on admittance to a palliative care unit [129]. In patients receiving opioids, the prevalence can increase to almost 90 % [130, 131]. Pathophysiologically speaking, immobility, a low-fibre diet, inflammatory edema, reduced intestinal secretion, changes in intestinal flora and secondary motility disorders, in particular as a drug-induced side effect, but also due to malignant infiltration of the intestinal wall play a significant role.

The definition of constipation in a palliative care situation is just as difficult as in any other circumstance. The lack of bowel movements is of minor importance if a patient is symptom-free. Action is driven by the patient's subjective impairment. In patients unable to communicate, it is particularly important to check the status of the abdomen. In cases of bloated abdomen or a pain reaction during examination, constipation should be considered.

The principles of good clinical practice with regard to carefully taking the medical history, physical examination and radiological and laboratory diagnostic measures do not greatly differ in palliative care from other clinical situations – it is always important to critically ask what the potential consequences of treatment are. Concerning treatment, the same possibilities as with curable patients are largely available to patients in palliative care. However, the question of long-term side-effects from laxatives is of less significance. Essentially, a proactive prophylactic approach is to be favoured over a therapeutic reactive approach.

The recommendations in this chapter refer exclusively to constipation and not to the treatment of malignant bowel obstruction (MBO). As in the international literature MBO is also considered to be a separate entity in German-speaking regions [132, 133]. A MBO is defined as an intestinal obstruction (Ileus) distal to the ligament of Treitz in known intra-abdominal incurable cancer or extra-abdominal cancer with a clear diagnosis of peritoneal carcinomatosis. Due to this reason the treatment of MBO will not be addressed here.

7.2. Assessment/diagnosis of constipation

No.	Recommendations	GoR	LoE	Sources
7.1.	As with all patients, for patients with incurable cancer normal frequency of defecation is in the range of 3x/day to 3x/week.	Statement		
7.2.	For the diagnosis of constipation in patients with incurable cancer, subjective parameters such as the feeling of an incomplete defecation, pressing and/or complaints as well as objective parameters such as hard stool consistency *must* be taken into account.	EC		
7.3.	In patients with incurable cancer, the assessment of constipation *must* include a specific medical history recording stool behaviour, medications, accompanying symptoms and illnesses, a physical examination as well as the exclusion of reversible causes.	EC		
7.4.	The amount of stool and frequency of defecation as well as the subjective impairment *must* be documented both initially and on an ongoing basis in patients with incurable cancer for an early diagnosis of constipation.	EC		

7.3. Prophylaxis

No.	Recommendations	GoR	LoE	Sources
7.5.	In patients with incurable cancer, drug-based prophylaxis *must* be started alongside the use of opioids and be regularly adjusted as needed.	EC		
7.6.	In patients with incurable cancer, physiotherapeutic treatments (active movement exercises, mobilisation and colon massage) *can* be used as a supportive measure.	EC		

7.4. Pharmacological treatment

7.4.1. Constipation (regardless of the cause)

No.	Recommendations	GoR	LoE	Sources
7.7.	In pharmacological mono- or combination therapy for the treatment of constipation in patients with incurable cancer, osmotic and/or stimulant laxatives *must* be administered.	A	1-	[127]

No.	Recommendations	GoR	LoE	Sources
7.8.	Osmotic salts, magnesium hydroxide or paraffin oil *should not* be administered to patients with incurable cancer and constipation.	B	1-	[127]
7.9.	In respect of defecation disorders in patients with incurable cancer, rectal measures *should* be used.	B	1-	[127]
7.10.	Pharmacological treatment with prokinetic or secretagogue agents *can* be administered in patients with incurable cancer and constipation when conventional treatment fails.	0	1-	[127]

7.4.2. Opioid-related constipation

See also chapter 0, from which the recommendations given here were taken.

No.	Recommendations	GoR	LoE	Sources
Pain 7.25.	Laxatives *must* be routinely prescribed for the management or prophylaxis of opioid-induced constipation.	A	1+	[50, 114]
Pain 7.26.	No evidence suggests that one laxative agent should be recommended over others.	Statement	1+	[50, 114]
Pain 7.27.	A combination of laxatives with different modes of action *can* be administered in resistant constipation.	0	1+	[50, 114]
Pain 7.28.	Subcutaneous methylnaltrexone should be considered in the treatment of opioid-related constipation when traditional laxatives are not effective.	A	1+	[50, 114]

7.4.3. Step-wise approach

No.	Recommendation	GoR	LoE	Sources
7.11	In the prophylaxis and treatment of constipation a standardised approach in the form of a step-wise approach should be chosen (see figure 1).		EC	

7.5. Non-pharmacological treatments

No.	Recommendation	GoR	LoE	Sources
7.12.	Supportive measures for the treatment of constipation *should* be used, such as • Practical behavioural advice • Physiotherapeutic measures		EC	

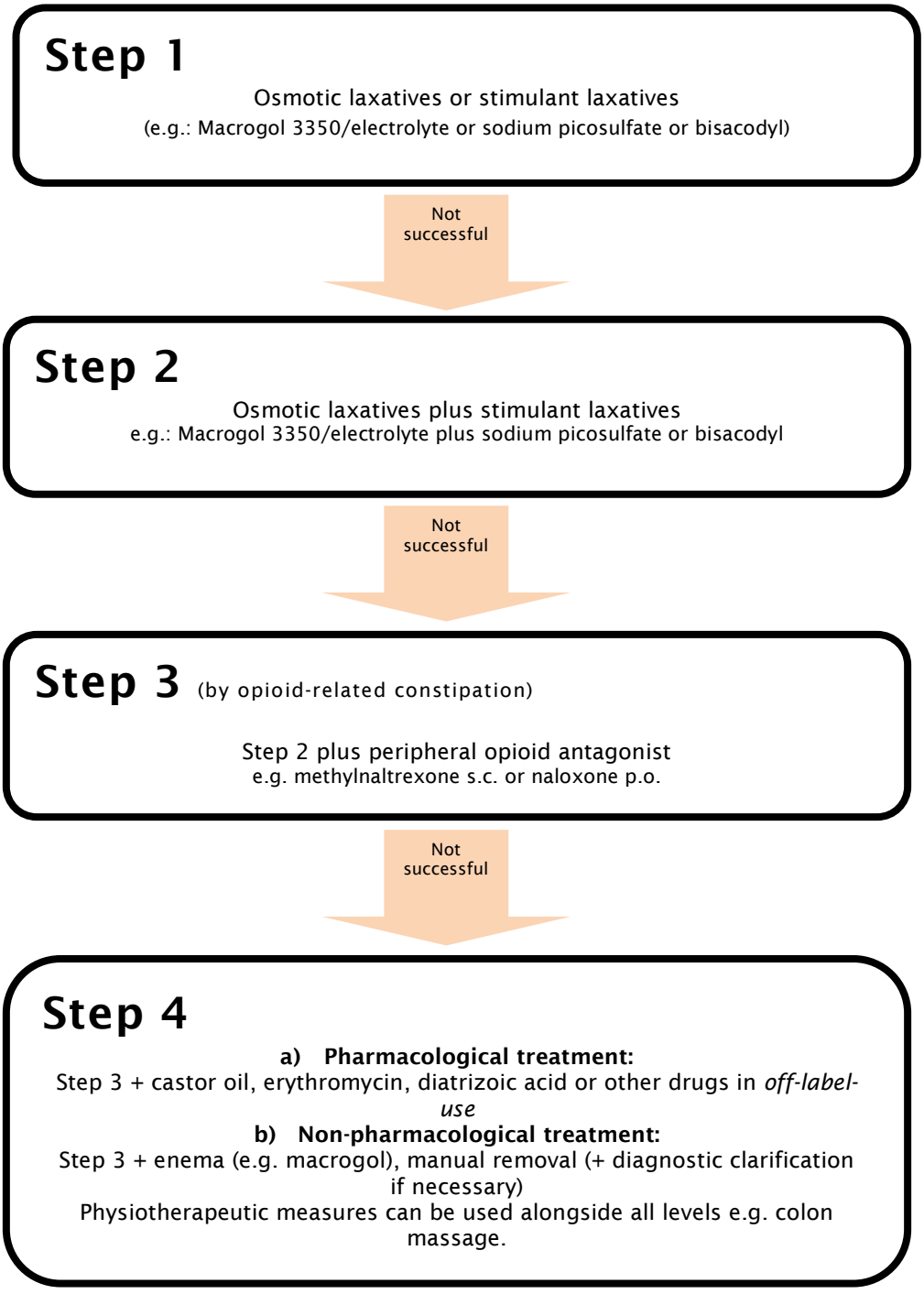

Figure 1: Step-wise approach for the treatment of constipation

8. Depression

8.1. Introduction

Low or depressed mood is not only common in palliative care. It is part of the "normal" expression of psychological feelings. This guideline's task is to look at depression as a comorbid problem in the context of incurable cancer and to give recommendations regarding differential diagnosis according to the ICD 10 classifications (International Statistical Classification of Diseases and Related Health Problems) as well as regarding the introduction of suitable treatment in the context of incurable cancer [134].

This guideline refers to the medical condition depression or depressive episode (according to ICD 10 Codes F32; F33) in its various degrees of severity as mild, moderate and severe as well as recurrent. Both terms are used in the text as synonyms.

During the development of the guideline, two guidelines were used for assistance: the European guideline from the European Association for Palliative Care (EAPC) "The management of depression in palliative care" [135], published in 2010, with direct relevance to palliative care and secondly the "S3-Guideline/National Disease Management Guideline (NDMG) Unipolar Depression", published in 2009 [136]. For the psycho-oncological support and treatment of patients with incurable cancer and depression we also refer to the S3-guideline "Psycho-oncology" [4].

8.2. Differential diagnosis of depression

Nr.	Recommendations	GoR	LoE	Sources
8.1.	In patients with incurable cancer and depressive symptoms, the differential diagnosis of this symptomatology *must* include adjustment disorder, dysthymia, a depressive episode, organic mood affective disorders or a reaction of grief.		EC	

Table 7 offers an overview of differential diagnostic criteria of depressive disorders according to ICD 10.

Table 7: Occurrence of depressive conditions in accordance with ICD 10 [134]

	Adjustment disorder (F 43.2)	Dysthymia (F 34.1)	Depressive episode or recurrent depressive disorder (F 32; F 33)	Organic mood [affective] disorders (F 06.3)
Severity of the depressive condition	Mild	Mild	Mild, moderate, severe	Inconsistent
Type and content of symptoms	Depressed mood The criteria for a mild or moderate depressive episode are never or very rarely fulfilled.	Depressed mood The criteria for a mild or moderate depressive episode are never or very rarely fulfilled.	Depressed mood Capacity for interest and enjoyment is reduced, reduction of energy, increased tiredness, psychomotor retardation/agitation, reduced concentration, reduced self-esteem, feelings of guilt, suicidal thoughts or acts, disturbed	Depressed mood

	Adjustment disorder (F 43.2)	Dysthymia (F 34.1)	Depressive episode or recurrent depressive disorder (F 32; F 33)	Organic mood [affective] disorders (F 06.3)
			sleep, diminished appetite Day-to-day variations possible, however little change in the low mood day-to-day	
Psychotic symptoms	No	No	Possible, then severe episode	Possible as part of the comorbidity with organic delusional disorder
Connection with a critical life event	Obligatory Starts within 1 month of a critical life event or severe physical illness	Possible	Possible	No
Organic cause	No Can however occur as a reaction to a severe physical illness.	No	No, can however occur as a reaction to a severe physical illness	Obligatory
Duration of symptom	Short reaction: no longer than 4 weeks Long reaction: no longer than 2 years	Long-lasting duration (at least 2 years), sometimes life-long	Minimum duration: approximately 2 weeks, if an unusually severe symptom then sometimes shorter, often recurrent with episodes from 3-12 months (on average 6 months)	Uncertain, Occurrence must follow a cerebral or other physical disorder Disappearance of symptom following removal of the cause

In patients with advanced cancer it can be particularly difficult to differentiate depression from a normal reaction of grief. Table 8 gives indications of the different characteristics. Patients who are sad or worried but who do not fulfill the criteria of depression can still benefit from support, provision of information, referral to a palliative care physician or psychological interventions.

Table 8: Characteristics of depression in comparison to a reaction of grief [137]

Depression	Reaction of grief
Feeling of being left out or being alone	Feeling of being in contact with others
Feeling of invariability	Feeling that it will be over at some point
Thoughts constantly going around in circles, hopelessness	Can enjoy memories
Strong feeling of worthlessness	Keeping a feeling of self-worth
Constant	Comes in waves
No hope, no interest in the future	Looking ahead
Only little enjoyment in activities	Remains able to enjoy things
Suicidal tendency	Will to live

8.3. Screening, diagnosis and assessment of severity of depression

8.3.1. Screening

No.	Recommendations	GoR	LoE	Sources
8.2.	In patients with incurable cancer, the existence of depression *must* be actively and regularly checked for.	A	4	-
8.3.	In patients with incurable cancer, screening *should* be used to recognise depression.	B	1+	[138-140]
8.4.	In patients with incurable cancer, the 2-question screening tool *can* be used to recognise depression: 1. During the past month, have you often been bothered by feeling down, depressed or hopeless? 2. During the past month, have you often been bothered by little interest or pleasure in doing things?	0	4	-

8.3.2. Diagnosing depression

No.	Recommendation	GoR	LoE	Sources
8.5.	If noticeable depression scores are detected in a screening, the diagnosis of depression in patients with incurable cancer *should* occur by the assessment of main and other symptoms according to the ICD-10-criteria with ascertaining the degree of severity and development.		EC	

Example questions for the assessment of symptoms and in this way for the diagnosis of depression are displayed in Table 9.

Table 9: Example questions for diagnosing depression [136]

Main symptoms	
Depressed mood	"Have you felt low or sad during the last two weeks?" "Were there times when your mood was better or worse?"
Loss of interest and a lack of enjoyment	"Have you lost interest or enjoyment in important activities (job, hobby, friends and family) of late?" "During the last two weeks, have you almost constantly had the feeling that you do not want to do anything?"
Increased tiredness and reduction of energy	"Have you noticed a decrease in your energy?" "Do you constantly feel tired and exhausted?" "Do you find it difficult to manage daily tasks as usual?"

Additonal symptoms	
Reduced concentration and attention span	"Do you find it difficult to concentrate?" "Do you find it an effort to read the newspaper, watch television or to follow a conversation?"
Reduced self-esteem and self-confidence	"Are you suffering from a lack of self-confidence and/or self-esteem?" "Do you feel as self-assured as you usually do?"
Feelings of guilt and worthlessness	"Do you often blame yourself for things?" "Do you often feel guilty for everything that happens?"
Negative and pessimistic views of the future	"Do you see the future more negatively than usual?" "Do you have any plans for the future?"
Suicidal thoughts/suicidal acts	"Are you feeling so bad that you think about death or that it would be better if you were dead?" "Have you had or do you have any plans to harm yourself?" "Have you tried to harm yourself?" "Is there anything which makes you want to stay alive?"
Disturbed sleep	"Has your sleep changed at all?" "Are you sleeping more/less than usual?"
Diminished appetite	"Has your appetite increased/decreased of late?" "Have you lost weight without intending to?"

8.3.3. Assessment of the severity

No.	Recommendation	GoR	LoE	Sources
8.6.	The severity of depression *should* be assessed according to the ICD 10 criteria (mild, moderate, severe).		EC	

Figure 2 gives an overview of the assessment of severity according to ICD 10.

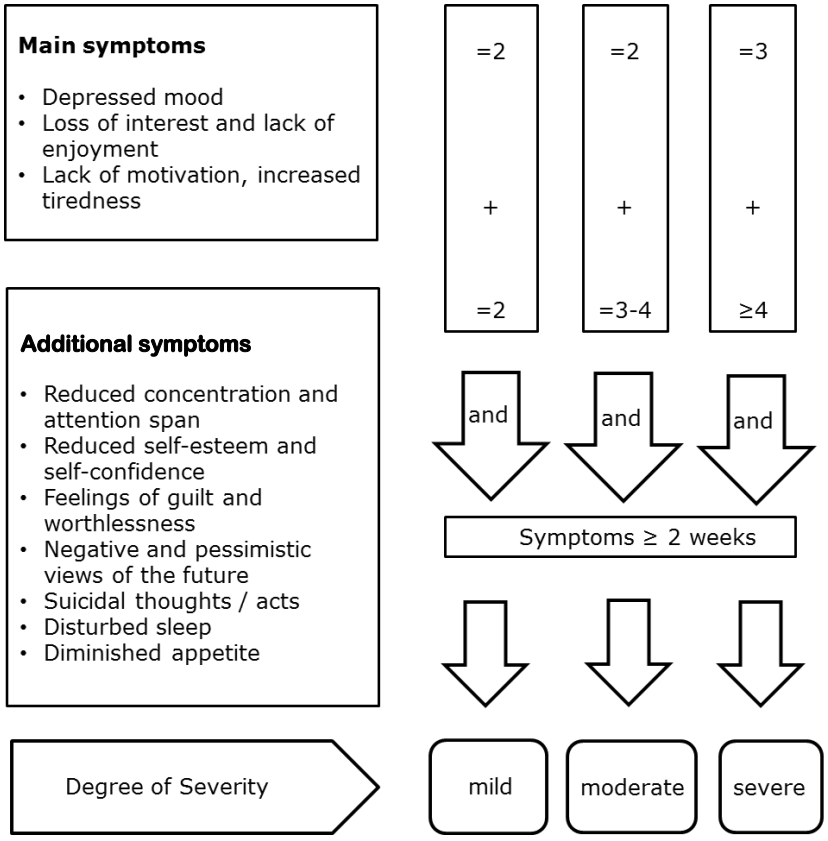

Figure 2: Diagnosis of depression according to ICD 10 (adapted figure from S3-Guideline/NDMG "Unipolar Depression" [136])

Depression is combined with an increased **risk of suicide** [136]. Depression is often found in connection with a wish for euthanasia or hastened death [141-144]. The following approach is recommended for the assessment and reduction of suicide risk:

1. Make time and space available (offer personal attention and support) [145];
2. Directly speak to patients with psychological problems about suicidal thoughts or plans [141].

Helpful questions for this approach are [145]:

- "Have you recently thought that you do not want to live anymore?"
- „Often?"
- "Without wanting to, have you had suicidal thoughts or in other words have suicidal thoughts come upon you?"
- "Could you brush these thoughts off?"
- "Do you have specific ideas of how you would do it?"
- "Have you made preparations?"
- "Or the other way around: Is there anything which is stopping you?"
- "Have you already spoken to someone about your suicidal thoughts?"
- "Have you ever attempted suicide?"
- "Has anyone in your family or among your friends or acquaintances committed suicide?"

8.4. Treating depression

8.4.1. The principles of treatment

No.	Recommendations	GoR	LoE	Sources
8.7.	Patients with incurable cancer and depression *must* receive both effective palliative care symptom control and professional psycho-social support.		EC	
8.8.	Patients *must* be integral part of the decision-making process with regard to treatment.		EC	
8.9.	The treatment of patients with incurable cancer and depression *must* be adapted to the severity of the depressive symptoms.		EC	
8.10.	A psychiatrist/psychotherapist *must* be involved in the following cases: • Uncertainty about the diagnosis and the treatment plan for depression • A complex psychiatric past medical history or symptomatology • Severe depressive symptoms with psychotic symptoms or depressive stupor • Acute suicidality • Endangerment of others • No response to antidepressant treatment		EC	

8.4.2. Treatment of mild, moderate or severe depression

No.	Recommendations	GoR	LoE	Sources
8.11.	Antidepressants *should not* be used generally in the initial treatment of mild depressive episodes, but only after carefully weighing the benefit-risk ratio		EC	[146]
8.12.	For the treatment of acute mild to moderate depressive episodes, psychotherapy *must* be offered.		EC	[146]
8.13.	For the treatment of acute moderate depressive episodes, patients *must* be offered antidepressant treatment.		EC	[146]
8.14.	In acute severe depressive episodes, combination treatment with pharmacotherapy and psychotherapy *must* be offered.		EC	[146]

8.4.3. Treatment of patients with short prognosis

No.	Recommendations	GoR	LoE	Sources
8.15.	Depression in patients with incurable cancer *must* also be treated in cases of a short life prognosis of a few weeks.		EC	
8.16.	In the dying phase[14], treatment with antidepressants *must* be stopped.		EC	

8.5. Non-pharmacological measures

No.	Recommendations	GoR	LoE	Sources
8.17.	Patients with incurable cancer and depression *must* receive basic psycho-social support.		EC	
8.18.	In cases of non-pharmacological treatment of depression, behavioural-therapy or depth psychology oriented methods *should* be delivered. Additionally, other methods (e.g. expressive therapy, mindfulness) *can* be used.		EC	

8.6. Pharmacological treatment

8.6.1. Antidepressants

Nr.	Recommendations	GoR	LoE	Sources
8.19.	The psychopharmacotherapy of patients with incurable cancer and depression *must* be in accordance with the available S3-Guideline/NDMG Unipolar Depression.		EC	
8.20.	In the pharmacological treatment of patients with incurable cancer and depression, there is no clear superior efficacy of one antidepressant over another.	Statement	1-	[147-149]
8.21.	The choice of antidepressive substance *must* be in consideration of the following criteria: • Tolerability and side-effect profile • Manageability • Experience of the prescribing physician • Response to previous treatments, risk of overdose and the patient's preference		EC	

[14] The "dying phase" refers to the final days of life (see chapter 10).

Nr.	Recommendations	GoR	LoE	Sources
8.22.	For prevention of recurrence, antidepressants *should* be taken for at least 4-9 months after remission following a depressive episode.	EC		[146]
8.23.	Antidepressants *should* be tapered off.	EC		

For the pharmacological treatment of depression there are various substances available (see Table 10).

Table 10: Medication for the treatment of depression modelled on Benkert/Hippius (2013) [150]; S3-Guideline/NDMG "Unipolar Depression" [136]

Drug	Half-life	Dosage form	Initial dose	Standard daily dose
Amitriptyline (TCA)	10-28 hours	Diverse dosages available, also sustained release (10 – 100 mg); Oral solution (40 mg/ml); Infusion solution (50 mg)	25 – 50 mg	75-150 mg/day (in clinic up to max. 300 mg/day) (Mainly evening administration)
Citalopram (SSRI)	26–40 hours	Tablets (10/20/40 mg); Infusion solution (20 mg)	10-20 mg	20-40 mg/day (max. 40 mg/day) (morning administration)
Mirtazapine (NaSSA)	20-40 hours	Tablets; orodispersible tablets (15/30/45 mg); Oral solution (15 mg/ml)	15 mg	15-45 mg/day (evening administration)
Sertraline (SSRI)	24-36 hours	Tablets (50/100 mg)	50 mg	50-100 mg/day (max 200 mg/day) (morning administration)
Venlafaxine (SSNRI)	5 hours, sustained release 14-18 hours	Tablets 37,5 mg; Sustained release capsules (37.5/75/150/225 mg)	37.5-75 mg	75-225 mg/day (max. 375 mg/day)

*NaSSA: Noradrenergic and Specific Serotonergic Antidepressant; SSNRI: Selective Serotonin-Noradrenalin-Reuptake-Inhibitor; SSRI: Selective Serotonin Reuptake Inhibitor; TCA: Tricyclic antidepressant.

Table 11 offers criteria for the selection of antidepressants.

Table 11: Selection criteria for antidepressants (table modelled on S3-Guideline/NDMG "Unipolar Depression" [136])

Tolerability/side-effect profile	Different side-effect profile of SSRI in comparison to TCA, in particular in out-patients and in comparison to classical, older TCA; In in-patient care hardly any differences in tolerability between TCA and SSRI; Qualitative differences in side-effect profiles of TCA and SSRI (more serious complications with TCA such as delirium, heart block/arrhythmias or urinary retention).
Risk of overdose	Taking a weekly ration of TCA can be lethal in suicidal patients; in out-patient care only smaller sized packets are prescribed.
Response in a previous illness	Effectiveness and compatibility of an earlier administration of antidepressants should

episode	be taken into consideration in the case of re-indication.
Manageability	TCA require more of an individual initial titration and control than the SSRI or new antidepressants (gradual dosing, plasma level, ECG-controls). Gradual dosing is also advisable with SSRI and new antidepressants like venlafaxine and mirtazapine.
Experience of use	The physician's individual experience of use with specific antidepressants is very important for the selection of the antidepressive substance.
Possibilities in cases of non-response	With TCA an assessment of the serum level is advisable because for most TCA a therapeutic serum level area is established. For TCA a high-dosage treatment is effective because a dose-response relationship exists.
Patient's preference	Patients have differing physical and psychological reactions with regard to the effect and side-effects of antidepressants, which is why the individual emphasis on undesired effects plays a role in the choice of the antidepressive substance.
SSRI: Selective Serotonin Reuptake Inhibitor; TCA: Tricyclic antidepressant.	

Tamoxifen in cases of breast cancer

A specific treatment situation arises in patients with breast cancer who are being treated with tamoxifen. Due to interactions in the Cytochrome-P450 system, breast cancer patients receiving tamoxifen should not receive SSRI or other medication with strong or moderate inhibitory CYP2D6 activity [141, 151, 152] because these will reduce the anti-cancer activity of tamoxifen [4].

8.6.2. Psychostimulants

No.	Recommendation	GoR	LoE	Sources
8.24.	In patients with incurable cancer and depression, psychostimulants *should not* be administered for the treatment of depression.	B	1-	[153, 154]

9. Communication

9.1. Introduction

Patient-centred communication with patients with incurable cancer and their family carers is an essential requirement for comprehensive treatment. Due to the specific life situation in which the affected persons find themselves and the existential dimensions of that situation, a particular challenge exists for all health care providers. This is partly the case because the reality of communication at the end of life reflects the societal and cultural way of dealing with incurable illness, death and dying. In spite of the topic's growing presence in the media and an increasing public acceptance of the hospice movement and palliative care, speaking about death and dying when one is specifically affected is challenging, often avoided, sometimes tabooed and only too often replaced by hope for new achievements in modern medicine. Likewise, communication plays a pivotal role in difficult treatment decisions which occur for patients with incurable cancer.

This guideline chapter focuses on five central areas of communication. Their importance is far-reaching in the context of palliative care.

The first section presents some basic principles of a patient-centred communication. It is of key importance for the provision of good palliative care to establish a communication based on the patient's current needs, problem areas and preferences.

When meeting palliative care patients, conversations about serious changes in the course of the disease and how to deal with these are of particular importance. The theoretical knowledge that every person dies becomes a concrete reality: "I will die." [155]. The second part gives practical tips with particular reference to the necessity of integrating the emotional level.

The third section addresses the question of death and dying. It deals with both the problem described at the beginning of an increasing societal taboo and handling a wish to die from affected patients which is gaining increased importance in the current context of ethical and legal discussions regarding physician assisted suicide.

The crucial role of friends and family in the context of palliative care will be acknowledged in the fourth section. This section will highlight the specific aspects of discussions with family carers, such as family meetings and also dealing with children.

Finally, the topic of the fifth section is looking ahead with treatment planning which, in the broadest sense of the term, addresses all patient's preferences with regard his/her final stage in life.

9.2. The principles of patient-centred communication

No.	Recommendations	GoR	LoE	Sources
9.1.	In order to ensure patient-centred communication with patients with incurable cancer, health care providers *must* • convey trust and safety to the patients through a relationship characterised by sincerity, empathy and appreciation; • Take notice of patients with their values, resources, needs, complaints, worries and fears and support them in the preserving as much autonomy and hope as possible; • Convey all information to the patients – in accordance with their current wishes and preferences – which will provide them with a comprehensive understanding of their situation and allow them to reach informed decisions.		EC	
9.2.	When communicating with patients with incurable cancer and various cultural and religious backgrounds, health care providers *must* take the personal, cultural and religiously linked principles and values into account.		EC	
9.3.	In cases of impaired communication of the patient with incurable cancer, non-verbal and technical possibilities for the improvement of communication *must* be offered.		EC	
9.4.	All health care providers who care patients with incurable cancer *must* train and develop their communicative competences through suitable further training. They *should* regularly reflect on their communicative competences e.g. through supervision/intervision.		EC	

9.3. Conversations about serious changes in the course of a disease

No.	Recommendations	GoR	LoE	Sources
9.5.	Information about the disease and its progression *must* primarily be initiated by the treating physician. When dealing with the information, the patient *must* be supported by all health care providers. For this purpose, the status of the information process *must* be documented comprehensibly.		EC	
9.6.	Before conveying information the patient *must* be asked about his/her knowledge, expectations, hopes and fears with regard to his/her disease when entering this conversation.		EC	

No.	Recommendations	GoR	LoE	Sources
9.7.	Information *must* be gradually conveyed with regular reassurance whether and to what extent the patient has understood. Furthermore the patient *must* be explicitly encouraged to ask questions.		EC	
9.8.	Emotional experience and spiritual needs *must* be given sufficient room. Both *should* be specifically discussed, even if the patient does not express it.		EC	

In day-to-day clinical practice, the **SPIKES-Model**, which was developed by Buckman and Baile, has proven to be a successful guide in many communicative situations [156]. The guide structures the conversation in six steps which encompass the essential elements of patient-centred communication:

- **S**etting: creating a suitable setting for the conversation
- **P**erception: assessing the patient's current knowledge/perception of the illness
- **I**nvitation: assessing the patient's information needs
- **K**nowledge: offering knowledge and information to the patient
- **E**xploration of Emotions: taking notice of and responding to the patient's emotions, reacting with empathy
- **S**trategy and Summary: planning and summarising

Understanding and considering the spiritual level is in accordance with the conception of palliative care and, in this respect, is the task of all health care providers. First studies have shown the "**SPIR**" tool, developed by E. Frick et al. and modelled after Puchalski, to be helpful as a partially structured interview [157-159]. The acronym, SPIR, is used to show how to communicate about the patient's spiritual needs and their meaning.

- **S**piritual and religious beliefs of the patient
- **P**lace and importance of the beliefs in the patient's life
- **I**ntegration in a spiritual, religious or church community or group
- **R**oll of health care providers: How should they address these beliefs?

9.4. Raising the issue of dying and death

No.	Recommendations	GoR	LoE	Sources
9.9.	In patients with incurable cancer, willingness to discuss dying from the disease *must* be expressed both early on and repeatedly; in doing so, words such as "dying" and "death" *should* be expressed in a sensitive and appropriate way by the health care providers.		EC	

No.	Recommendations	GoR	LoE	Sources
9.10.	If a patient with incurable cancer expresses a wish to hasten death, this *must* be met with empathy and willingness to communicate.		EC	
9.11.	The subtext, which possibly lies behind a wish to hasten death, *must* be explored in a sensitive manner. Such subtexts are e.g. the desire for assistance and support to continue living (in terms of a will to live), longing for death, an active desire for assisted suicide or voluntary euthanasia.		EC	
9.12.	Possible causes for a wish to hasten death *must* be investigated (e.g. the fear of being a burden to others, loss of autonomy, the burden of physical symptoms, depression and hopelessness, existential concerns and fear of the future).		EC	

9.5. Communication with family carers

No.	Recommendations	GoR	LoE	Sources
9.13.	Family carers *must* be appreciated in their role as providers of support and as affected persons. They *must* be asked about their needs and if necessary encouraged to accept support offers.		EC	
9.14.	Family meetings *must* be arranged with the patient's consent, • if a patient and family carer need to be given information together; • if a patient and family carer require support when entering an advanced stage of the disease or concerning future changes in treatment goals; • if diverging opinions come to the fore in the family in the course of palliative care. The facilitator of the family meeting *must* bring up various points of view and encourage all those involved to take part in the communication.		EC	
9.15.	If the patient agrees, family carers *must* be informed about the progression of the disease together with the patient. If the patient or his/her family carer does not wish to speak openly about the disease, this *must* be respected and communication about underlying fears must be offered.		EC	
9.16.	The needs of parents with incurable cancer regarding information, family meetings and if necessary further support with re-		EC	

No.	Recommendations	GoR	LoE	Sources
	spect to dealing with children *must* be investigated. The affected parents with incurable cancer *must* be encouraged to communicate openly with their children and if desired, be provided with support. After consulting the parents, underage children of patients with incurable l cancer *must* be involved in communication about the disease in all phases of treatment in an age appropriate manner and in accordance with their needs.			
9.17.	Underage children as family of patients with incurable cancer *must* receive support from qualified specialists if necessary.		EC	

The term family meeting refers to a gathering of the patient's most important close family and friends (family in the biological sense, legal representatives and important people outside of the family) [160]. In addition to topics related to illness and treatment, the expected disease progression and what is expected to happen in the dying phase should be discussed. The family carers should be assured that adequate symptom control will be provided in the final stages of life [161-163].

Underage children of terminally ill parents form a specific subgroup of family carers. In a collaborative project, funded by the German Cancer Aid, "Kinder krebskranker Eltern" – (children of parents with cancer), specific consultation concepts for parents, children and adolescents were compiled and the specific requirements for the palliative treatment situation were focused on [164]. Referring to qualified specialists and regional initiatives for children of parents with cancer (www.dapo-ev.de [Deutsche Arbeitsgemeinschaft für Psychosoziale Onkologie e.V.], www.verbund-kinder-krebskranker-eltern.de) offers further possibilities to introduce support on-site.

9.6. Advance Care Planning (ACP)

No.	Recommendations	GoR	LoE	Sources
9.18.	The topics of discussions in Advance Care Planning *must* be: • Scope and limitations of treatment in the case of (illness) typical situations as well as frequent and possible complications; • Individual preferences regarding the provision of care in the final stages of life, the place of care and death as well as funeral arrangements if appropriate; • Arranging a health care proxy or suggesting a person to act as a legal representative.		EC	
9.19.	Patients with incurable cancer *must* receive the offer of Advance Care Planning.		EC	

No.	Recommendations	GoR	LoE	Sources
9.20.	Facilitating communication about Advance Care Planning *must* be offered early on and repeated in the case of considerable changes in the state of health and prognosis.		EC	
9.21.	Conversations on Advance Care Planning *should* be supported by informative written material and content and outcomes *should* be documented.		EC	
9.22.	With the patient's agreement, family carers and, if appropriate, the health care proxy agent/legal representative *must* be involved in conversations on Advance Care Planning.		EC	

Advance Care Planning refers to a systematic, inter-professional communication and implementation process between patients, family carers and health care providers. The process encompasses the best possible sensitisation, reflection, documentation and, where appropriate, applying the patient's treatment preferences in clinical practice with regard to hypothetical future clinical situations. In German-speaking countries, various terms are used for the English term *Advance Care Planning (ACP)*. There is no standard terminology in use. This is partly due to the lack of a consistent understanding of what ACP is. In the context of this guideline, the term "vorausschauende Versorgungsplanung – Forward-looking care planning" was chosen in the original German version because it best encompasses all the aspects of ACP. The terminology used in Germany, "gesundheitliche Vorsorgeplanung/Vorausplanung – health care planning or forward-looking planning" particularly focusses on the patient's living will but this would be too narrowly defined for this guideline. Finally, the term "umfassende Versorgungsplanung – comprehensive care planning" integrates a wide variety of topics which must be discussed at the end of life but is further away from the English term, *Advanced Care Planning*.

10. The dying phase

10.1. Introduction

869,582 people died in Germany in 2012 and 221,611 of those who died were suffering from cancer. Cancer, with 25%, is the second most common cause of death in Germany after cardiovascular related deaths [165]. Almost 40% of people who are diagnosed with having cancer will die from the illness [166].

The dying phase refers to the last days of life when, due to the illness, the physical and psychological abilities of the dying person are increasingly limited. Based on international expert recommendation and the available evidence, this guideline defines the dying phase as the last three to seven days of life [10, 11].

The dying phase of patients with terminal cancer is typically characterised by a dynamic development with various challenges to the physical, psychological, social and/or spiritual care of the patient and their family. Various symptoms can be a burden for both patients and their family carers. Increasing weakness and immobility, the loss of interest in eating and drinking, restrictions in mental capacity with a reduction in the possibility to communicate verbally as well as changes in breathing and existential uncertainty can all occur in the final days of life [167].

Due to these various problems, comprehensive offers of support as well as open and honest communication with the patient and their family are necessary. Often, treatment decisions have to be made, which need consideration in light of the medical indication, the (presumed) wish of the patient but also the appropriateness of the measures. When caring for dying patients it is of utmost importance that dying is accepted as a natural process by the health care providers. All measures should be oriented towards the goals of ensuring both the best quality of life, even in the final stage of life, and dying with dignity.

10.2. Diagnosing dying

No.	Recommendations	GoR	LoE	Sources
10.1.	To assess whether the dying phase in a patient with terminal cancer has begun, the following criteria *can* be considered, if acute reversible causes have been excluded: • Changes in breathing, emotions and consciousness • Increased weakness and a worsening of the patient's general condition • Skin changes; confusion; loss of interest in nutritional and fluid supplies • Intuition of those involved in the treatment	0	4	[10, 11, 168]
10.2.	The assessment of whether the dying phase has begun in a patient with terminal cancer *should* occur as part of an interprofessional discussion.	B	4	[10, 11, 168]

In order to avoid the use of distressing measures for patients in the final days of life, but also in order to prepare the surrounding family for this phase and to adequately support them, it is helpful for the day-to-day clinical practice to be better able to diagnose the onset of this phase. Although clear predictors seem to be largely missing, in cases of advanced, terminal cancer the occurrence of or an increase in changes in breathing (e.g. pattern, rhythm or additional sounds like rattle), changes in emotion (e.g. increased anxiety or agitation) or consciousness (e.g. somnolence), increased weakness and deteriorated general condition, skin changes, confusion, and the loss of interest in food or liquid supply can be indirect indications for the dying phase. This list of observable signs does not claim to be complete or lacking ambiguity. In a Delphi survey among international palliative care experts from various professional groups (e.g. medicine, nursing, pastoral care), the changes in the following categories (which describe a variety of phenomena) were classified as being very relevant for diagnosing the dying phase: breathing, deteriorated general condition, consciousness, skin, intake of nutrition and fluids, emotional condition and opinions expressed by health care providers [10]. According to expert opinion, the intuition of those involved in the care of the patient ("gut feeling") was classified as clinically relevant [10].

10.3. Principles and practical issues of care in the dying phase

No.	Recommendations	GoR	LoE	Sources
10.3.	When a patient with terminal cancer is dying this *must* be recognised as a natural part of life by health care providers. The dying process *must* be neither hastened nor delayed.		EC	
10.4.	The dying patient and their family carers *must* be the focus of care respecting the physical, psychological, social and spiritual dimensions of dying.		EC	
10.5.	Treatment decisions and measures in the dying phase *must* be in accordance with the needs of the dying patient and their family carers, while preserving the patient's dignity.		EC	
10.6.	Treatment decisions and measures in the dying phase *must* be documented and continually reassessed.		EC	
10.7.	The dying patient and his/her family carers *must* be adequately informed about the approaching death and the changes to be expected in the dying phase.		EC	
10.8.	Family carers of the dying patient *must* have the opportunity to participate in the care of the dying patient, taking into account their wishes and resources and respecting the wishes of the dying patient. They *must* receive offers of support.		EC	

No.	Recommendations	GoR	LoE	Sources
10.9.	In dying patients who can no longer communicate verbally or are impaired in their communicative capacity, facial expressions, gestures, breathing, muscle tone, eye contact, movement patterns, reactions and para-verbal sounds *must* be carefully observed by the health care providers and their meaning assessed.		EC	
10.10.	The wish of a patient with terminal cancer concerning the place of death *should* be complied with.		EC	
10.11.	Involving competent volunteers in multi-professional care during the dying phase of a patient with terminal cancer *should* be part of palliative care.		EC	

10.4. Treatment of the most common symptoms

For the symptoms breathlessness and pain, see chapters 5 and 6 of this guideline.

10.4.1. Delirium in the dying phase

No.	Recommendations	GoR	LoE	Sources
10.12.	The symptoms of delirium *must* be detected as early as possible: i.a. sudden onset and fluctuating course, impaired consciousness, disturbance of attention, thinking and sleep-wake cycle.		EC	
10.13.	The team *should* be trained in the early diagnosis of delirium in dying patients and in how to deal with delirious patients in both verbal and nonverbal ways.		EC	
10.14.	Dying patients with delirium symptoms *should* be treated using the following general measures: calm and reassuring setting providing orientation, fall prevention, calm communication and continuity in care.	B	4	-
10.15.	In dying patients with delirium and the need for pharmacological treatment, haloperidol *should* be administered for the treatment of delirium.	B	1-	[169-172]

10.4.2. Death rattle

No.	Recommendations	GoR	LoE	Sources
10.16.	Artificial hydration *should* not be administered in the dying phase when death rattle is present.		EC	

No.	Recommendations	GoR	LoE	Sources
10.17.	Family carers of dying patients *must* be informed early of the cause, the course and the consequence of death rattle. The use of information brochures *can* provide additional help for family carers.		EC	
10.18.	In dying patients with distressing death rattle, suitable positioning for the mobilisation and drainage of secretion *can* be used.	0	4	-
10.19.	In dying patients with distressing death rattle, anticholinergic drugs *can* be administered to reduce the death rattle.	0	1-	[173-175]
10.20.	In dying patients with distressing death rattle (without tracheostomy or endotracheal tube), tracheal secretion *should not* be sucked.	B	4	-

10.4.3. Dry mouth (Xerostamia)

No.	Recommendations	GoR	LoE	Sources
10.21.	Dry mouth *must* be regularly assessed, including the causes (e.g. medication), the level of distress and whether the xerostomia requires treatment.		EC	
10.22.	In cases of distressing xerostomia, the oral mucosa *should* be regularly moistened, in accordance with the dying patient's needs. Suitable substances *should* be used which are in accordance with the dying patient's habits and preferences and which are aimed at ensuring well-being.	B	4	-

10.4.4. Anxiety and agitation in the dying phase

No.	Recommendations	GoR	LoE	Sources
10.23.	The emergence of anxiety *must* be regularly assessed in the dying phase. In addition to verbal statements, clinical signs such as agitation, sweating, facial expressions or defence reactions *must* be observed.		EC	
10.24.	In cases of agitation during the dying phase, the main triggering causes *must* be determined, e.g. pain, constipation, urinary retention, breathlessness, anxiety and/or delirium.		EC	

No.	Recommendations	GoR	LoE	Sources
10.25.	Dying patients with anxiety – with or without accompanying symptoms of agitation – *must* be supported with the use of general measures: e.g. calm setting, trust-building communication and continuity in care.		EC	
10.26.	Benzodiazepines can be administered in the dying phase to relieve anxiety, whether accompanying symptoms of agitation are present or not.		EC	
10.27.	In cases of agitation as part of delirium in the dying phase, the delirium *must* primarily be treated.		EC	

10.5. Medication and measures in the dying phase/Withdrawal of medication and measures in the dying phase

No.	Recommendations	GoR	LoE	Sources
10.28.	The patient's wishes are also to be considered in the dying phase. If the dying patient is not able to express themselves, the health care proxy agent (by means of a written power of attorney for personal welfare or a legal representative) determines the will of the patient and discusses this with the physician. At the same time, a written living will or other wishes expressed by the dying patient (e.g. oral or written treatment wishes, other expressed wishes) are to be taken into account.		Statement	EC
10.29.	All measures taken in the dying phase *must* be in accordance with the needs of the dying patient with regard to their frequency and form. At the same time, all dimensions of quality of life (physical, psychological, social and spiritual), as well as cultural and religious aspects *must* be considered.		EC	
10.30.	Only drugs that aim to ensure the best possible quality of life in the dying phase *must* be started or continued. This particularly includes the substances from the groups of opioids, antipsychotics, benzodiazepines and anticholinergics.		EC	
10.31.	Cancer-specific drugs and treatment measures *must* be stopped in the dying phase.		EC	

No.	Recommendations	GoR	LoE	Sources
10.32.	All medical, nursing and physiotherapeutic treatment measures, which do not support the treatment goal of ensuring the best possible quality of life, *must not* be introduced or, if they were introduced previously, *must* be stopped: e.g. ventilation, dialysis/hemofiltration, intensive care, positioning for decubitus or pneumonia prevention.		EC	
10.33.	Measuring and documenting blood pressure, pulse, respiration rate, blood glucose level, oxygen saturation and body temperature *must* be stopped when there is no benefit concerning symptom relief.		EC	
10.34.	If drugs for symptom relief can no longer be administered enterally, an adjusted dose *must* be given using a parenteral (subcutaneous, intravenous), transmucosal (nasal, buccal, sublingual) or rectal route of administration. A sufficiently effective transdermal treatment *can* also be continued in the dying phase.		EC	
10.35.	In dying patients who have an implanted cardioverter-defibrillator (ICD), the cardioverter function *should* be deactivated in the dying phase.		EC	
10.36.	Palliative sedation *must* be carried out by competent physicians and nurses experienced in palliative care.		EC	

Certain types of drugs, which were necessary in other stages of the disease, can be foregone in the dying phase. Drugs which fall under this category are e.g. antibiotics, antidepressants, anticoagulants, chemotherapeutic drugs or other cancer-specific medication, diuretics, insulin, cardiac medication, corticosteroids, laxatives, oxygen or blood products.

In rare cases, it is not possible to relieve the patient's suffering in a satisfactory manner by either causal or symptomatic treatment or by withdrawing measures. In such cases, palliative sedation can be considered as a last resort. Palliative sedation includes the monitored use of drugs for patients who are suffering from therapy-refractory symptoms. Palliative sedation can be indicated in the dying phase for symptoms such as agitated confusion, breathlessness, pain, epileptic seizures, heavy bleeding or asphyxia as well as non-physical symptoms such as depressive conditions which are unresponsive to medication, fear or existential suffering [176, 177]. However, there is no consensus across the board that palliative sedation is indicated for these non-physical symptoms [177, 178].

The aim of sedation is the relief of suffering from symptoms in a way which is ethically acceptable for the patient, the family carers and members of staff and not the premature ending of life [176].

10.6. Artificial nutrition and hydration

No.	Recommendation	GoR	LoE	Sources
10.37.	Following a thorough investigation on an individual basis (e.g. satisfying hunger or thirst), artificial nutrition and hydration *should not* be administered to dying patients.	B	2	[179-181]

Caring for dying patients with artificial nutrition and hydration is common practice with the motivation of, for example, relieving symptoms such as fatigue, somnolence, confusion or nausea. However, artificial nutrition and/or hydration have potential side-effects (e.g. peripheral edema, pulmonary edema, increased death rattle), require an invasive route of application (i.v, subcutaneous, PEG) and lead to an increased medical and nursing input which could be inappropriate or unwanted during the dying phase.

The main focus of attention when caring for dying people is comfort and optimal symptom control [182]. Due to the fact that artificial hydration does not relieve xerostomia, mouth care is advisable independent from rehydration (see also chapter 10.4.3) [183].

Due to the fact that dying patients and in particular their family carers often value artificial nutrition and hydration positively and – in contrast to palliative care experience and evidence – connect it with the hope of a dignified death and an improvement of symptoms, it is necessary that communication on this matter is sensitive with sufficient explanation and provision of information in the decision-making process when reaching a decision [184, 185].

10.7. The aftermath of death: the deceased and grief

No.	Recommendations	GoR	LoE	Sources
10.38.	The family carers of the deceased *must* be informed of the death in a sensitive and timely manner.		EC	
10.39.	Following the death the family carers *must* be allowed to say goodbye in accordance with their needs and resources, cultural practices and religious duties.		EC	
10.40.	The people, who were involved in the care of the patient with terminal cancer, *should* be informed about the patient's death in an appropriate manner.		EC	

10.8. Dying and death and the health care team

No.	Recommendations	GoR	LoE	Sources
10.41.	For the dignified care of dying people and their family carers, supportive conditions *must* be implemented in the team e.g. an open culture of communication, joint definition of goals, defined team roles and sufficient staff and time for individual care of those affected.		EC	
10.42.	In order to stabilise teamwork and to reduce distress, reliable and transparent ways of decision-making *must* be jointly agreed upon and defined. Decisions concerning treatment and care *must* be adequately communicated within the team. Changes in treatment goals and adjustments in treatment measures *must* be transparently documented for the whole team.		EC	
10.43.	Mutual support, both emotionally and in practice, as the predominant protective factor against stress in a team *must* be maintained in an appropriate culture.		EC	
10.44.	Rituals for saying goodbye *can* be introduced for support and coping. Such rituals *should* be jointly developed and agreed upon.		EC	
10.45.	Suitable room for reflection such as case conferences, supervision, team days and further training *must* be implemented for teams that care for dying patients.		EC	

11. Organisation of palliative care

11.1. Introduction

The rapid development experienced by palliative care has been unlike that of most other areas of healthcare. This area of medicine has received considerable socio-political support which is likely due to the epidemiological developments expected in our society. The consistent focus that palliative care affords to the needs of both patients and their family carers in such an existential situation has certainly also led to its rapid development.

The 5-year cancer prevalence in Germany for the year 2010 was 1,863 per 100,000 residents, the mortality was 267 per 100,000 (see www.krebsdaten.de/Krebs/DE/Datenbankabfrage/datenbankabfrage_stufe1_node.html). One in four men and one in five women died from cancer [186]. On the European level, the need for palliative care for patients with cancer was estimated in a WHO-report from 2014 as 218 per 100,000 adults [187].

Both currently and in the coming years a rapid development of models for the integration of palliative care into standard care is to be expected. The first of these initiatives during the 1980s (first palliative care unit 1983 Cologne, first in-patient hospices 1986 Aachen and Recklinghausen, first hospice association 1985 Munich) were the personal initiatives of committed pioneers in the field. The introduction of these models in standard care – starting firstly with hospice services and in-patient hospices, followed by palliative care units and finally by specialist palliative home care services – was based on the provision of financial resources, which were primarily due to political activities and not scientific data. The future development concerning the further development of the Charter for the Care of Severely Ill and Dying People (Charta zur Betreuung Schwerkranker und Sterbender) is also primarily being politically decided upon as part of a national strategy. Scientific data can act as support for further structural development if it shows the effectiveness or lack of effectiveness of new or already existing structures.

This chapter aims to compile the evidence for new health care services and to adapt international experiences, where possible, to develop valid recommendations for Germany. The focus here is on the needs of patients and family carers from the time of diagnosis of incurable cancer. This is reflected in structuring this chapter in accordance with the patient oriented clinical pathway (see chapter 11.2).

It was likewise decided to base the chapter on a division of palliative care into specialist and generalist palliative care even though the international model is rather divided into three or even four tiers (see WHO [188], White Paper [1, 2]). This is due to the fact that the home care area of SAPV (Spezialisierte Ambulante Palliativversorgung - specialist palliative home care) is now defined by law, but the other forms of generalist palliative care have not been differentiated far enough in Germany so that one cannot speak of a further subdivision of this form of care yet.

In particular for the section about the organisation of palliative care, this guideline is often based on the expert opinion of the guideline group and gives a snapshot of the situation in Germany.

11.2. Clinical pathway for patients and family carers

The clinical pathway for patients with terminal cancer and their family carers (Figure 3) displays the various steps of palliative care which are offered to the patient and their family carers. The pathway begins with the diagnosis of incurable cancer and goes beyond the death of the patient to grief counselling for family carers. The individual steps and offers are explained in depth in the next chapters.

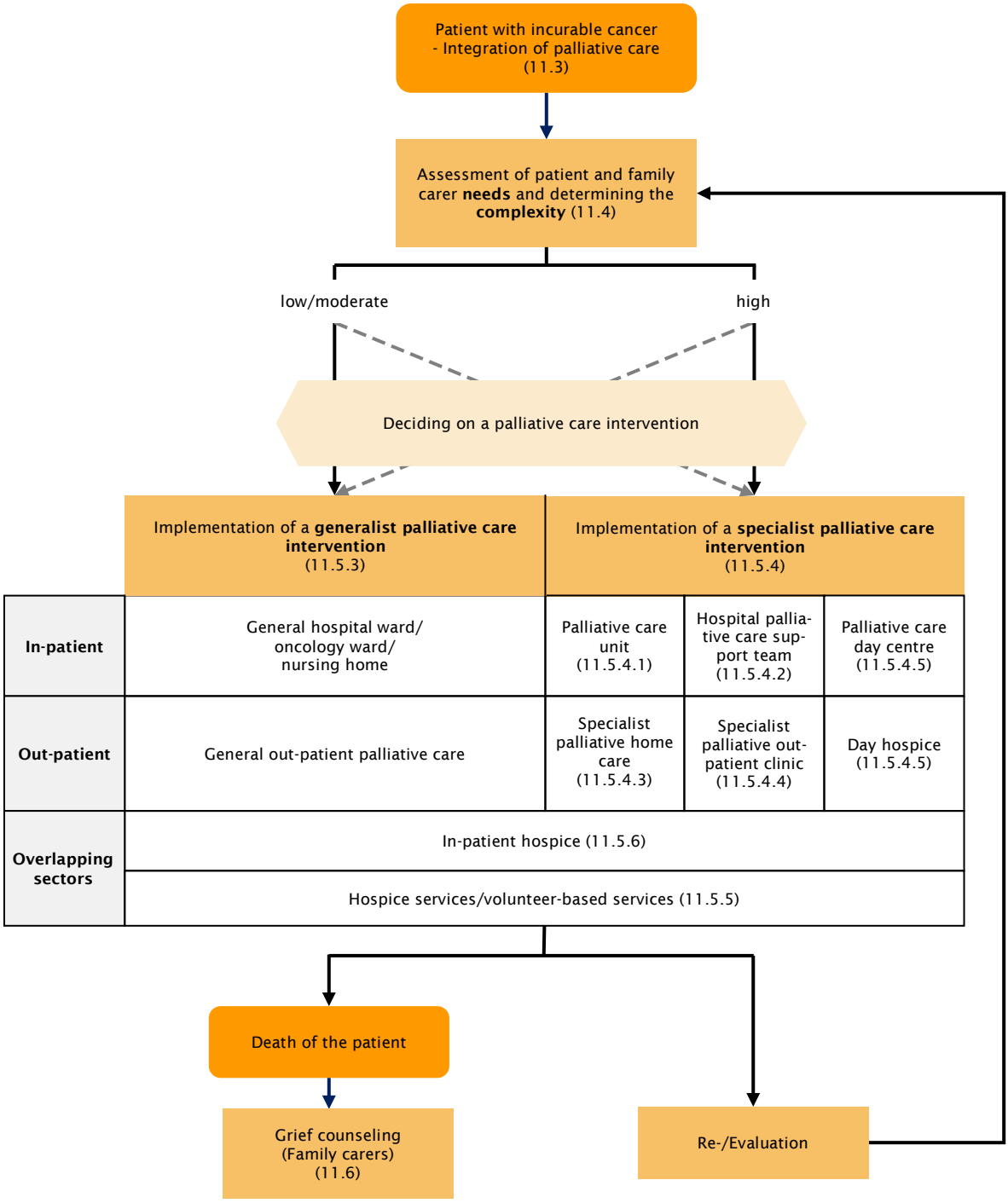

Figure 3: Clinical pathway for patients and family carers

11.3. Integration of palliative care

11.3.1. Time of palliative care integration

No.	Recommendations	GoR	LoE	Sources
11.1.	All patients with cancer *must* have access to information about palliative care, regardless of what disease stage they are in.		EC	
11.2.	All patients *must* be offered palliative care following the diagnosis of incurable cancer, regardless of whether cancer-specific therapy is being implemented.		EC	

The assessment that a cancer is "incurable" is based on prognostic probabilities. These statistical findings are always associated with a prognostic uncertainty in isolated cases, which means that every case has to be individually assessed [189]. Alongside biological properties of the tumour which enable an estimation of prognosis, factors individual to the patient such as comorbidity and social integration play a significant role.

Whether a consultation on the topic of palliative care is urgently required can be assessed by the use of the so called *surprise question:* "Would you be surprised if your patient died within the next 6-12 months?" [190, 191]. This question should be addressed by means of self-reflection and also in an exchange with colleagues. If the question is answered with "No" (I would not be surprised), one should critically reflect whether the patient's prognosis is worse than was previously assumed.

11.3.2. Integration of oncological services and palliative care

No.	Recommendation	GoR	LoE	Sources
11.3.	Specialist palliative care *must* be integrated into oncological decision-making processes, e.g. by means of participation in interdisciplinary tumour conferences.		EC	

11.4. Assessment of patient needs and determining complexity

No.	Recommendations	GoR	LoE	Sources
11.4.	In cases of incurable cancer, the patient and family carers' physical, psychological, social and spiritual needs as well as their sources of distress and need for information *must* be assessed repeatedly and when there is a change in the clinical situation.		EC	

No.	Recommendations	GoR	LoE	Sources
11.5.	In cases of incurable cancer, the patient and family carers' needs as well as their sources of distress and need for information *should* be assessed with the help of validated multi-dimensional assessment tools.		EC	
11.6.	In patients with incurable cancer, the complexity of the situation *must* be repeatedly assessed; this includes the needs of the patient and family carers, the functional status of the patient and the phase of illness.		EC	
11.7.	Patients with incurable cancer and a highly complex situation *must* receive specialist palliative care.		EC	

Following an assessment of patient needs and problems, the complexity of the entire situation will be evaluated with the help of the available information and then assigned to the category low/moderate or high. The complexity is determined by many different factors – the factors specified in Table 12 have proven to be particularly relevant. The complexity is influenced by the **intensity** of individual symptoms or psychosocial, spiritual or ethical problems as well as by their simultaneous occurrence (**simultaneity**; including the simultaneous occurrence of comorbidity).

The determination of complexity mentioned here is based on a model which was primarily developed in Australia, has been used for many years with positive experiences and is being increasingly implemented in other countries (e.g. England). The complexity of the patient's situation can best be ascertained from the assessed **needs, problems and sources of distress of patients and family carers**, but is also described based on the **functional status of the patient** in connection with the **phase of illness** [192]. Functional status refers to the quantification of the general condition and day-to-day activities. The phases of illness, in the sense they are referred to here, are characterized as stable, unstable, deteriorating and dying (terminal) [192] (see Table 12).

Table 12: Influencing factors for complexity and possible assessment tools

Influencing factor for complexity	Possible assessment tool
1. Problems and needs of the patient	e.g. Minimales Dokumentationssystem (MIDOS 2) [193] (German version of the Edmonton Symptom Assessment Scale), Edmonton Symptom Assessment System (ESAS/revised version ESAS-r) [193, 194], Palliative Care Outcome Scale (POS) [195, 196], Distress-Thermometer and problem list [197]
2. Distress of family carers	e.g. German version of the Zarit Burden Interview (G-ZBI) [198], Häusliche Pflegeskala (HPS) der DEGAM (Home care scale from the German College of General Practitioners and Family Physicians)
3. Functional status	Functional status particularly concerning activity, self-sufficiency and self-determination. e.g. Australian-modified Karnofsky-Performance Status (AKPS) [199], Eastern Cooperative Oncology Group (ECOG) [200], Activities of Daily Living (ADL) [201], Barthel Index [202]
4. Phase of illness:	**Description**
a) stable	Symptoms under control, patient needs satisfied by care plan, stable family situation

Influencing factor for complexity	Possible assessment tool
b) unstable	New major problems or sudden increase in already existing problems within a few days, urgent or less urgent changes in care plan necessary in order to satisfy patient needs
c) deteriorating	Symptoms worsen gradually or steadily over weeks, or development of new but expected problems in days/weeks, with necessity to adjust and regularly check the care plan, with increased family distress and/or social/practical distress.
d) dying (terminal)	Death within the next days probable with necessity of regular, usually daily checking of the care plan and regular support of the family.

In order to develop a suitable treatment and care plan, assessing the complexity is essential. The complexity of the patient and family carer's situation is assigned one of two levels – **low/moderate** or **high**. Depending on what complexity category is assigned to a patient, it is decided which level of intervention – whether generalist or specialist palliative care – is to be offered to the patient. Patients with a highly complex situation should as a rule receive specialist palliative care. However, it is important to note that the decision, whether generalist or specialist palliative care will be implemented, is dependent on the respective patient situation and should therefore be assessed on an individual basis.

Guide for the assessment of complexity in two categories:

- Low/moderate: low-intensity symptoms, slow or moderate progression of the underlying illness, no other illnesses/no distressing other illnesses – particularly no active psychological illnesses. A balanced psychological state and a stable family situation rather infer a low complex situation.
- High: intense symptoms that are difficult to treat, ulcerating tumours or imminent paraplegia infer a highly complex medical situation. Intense states of anxiety, a lack of coping with the illness or difficult family relationships, which are a cause of distress and not supportive for the patient, can be described as highly complex patient situations. One of the characteristics of highly complex situations is a need for continual adjustment and regular checking of the treatment plan due to the changing situation.

11.5. Deciding on a palliative care intervention

11.5.1. Differentiation between generalist and specialist palliative care

Generalist palliative care (Allgemeine Palliativversorgung, APV)

There is no standardly accepted definition of generalist palliative care. Indicators for assigning a care service to the category of generalist palliative care are:

- Treatment service is provided by staff whose main field of work is not in palliative care.
- The patient situation is less complex than in specialist palliative care.

- It is not compulsory that the care service is linked with specific structural requirements.

In chapter 11.5.3, the tasks and possibilities of generalist palliative care will be defined and described

Specialist palliative care (Spezialisierte Palliativversorgung, SPV)

In Germany, specialist palliative care in the home care sector is specifically defined by law as SAPV (Spezialisierte Ambulante Palliativversorgung – specialist palliative home care). It is based on the entitlement to SAPV in SGB V (§ 37b, § 132d), as well as the guidelines from the *Gemeinsamen Bundesausschusses* (Joint Federal Committee[15]) and the recommendations from the *GKV-Spitzenverband* (National Association of Statutory Health Insurance Funds). In the in-patient sector, the *Spezialisierte Stationäre Palliativversorgung* (SSPV) (specialist in-patient palliative care) is formally defined by the minimum characteristics of OPS 8-982 and 8-98e.

Indicators for assigning a health care service to the category of specialist palliative care are (see also chapter 0):

- Patient needs require a complex and more extensive care service than in generalist palliative care.
- Treatment is provided by staff whose main field of work is primarily or exclusively in specialist palliative care.
- Treatment is provided by staff who possesses specific qualifications and experience in palliative care.
- Team approach and multi-professionalism are a conceptual and structural prerequisite [203].
- 24h availability of appropriate service for complex problems is guaranteed.

In the understanding of the guideline, the term specialist palliative care is used for content concerning health care and structures which adhere to these characteristics, regardless of the existing legal regulations.

Two health care services can be associated with both generalist and specialist palliative care (generalist and specialist palliative care): the in-patient hospice (see chapter 11.5.5) and the hospice service or voluntary work (see chapter 11.5.6). Thus, they are addressed following the chapter on generalist (see chapter 11.5.3) and specialist palliative care (see chapter 0) in an individual chapter.

11.5.2. Qualifications in palliative care

There are currently inconsistencies between the palliative care qualifications of individual professional groups, in some professional groups there are no recognised qualifications yet (as of 07.2014). Additionally, it is often not possible to categorise qualifications into either basic or specialised. Due to this, the guideline group decided to make a distinction between basic and specialised qualifications, with which the current qualifications of the individual professional groups are descriptively assigned to one of the two qualification levels.

For this guideline the two qualification levels are described and used as follows:

[15] The Federal Joint Committee (G-BA) is the highest decision-making body of the joint self-government of physicians, dentists, hospitals and health insurance funds in Germany.

1. **Basic qualification**: basic knowledge, attitudes and skills in palliative care which make generalist palliative care possible:

   Acquired, in particular, by palliative care content integrated in the training course and/or through further education, e.g. a one/several week long course and/or by work experience of caring for severely ill or dying patients stretching over several years (particularly in generalist palliative care)

2. **Specialist qualification:** Specialist palliative care knowledge, skills and attitudes with practical experience which make specialist palliative care possible:

   Acquired by training course or further education in specialist palliative care stretching over several years with the acquirement of theoretical knowledge (e.g. from advanced training courses) and practical work for at least one year in specialist palliative care (work experience in specialist palliative care)

11.5.3. Generalist palliative care

No.	Recommendations	GoR	LoE	Sources
11.8.	Everyone who is affected by incurable cancer *must* have access to generalist palliative care.		EC	
11.9.	Everyone involved in the care of patients with incurable cancer *must* be able to assess palliative care needs and recognise need for palliative action in order to initiate palliative care.		EC	
11.10.	Generalist palliative care of a patient with incurable cancer *must* contain the following scope of duties: • Treatment of symptoms and supervision of problems with low to moderate complexity in all four dimensions (physical, psychological, social and spiritual) • Communication • Establishing treatment goals • Coordinating care • Involving specialist palliative care, if indicated		EC	
11.11.	Every physician involved in generalist palliative care of a patient with incurable cancer *must* be able to assess the indication for specialist palliative care and integrate this into the treatment based on the patient's needs.		EC	
11.12.	Everyone involved in generalist palliative care of a patient with incurable cancer *must* provide a basic qualification in palliative care which has been acquired by means of a training course or further education and is regularly updated.		EC	

11.5.4. Specialist palliative care

No.	Recommendations	GoR	LoE	Sources
11.13.	A specialist palliative care core team *must* comprise members from at least three professional groups (physician, nursing profession and other professional group). Of these at least the physician and nurse *must* possess a specialist palliative care qualification.	A	1-	[204-210]
11.14.	Members of the specialist palliative care core team *should* primarily or exclusively work in specialist palliative care.	EC		

11.5.4.1. Palliative care unit

No.	Recommendations	GoR	LoE	Sources
11.15.	A palliative care unit is an in-patient specialist palliative care service and part of a hospital. It is available for patients with incurable cancer and limited life expectancy with the aim of improving quality of life. A requirement for the referral to a palliative care unit is the need for hospital care.	Statement		
11.16.	The admission of a patient with incurable cancer on a palliative care unit *can* occur if the need for in-patient care exists and one of the following indications is present: • Complex symptoms or distress due to problems • Uncertainty in setting treatment goals • Complex medical or nursing care • Home care is overstrained or uncertain	0	4*	-
11.17.	A palliative care unit *must* provide the following components of care: • Assessing symptoms and needs of patients and family carers in all four dimensions • Treatment of symptoms and problems in all four dimensions • Resource-based support of patients and their family carers, particularly when establishing treatment goals and discussing the illness • Palliative care also in terms of respite care • Advance care planning • Coordination and organisation of palliative care • Attendance from competent volunteers	A	4	-

* For the recommendations in this chapter that have a LoE 4 a systematic literature search was only conducted for RCTs, CCTs, controlled pre-post studies and ITS (interrupted time series), thus for a Level-of-evidence 1 to 2 in accordance with SIGN. For LoE 4 (expert opinion) the SIGN-levels 2 (partly) and 3 were skipped and for this no supplementary literature search was carried out due to the fact that a statement concerning the effectiveness of interventions on the basis of SIGN-levels 2 and 3 could not be made.

No.	Recommendations	GoR	LoE	Sources
	• Caring for the patient during the dying phase • Rituals of saying goodbye and remembering • Arranging grief counseling			
11.18.	Treatment and care on a palliative unit *must* be provided by an independent, specialised, qualified and multi-professional team.	A	4	-
11.19.	The palliative care unit *must* act as an independently organised and spatially separated unit.	A	4	-
11.20.	Treatment on a palliative care unit *should* be provided in an appropriate setting such as providing single rooms, overnight stay possibilities for family carers, homelike communal meeting areas and access to outdoor areas.	B	4	-
11.21.	To ensure qualified treatment on a palliative care unit, a medical and nursing service with a specialised palliative care qualification *must* be made available 24 hours a day and 7 days a week.	A	4	-
11.22.	The team on a palliative care unit *must* carry out the following measures to ensure process quality: • Individual treatment planning • Regular evaluation of treatment goals • Regular evaluation of performed treatment measures • Exchange between referrers and those continuing the treatment, as well as coordination between in-patient and out-patient care and treatment offers • Multi-professional, regular team meetings for case conferences • Joint multi-professional documentation • Offer of an external supervision for all team members.	A	4	-

11.5.4.2. Hospital palliative care support team

No.	Recommendations	GoR	LoE	Sources
11.23.	A hospital palliative care support team is an in-patient specialist palliative care service and cares for patients with incurable cancer and limited life expectancy who are not treated on a palliative care unit. Such a team is available for shared care (one or repeated visits) with the aim of improving quality of life.	Statement		

No.	Recommendations	GoR	LoE	Sources
11.24.	Every hospital that treats patients with incurable cancer *must* provide a palliative care support team.	0	4*	-
11.25.	Patients with incurable cancer *must* be offered a contact to a palliative care support team during a hospital stay.	A	1+	[207, 211, 212]
11.26.	A hospital palliative care support team *must* provide the following components of care: • Assessing symptoms and needs of patients and family carers in all four dimensions. • Treatment of symptoms and problems in all four dimensions • Resource-based support of patients and their family carers, particularly when establishing treatment goals and discussing the illness • Palliative care also in terms of respite care • Advance care planning • Coordination and organisation of palliative care • Shared care for the patient during the dying phase • Rituals of saying goodbye and remembering • Arranging grief counseling • Supporting members of the main care team	A	4	-
11.27.	A hospital palliative care support team *should* fulfil the following structural quality criteria: • Independent team • Multi-professional team with at least three different professional groups: physicians, nursing professionals, and a representative of another field of treatment • Own room for consultations and documentation • Available at the regular working hours in a hospital • Communication of indication criteria, team structure, availability and working methods of the palliative care support team to all departments which treat patients with incurable cancer.	B	4	-
11.28.	Consultation and shared treatment by the hospital palliative care support team *must* take place in close coordination with the main care team.	A	4	-

*For the recommendations in this chapter that have a LoE 4 a systematic literature search was only conducted for RCTs, CCTs, controlled pre-post studies and ITS (interrupted time series), thus for a Level-of-evidence 1 to 2 in accordance with SIGN. For LoE 4 (expert opinion) the SIGN-levels 2 (partly) and 3 were skipped and for this no supplementary literature search was carried out due to the fact that a statement concerning the effectiveness of interventions on the basis of SIGN-levels 2 and 3 could not be made.

No.	Recommendations	GoR	LoE	Sources
11.29.	The hospital palliative care support team *should* carry out the following measures to ensure process quality: • Individual treatment planning • Regular evaluation of treatment goals • Regular evaluation of performed treatment measures • Exchange between referrers and those continuing the treatment, as well as coordination between in-patient and out-patient care and treatment offers • Multi-professional, regular team meetings for case conferences • Joint multi-professional documentation • Offer of an external supervision for all team members.	B	4	-

A hospital palliative care support team is a multi-professional, specialised team that provides specialist palliative care for in-patients outside of a palliative care unit [213]. This implies continual, palliative care consultation and shared treatment in the case of complex symptoms and needs. In this way, the content and structure of a palliative service are rather in accordance with the established term for psychiatric/psychotherapeutic care, "liaison services", which goes beyond a mere consulting, short term consulting activity in the narrow sense. Therefore, this guideline forgoes using the often used term "palliative care consult".

11.5.4.3. Specialist palliative home care

No.	Recommendations	GoR	LoE	Sources
11.30.	Specialist palliative home care is available for patients with incurable cancer and a limited life expectancy if intense symptoms and/or high demand for coordination lead to a complex care situation and it is in accordance with the patient's wishes to be cared for in his/her home or family environment. SAPV is in accordance with the entitlement specified in §§ 37b, 132d SGB V.	Statement		
11.31.	Specialist palliative homecare *must* complement already existing health care services if these are not able to ensure the appropriate and sufficient care of a patient in the setting of his choice in the home environment (including nursing homes).	0	4*	-

* For the recommendations in this chapter that have a LoE 4 a systematic literature search was only conducted for RCTs, CCTs, controlled pre-post studies and ITS (interrupted time series), thus for a Level-of-evidence 1 to 2 in accordance with SIGN. For LoE 4 (expert opinion) the SIGN-levels 2 (partly) and 3 were skipped and for this no supplementary literature search was carried out due to the fact that a statement concerning the effectiveness of interventions on the basis of SIGN-levels 2 and 3 could not be made.

No.	Recommendations	GoR	LoE	Sources
11.32.	Specialist palliative home care *must* provide the following components when caring for patients with incurable cancer to improve quality of life: • Assessing symptoms and needs of patients and family carers in all four dimensions. • Treatment of symptoms and problems in all four dimensions • Resource-based support of patients and their family carers, particularly when establishing treatment goals and discussing the illness • Advance care planning • Coordination and organisation of palliative care • Care for the patient during the dying phase • Rituals of saying goodbye and remembering • Arranging grief counseling • Supporting members of the main care team	A	1-	[203, 205, 214, 215]
11.33.	Specialist palliative home care *must* be available round-the-clock.	A	4	-
11.34.	The specialist palliative home care team *must* work as an independent and multi-professional team (physician, nurse and another professional group).	A	1-	[204-208, 216, 217]
11.35.	A specialist palliative home care team *must* carry out the following measures to ensure process quality: • Individual treatment planning • Regular evaluation of treatment goals • Regular evaluation of performed treatment measures • Exchange between referrers and those continuing the treatment, as well as coordination between in-patient and out-patient care and treatment offers • Multi-professional, regular team meetings for case conferences • Joint multi-professional documentation • Independent team that regularly works together • Offer of an external supervision for all team members.	A	4	-
11.36.	Specialist palliative home care *must* be integrated into already existing health care structures and, in collaboration with the main health care providers (e.g. general practitioner, oncologist, nursing service), optimally ensure palliative care across sectors.	A	4	-

The aim of **specialist palliative home care** is to provide specialised care to patients with incurable cancer and at the same time a situation of high complexity and a high demand for care in the patients' familiar setting (at home, nursing home, hospice) so that these patients can live and die in their familiar surroundings.

In Germany, as of 2007 people who are insured with the public health care system are entitled to **"SAPV"** (specialist palliative home care) in accordance with §§ 37b und 132d SGB V, if they are suffering from a terminal, advanced and progressing illness, due to which their life-expectancy is limited and when complex problems are present which require particularly complex care. The entitlement to care exists for patients who wish to be cared for in their home or other familiar settings (including nursing homes).

In the context of this guideline, the abbreviation "SAPV" refers to the care entitlement stated by law. The written out term "specialist palliative home care" ("Spezialisierte ambulante Palliativversorgung") is used to describe the provision of services, on which this guideline has reached a consensus from both clinical experience and study evidence, which goes beyond the legislative text in some parts (e.g. definition of complexity).

11.5.4.4. Specialist palliative out-patient clinic

No.	Recommendations	GoR	LoE	Sources
11.37.	A palliative out-patient clinic is an integral part of specialist ambulatory palliative care.	Statement		
11.38.	A palliative out-patient clinic *should* be offered to out-patients with incurable cancer as an addition to already existing health care services.	B	1+	[209, 210]
11.39.	A palliative out-patient clinic *must* provide the following components when caring for patients with incurable cancer to improve quality of life: • Assessing symptoms and needs of patients and family carers in all four dimensions • Treatment of symptoms and problems in all four dimensions • Resource-based support of patients and their family carers, particularly when establishing treatment goals and discussing the illness • Advance care planning • Coordination and organisation of palliative care • Supporting members of the main care team or the main health care provider	A	1+	[209, 210]
11.40.	Consultation and shared treatment in the palliative out-patient clinic *must* take place in close coordination with the main health care provider or the main care team.	A	1+	[209, 210]

A palliative out-patient clinic is a facility for out-patients with the offer of specialist palliative care without home care (this can, however, be offered additionally in cooperation with a service from the specialist palliative home care). A palliative out-patient clinic can be part of a hospital or medical centre or part of an established practice (general practitioner, oncologists or out-patient pain clinic) and is comparable with an out-patient oncological or pain clinic.

11.5.4.5. Palliative day-care centre and day hospice

No.	Recommendation	GoR	LoE	Sources
11.41.	The palliative day-care centre and the day hospice are specialist offers for out-patients with incurable cancer and limited life-expectancy.	Statement		

In most cases, the palliative day-care centre or the day hospice is part of another facility (e.g. hospital, in-patient hospice, hospice service) which provide a day treatment service to out-patients.

11.5.5. In-patient hospice

No.	Recommendations	GoR	LoE	Sources
11.42.	An in-patient hospice is part of generalist and specialist palliative care with the aim of providing palliative care and hospice care in the final stage of life until death and is seen as an independent organization on the basis of the legal regulations §39 a, Abs.1 SGB V and the general agreement in connection with these.	Statement		
11.43.	Palliative care treatment and hospice care in an in-patient hospice *must* be offered to people with incurable cancer with a limited life-expectancy of days, weeks or months if care cannot be guaranteed or is not sufficient either at home or elsewhere in an in-patient care facility.	A	4*	-
11.44.	An in-patient hospice *must* offer the following components of palliative care treatment and hospice care: • Assessing symptoms and needs of patients and family carers in all four dimensions • Basic symptom control, together with visiting physician • Supporting the patient and their family carers in understanding the illness • Resource-based support of patients and their family carers,	A	4	-

* For the recommendations in this chapter that have a LoE 4 a systematic literature search was only conducted for RCTs, CCTs, controlled pre-post studies and ITS (interrupted time series), thus for a Level-of-evidence 1 to 2 in accordance with SIGN. For LoE 4 (expert opinion) the SIGN-levels 2 (partly) and 3 were skipped and for this no supplementary literature search was carried out due to the fact that a statement concerning the effectiveness of interventions on the basis of SIGN-levels 2 and 3 could not be made.

No.	Recommendations	GoR	LoE	Sources
	particularly psychosocial and spiritual support • Basic nursing and treatment care • Psychosocial and spiritual support • Care from competent volunteers • Care for the patient during the dying phase • Rituals of saying goodbye and remembering • Dignified lying out in accordance with the wishes of the patient and family carers • Arranging grief counseling			
11.45.	Palliative and hospice care *must* be provided by a qualified multi-professional team with specialist palliative nursing that ensures round-the-clock care and considers the special needs of the severely ill resident and their family carers.	A	4	-
11.46.	Medical care *should* be provided by the general practitioner or physicians with a basic qualification in palliative care who are available 24h a day, 7 days a week.	B	4	-
11.47.	If necessary, specialist palliative home care *must* be consulted.	A	4	-
11.48.	An in-patient hospice *must* be a place to live for patients and their family carers in the final stage of life with single rooms and overnight stay possibilities for family carers. The setting *must* have a comfortable-familiar character with communal meeting areas and areas to enable privacy.	A	4	-

Care in an in-patient hospice means that the place of residence of the affected person by law is an in-patient facility in accordance with §39a paragraph 1 SGB V. This means that the nursing care service and the services of other non-medical professional groups are provided by members of staff from an in-patient facility but the medical services are normally provided by independently working physicians as part of their statutory duties or as part of the specialist palliative home care.

In-patient hospices cannot be clearly assigned to either generalist or specialist palliative care and are assigned to both areas (generalist and specialist palliative care) for the purpose of this guideline.

11.5.6. Hospice services/volunteer-based services

No.	Recommendation	GoR	LoE	Sources
11.49.	Patients with incurable cancer in palliative care and their family carers *should* be provided with support from hospice volunteers regardless of age, care setting, phase of illness or the type of palliative care services being offered.		EC	

11.5.7. Family carers

See also chapter 9.5.

No.	Recommendations	GoR	LoE	Sources
11.50.	Family carers of patients with incurable cancer *must*, with the patient's agreement, be informed of treatment decisions and treatment and care planning, be involved in discussions on diagnosis and prognosis and receive the opportunity to active participation.	A	4*	-
11.51.	Family carers of patients with incurable cancer *must* be considered, supported and cared for in their experience and coping with the patient's illness, in accordance with their needs and with consideration of specific and individual distress factors.	A	1+	[218]
11.52.	Family carers of patients with incurable cancer *must* be informed of available support offers such as self-help groups and training for family carers.	EC		

11.6. Grief and bereavement counseling

No.	Recommendations	GoR	LoE	Sources
11.53.	Facilities, which care for and treat dying people, *must* develop a culturally sensitive way of saying goodbye and grieving, personal to their own facility, which enables a dignified farewell for patients, family carers and members of staff.	A	4*	-
11.54.	Patients with incurable cancer and their family carers *must* have access to information on grief counseling at all stages of the illness.	A	4	-
11.55.	If desired, family carers of patients with incurable cancer *should* be informed of the offer of qualified grief counseling, also following the patient's death.	B	4	-

* For the recommendations in this chapter that have a LoE 4 a systematic literature search was only conducted for RCTs, CCTs, controlled pre-post studies and ITS (interrupted time series), thus for a Level-of-evidence 1 to 2 in accordance with SIGN. For LoE 4 (expert opinion) the SIGN-levels 2 (partly) and 3 were skipped and for this no supplementary literature search was carried out due to the fact that a statement concerning the effectiveness of interventions on the basis of SIGN-levels 2 and 3 could not be made.

* For the recommendations in this chapter that have a LoE 4 a systematic literature search was only conducted for RCTs, CCTs, controlled pre-post studies and ITS (interrupted time series), thus for a Level-of-evidence 1 to 2 in accordance with SIGN. For LoE 4 (expert opinion) the SIGN-levels 2 (partly) and 3 were skipped and for this no supplementary literature search was carried out due to the fact that a statement concerning the effectiveness of interventions on the basis of SIGN-levels 2 and 3 could not be made.

When and by whom information concerning grief services and counseling should be provided is shown in Table 13.

Table 13: Grief counseling and mourning culture in facilities and hospitals which care for and treat severely ill and dying people

Time/trigger point	Offer/intervention	Addressees	Person responsible
Mourning culture for dealing with loss and grief of patients, family carers and members of staff for the entire facility/hospital			
Diagnosis of terminal cancer	Information about grief counseling offers	• Patients • Family carers	Competent team members in palliative care
Request/needs of the patient or their family carers in the course of treatment	Timely grief counseling in one-on-one discussions or groups	• Patients • Family carers	Qualified grief counselor, e.g. from hospice care, pastoral care or psycho-oncologists
Following the death of the patient: • At the request of family carers • Team is particularly affected	• Grief counseling in one-to-one settings or groups • Identification of possible emergence of complicated grief	• Family carers • Team of carers	Qualified grief counselor, e.g. from hospice care, pastoral care or psycho-oncologists
In cases of already diagnosed or suspicion of complicated grief	Psychotherapeutic grief counseling in one-to-one settings or in a group setting	Family carers with complicated grief reactions	Qualified psychotherapists, psychologists, psychiatrists

12. Quality indicators (QIs)

Quality indicator	Reference recommen-dation	Evidence basis
General remarks: The QIs 1, 2, 3, (4) and 10 must be assessed with the screening instruments IPOS or MIDOS. Another instrument must only be used for QI 8. The denominator of the QIs addresses explicitly patients receiving generalist and specialist palliative care. This reflects the idea that the QIs should be put into practice for both sectors of palliative care provision.		
QI 1: Reduction of breathlessness		
Numerator: Number of patients with reduction of breathlessness within 48h **Denominator:** All patients with the diagnosis "incurable cancer" (generalist and specialist palliative care) and with moderate/severe breathlessness **Screening instruments** (open list of validated instruments): Modified Borg Dyspnea Scale, Visual Analog Scale, Numeric Rating Scale, MIDOS, IPOS (HOPE/national palliative care registry)	**5.3**	**EC**
QI 2: Reduction of pain		
Numerator: Number of patients with reduction of pain within 48h **Denominator:** All patients with the diagnosis "incurable cancer" (generalist and specialist pallia-tive care) and with moderate/severe pain **Screening instruments** (open list of validated instruments): McGill Pain Questionnaire, Verbal Rating Scale, Numeric Rating Scale, MIDOS, IPOS, (HOPE/national palliative care registry), in case of suspicion of neuropathic pain, also painDETECT or DN4	**6.1**	**EC**
QI 3: Opioids and laxatives		
Numerator: Number of patients without therapy with osmotic and/or stimulant laxatives **Denominator:** All patients with the diagnosis "incurable cancer" (generalist and spe-	**6.25**	**GoR A, LoE: 1+** [50],[114]) **GoR A,**

Quality indicator	Reference recommen-dation	Evidence basis
cialist palliative care) on opioids **Quality target:** low	**7.7**	**LoE: 1-** [127]
QI 4: Symptom assessment in the dying phase		
Numerator: Number of patients with symptom assessment by means of a validated screening instrument in the last 72h before death **Denominator:** All deceased patients (generalist and specialist palliative care) **Screening instruments** (open list of validated instruments): IPOS, MIDOS, HOPE/national palliative care registry)	**10.23**	**EC**
QI 5: Assessment of agitation in the dying phase		
Numerator: Number of patients with agitation assessment in the last 72h before death **Denominator:** All deceased patients (generalist and specialist palliative care) **Screening instruments:** Agitation will be assessable with IPOS and MIDOS in the future.	**10.24**	**EC**
QI 6: Stopping cancer-specific measures in the dying phase		
Numerator: Number of patients with cancer-specific measures (systematic therapies, radiotherapy) within 14 days before death **Denominator:** All deceased patients (generalist and specialist palliative care) **Quality target:** low	**10.31**	**EC**
QI 7: Stopping medical treatment measures in the dying phase		
Numerator: Number of patients with dialysis or hemofiltration or ventilation within 7 days before death **Denominator:** All deceased patients (generalist and specialist palliative care)	**10.32.**	**EC**

Quality indicator	Reference recommen-dation	Evidence basis
Quality target: low		
QI 8: Screening for depression		
Numerator: Number of patients with screening for depression when planning the treatment **Denominator:** All patients with the diagnosis "incurable cancer" (generalist and specialist palliative care) **Screening instruments:** HADS, Self assessment process ("During the past month, have you often been bothered by feeling down, depressed or hopeless?"; "During the past month, have you often been bothered by little interest or pleasure in doing things?")	8.2	GoR A, LoE 4
QI 9: Advance Care Planning		
Numerator: Number of patients with conversations about Advance Care Planning by treatment planning **Denominator:** All patients with the diagnosis "incurable cancer" (generalist and specialist palliative care) **Note:** Advance Care Planning comprises conversations about e.g. (see recommendation 9.18): • Scope and limitations of treatment in the case of (illness) typical situations as well as frequent and possible complications; • Individual preferences regarding the provision of care in the final stages of life, the place of care and death as well as funeral arrangements if appropriate; Arranging a health care proxy or suggesting a person to act as a legal representative.	9.19. 9.20.	GoR A, LoE 4
QI 10: Screening by means of MIDOS and IPOS		

Quality indicator	Reference recommendation	Evidence basis
Numerator: Number of patients with screening by means of validated tools (e.g. MIDOS or IPOS) when planning the treatment **Denominator:** All patients with the diagnosis "incurable cancer" (generalist and specialist palliative care)	11.4	EC

13. List of figures

14. List of tables

15. Bibliography

1. Radbruch, L. and S. Payne, *White Paper on standards and norms for hospice and palliative care in Europe: part 1* European Journal of Palliative Care, 2009. **16**(6): p. 278-289.
2. Radbruch, L. and S. Payne, *White Paper on standards and norms for hospice and palliative care in Europe: part 2* European Journal of Palliative Care, 2010. **17**(1): p. 22-33.
3. Nationale Akademie der Wissenschaften Leopoldina und Union der deutschen Akademien der Wissenschaften. *Palliativversorgung in Deutschland – Perspektiven für Praxis und Forschung*. 2015; Available from: www.leopoldina.org/uploads/tx_leopublication/2015_Palliativversorgung_LF_DE.pdf; www.leopoldina.org.
4. Leitlinienprogramm Onkologie, *Psychoonkologische Diagnostik, Beratung und Behandlung von erwachsenen Krebspatienten, Langversion 1.1*, in *http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html*2014, Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF: AWMF-Registernummer: 032/051OL.
5. Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften - Ständige Kommission, L. *AWMF-Regelwerk "Leitlinien"*. 1. Auflage 2012 [cited 09.12.2013; Available from: http://www.awmf.org/leitlinien/awmf-regelwerk/awmf-regelwerk.html.
6. WHO. *The Ottawa Charter for Health Promotion*. 1986; Available from: http://www.who.int/healthpromotion/conferences/previous/ottawa/en/index.html.
7. WHO. *Definition of Palliative Care*. 2002; Available from: http://www.who.int/cancer/palliative/definition/en/.
8. Saunders, C., *The evolution of palliative care.* J R Soc Med, 2001. **94**(9): p. 430-2.
9. Nolan, S., P. Saltmarsh, and C. Leget, *Spiritual care in palliative care: working towards an EAPC Task Force.* European Journal of Palliative Care, 2011. **18**(2): p. 86-89.
10. Domeisen Benedetti, F., et al., *International palliative care experts' view on phenomena indicating the last hours and days of life.* Support Care Cancer, 2012.
11. Eychmüller, S., et al., *"Diagnosing dying" in cancer patients - a systematic literature review.* European Journal of Palliative Care, 2013. **20**(6): p. 292-296.
12. WHO, *Palliative Care; Cancer control : knowledge into action : WHO guide for effective programmes ; module 5*, W.H. Organization, Editor 2007.
13. Hanisch, H., *Team und Typ-Knigge 2100: Ich und Wir, Typen und Charaktere, Team-Entwicklung*2012, Norderstedt: Books on Demand.
14. Vergnaud, M., *Teamentwicklung*2004, Munich: Elsevier.
15. *Dyspnea. Mechanisms, assessment, and management: a consensus statement. American Thoracic Society.* Am J Respir Crit Care Med, 1999. **159**(1): p. 321-40.
16. Parshall, M.B., et al., *An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea.* Am J Respir Crit Care Med, 2012. **185**(4): p. 435-52.
17. Abernethy, A.P., et al., *Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnoea: a double-blind, randomised controlled trial.* Lancet, 2010. **376**(9743): p. 784-93.
18. Reddy, S.K., et al., *Characteristics and correlates of dyspnea in patients with advanced cancer.* J Palliat Med, 2009. **12**(1): p. 29-36.
19. Bailey, P.H., *The dyspnea-anxiety-dyspnea cycle--COPD patients' stories of breathlessness: "It's scary /when you can't breathe".* Qual Health Res, 2004. **14**(6): p. 760-78.
20. Simon, S., et al., *Atemnotattacken: Übersetzung und Konsentierung der internationalen Definition im Rahmen einer Delphi-Befragung; Episodic breathlessness: Translation of the international definition using the Delphi-method.* Dtsch Med Wochenschr, accepted.
21. Simon, S.T., et al., *Episodic and continuous breathlessness – a new categorization of breathlessness.* J Pain Symptom Manage, 2013. **45**(6): p. 1019-1029.
22. Altfelder, N., et al., *Characteristics of patients with breathlessness - a German national survey on palliative care in-patient units.* . Palliative Med, 2010. **24**: p. 37.
23. Currow, D.C., et al., *Do the trajectories of dyspnea differ in prevalence and intensity by diagnosis at the end of life? A consecutive cohort study.* J Pain Symptom Manage, 2010. **39**(4): p. 680-90.
24. Reuben, D.B. and V. Mor, *Dyspnea in terminally ill cancer patients.* Chest, 1986. **89**(2): p. 234-6.

25. Walsh, D., S. Donnelly, and L. Rybicki, *The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients.* Support Care Cancer, 2000. **8**(3): p. 175-9.
26. Alt-Epping, B., et al., *What is special about patients with lung cancer and pulmonary metastases in palliative care? Results from a nationwide survey.* J Palliat Med, 2012. **15**(9): p. 971-7.
27. Conill, C., et al., *Symptom prevalence in the last week of life.* J Pain Symptom Manage, 1997. **14**(6): p. 328-31.
28. Bausewein, C., et al., *Individual breathlessness trajectories do not match summary trajectories in advanced cancer and chronic obstructive pulmonary disease: results from a longitudinal study.* Palliat Med, 2010. **24**(8): p. 777-86.
29. Gysels, M.H. and I.J. Higginson, *Caring for a person in advanced illness and suffering from breathlessness at home: threats and resources.* Palliat Support Care, 2009. **7**(2): p. 153-62.
30. Edmonds, P., et al., *A comparison of the palliative care needs of patients dying from chronic respiratory diseases and lung cancer.* Palliat Med, 2001. **15**(4): p. 287-95.
31. Tishelman, C., et al., *Symptoms in patients with lung carcinoma: distinguishing distress from intensity.* Cancer, 2005. **104**(9): p. 2013-21.
32. Henoch, I., B. Bergman, and E. Danielson, *Dyspnea experience and management strategies in patients with lung cancer.* Psychooncology, 2008. **17**(7): p. 709-15.
33. Smoller, J.W., et al., *Panic anxiety, dyspnea, and respiratory disease. Theoretical and clinical considerations.* Am J Respir Crit Care Med, 1996. **154**(1): p. 6-17.
34. Davis, C.L., *ABC of palliative care. Breathlessness, cough, and other respiratory problems.* BMJ, 1997. **315**(7113): p. 931-934.
35. Booth, S., S. Silvester, and C. Todd, *Breathlessness in cancer and chronic obstructive pulmonary disease: using a qualitative approach to describe the experience of patients and carers.* Palliat Support Care, 2003. **1**(4): p. 337-44.
36. Abernethy, A.P., et al., *Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea.* British Medical Journal, 2003. **327**(7414): p. 523-526.
37. Allard, P., et al., *How effective are supplementary doses of opioids for dyspnea in terminally ill cancer patients? A randomized continuous sequential clinical trial.* Journal of Pain & Symptom Management, 1999. **17**(4): p. 256-65.
38. Bruera, E., et al., *Nebulized versus subcutaneous morphine for patients with cancer dyspnea: a preliminary study.* Journal of Pain & Symptom Management, 2005. **29**(6): p. 613-8.
39. Charles, M.A., L. Reymond, and F. Israel *Relief of incident dyspnea in palliative cancer patients: a pilot, randomized, controlled trial comparing nebulized hydromorphone, systemic hydromorphone, and nebulized saline.* Journal of pain and symptom management, 2008. 29-38.
40. Grimbert, D., et al., *[Dyspnea and morphine aerosols in the palliative care of lung cancer].* Revue des maladies respiratoires, 2004. **21**(6 Pt 1): p. 1091-7.
41. Jennings, A.L., et al., *Opioids for the palliation of breathlessness in terminal illness.* Cochrane Database Syst Rev, 2001(4): p. CD002066.
42. Jensen, D., et al. *Inhaled Fentanyl Citrate Improves Dynamic Airway Function, Exertional Dyspnea And Exercise Endurance In COPD [Abstract].* American Journal of Respiratory and Critical Care Medicine, 2011. A5627.
43. Johnson, M.J., et al., *Morphine for the relief of breathlessness in patients with chronic heart failure - A pilot study.* European journal of heart failure, 2002. **4**(6): p. 753-756.
44. Mazzocato, C., T. Buclin, and C.H. Rapin, *The effects of morphine on dyspnea and ventilatory function in elderly patients with advanced cancer: A randomized double-blind controlled trial.* Annals of Oncology, 1999. **10**(12): p. 1511-1514.
45. Navigante, A.H., M.A. Castro, and C. Cerchietti Leandro, *Morphine Versus Midazolam as Upfront Therapy to Control Dyspnea Perception in Cancer Patients While Its Underlying Cause Is Sought or Treated.* Journal of pain and symptom management, 2010. **39**(5): p. 820-830.
46. Navigante, A.H., et al., *Midazolam as adjunct therapy to morphine in the alleviation of severe dyspnea perception in patients with advanced cancer.* Journal of Pain & Symptom Management, 2006. **31**(1): p. 38-47.
47. Oxberry, S.G., et al., *Short-term opioids for breathlessness in stable chronic heart failure: A randomized controlled trial.* European journal of heart failure, 2011. **13**(9): p. 1006-1012.
48. King, S., et al., *A systematic review of the use of opioid medication for those with moderate to severe cancer pain and renal impairment: a European Palliative Care Research Collaborative opioid guidelines project.* Palliat Med, 2011. **25**(5): p. 525-52.

49. Twycross, R., Wilcock, A., *Palliative Care Formulary*. 4 ed2011, Nottingham: Palliativedrugs.com Ltd.
50. Caraceni, A., et al., *Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC.* Lancet Oncol, 2012. **13**(2): p. e58-68.
51. Murtagh, F.E., et al., *The use of opioid analgesia in end-stage renal disease patients managed without dialysis: recommendations for practice.* J Pain Palliat Care Pharmacother, 2007. **21**(2): p. 5-16.
52. Simon, S.T., et al., *Benzodiazepines for the relief of breathlessness in advanced malignant and non-malignant diseases in adults.* Cochrane Database Syst Rev, 2010(1): p. CD007354.
53. Stege, G., et al., *Temazepam 10mg does not affect breathing and gas exchange in patients with severe normocapnic COPD.* Respir Med, 2010. **104**(4): p. 518-24.
54. Allcroft, P., et al., *The role of benzodiazepines in breathlessness: a single site, open label pilot of sustained release morphine together with clonazepam.* J Palliat Med, 2013. **16**(7): p. 741-4.
55. O'Neill, P.A., P.B. Morton, and R.D. Stark, *Chlorpromazine - A specific effect on breathlessness?* British Journal of Clinical Pharmacology, 1985. **19**(6): p. 793-797.
56. Rice, K.L., et al., *Effects of chronic administration of codeine and promethazine on breathlessness and exercise tolerance in patients with chronic airflow obstruction.* British Journal of Diseases of the Chest, 1987. **81**(3): p. 287-292.
57. Stark, R.D., S.A. Gambles, and J.A. Lewis, *Methods to assess breathlessness in healthy subjects: A critical evaluation and application to analyse the acute effects of diazepam and promethazine on breathlessness induced by exercise or by exposure to raised levels of carbon dioxide.* Clinical Science, 1981. **61**(4): p. 429-439.
58. Woodcock, A.A., E.R. Gross, and D.M. Geddes, *Drug treatment of breathlessness: contrasting effects of diazepam and promethazine in pink puffers.* British Medical Journal, 1981. **283**(6287): p. 343-346.
59. Argyropoulou, P., et al., *Buspirone effect on breathlessness and exercise performance in patients with chronic obstructive pulmonary disease.* Respiration, 1993. **60**(4): p. 216-20.
60. Borson, S., et al., *Improvement in mood, physical symptoms, and function with nortriptyline for depression in patients with chronic obstructive pulmonary disease.* Psychosomatics, 1992. **33**(2): p. 190-201.
61. Eiser, N., et al., *Effect of treating depression on quality-of-life and exercise tolerance in severe COPD.* COPD, 2005. **2**(2): p. 233-41.
62. Lacasse, Y., et al., *Randomized trial of paroxetine in end-stage COPD.* Monaldi Archives for Chest Disease, 2004. **61**(3): p. 140-7.
63. Perna, G., R. Cogo, and L. Bellodi, *Selective serotonin re-uptake inhibitors beyond psychiatry: Are they useful in the treatment of severe, chronic, obstructive pulmonary disease?* Depression and Anxiety, 2004. **20**(4): p. 203-204.
64. Singh, N.P., et al., *Effects of buspirone on anxiety levels and exercise tolerance in patients with chronic airflow obstruction and mild anxiety.* Chest, 1993. **103**(3): p. 800-4.
65. Smoller, J.W., et al., *Sertraline effects on dyspnea in patients with obstructive airways disease.* Psychosomatics, 1998. **39**(1): p. 24-9.
66. Ström, K., et al. *Effect of protriptyline, 10 mg daily, on chronic hypoxaemia in chronic obstructive pulmonary disease.* The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology, 1995. 425-9.
67. Aaron, S.D., et al., *Outpatient oral prednisone after emergency treatment of chronic obstructive pulmonary disease.* N Engl J Med, 2003. **348**(26): p. 2618-25.
68. Choudhury, A.B., et al., *Withdrawal of inhaled corticosteroids in people with COPD in primary care: a randomised controlled trial.* Respir Res, 2007. **8**: p. 93.
69. du Bois, R.M., et al., *Randomized trial of inhaled fluticasone propionate in chronic stable pulmonary sarcoidosis: a pilot study.* European Respiratory Journal, 1999. **13**(6): p. 1345-50.
70. Guenette, J.A., et al., *Effect of adjunct fluticasone propionate on airway physiology during rest and exercise in COPD.* Respiratory Medicine, 2011. **105**(12): p. 1836-45.
71. Melani, A.S. and A. Di Gregorio, *Four-week nebulized beclomethasone dipropionate in stable COPD patients with exertional dyspnoea.* Monaldi Archives for Chest Disease, 1999. **54**(3): p. 224-7.
72. Milman, N., et al., *No effect of high-dose inhaled steroids in pulmonary sarcoidosis: a double-blind, placebo-controlled study.* J Intern Med, 1994. **236**(3): p. 285-90.
73. Rice, K.L., et al., *Withdrawal of chronic systemic corticosteroids in patients with COPD: a randomized trial.* American Journal of Respiratory & Critical Care Medicine, 2000. **162**(1): p. 174-8.

74. Sayiner, A., et al., *Systemic glucocorticoids in severe exacerbations of COPD.* Chest, 2001. **119**(3): p. 726-30.
75. Shmelev, E.I. and Y.L. Kunicina, *Comparison of fenspiride with beclomethasone as adjunctive anti-inflammatory treatment in patients with chronic obstructive pulmonary disease.* Clinical Drug Investigation, 2006. **26**(3): p. 151-9.
76. Tashkin, D.P., et al., *Efficacy and safety of budesonide and formoterol in one pressurized metered-dose inhaler in patients with moderate to very severe chronic obstructive pulmonary disease: results of a 6-month randomized clinical trial.* Drugs, 2008. **68**(14): p. 1975-2000.
77. Thompson, W.H., et al., *Controlled trial of oral prednisone in outpatients with acute COPD exacerbation.* American Journal of Respiratory & Critical Care Medicine, 1996. **154**(2 Pt 1): p. 407-12.
78. van den Boom, G., et al., *The cost effectiveness of early treatment with fluticasone propionate 250 microg twice a day in subjects with obstructive airway disease. Results of the DIMCA program.* American Journal of Respiratory & Critical Care Medicine, 2001. **164**(11): p. 2057-66.
79. Vestbo, J., et al., *Early onset of effect of salmeterol and fluticasone propionate in chronic obstructive pulmonary disease.* Thorax, 2005. **60**(4): p. 301-4.
80. Walters, J.A., E.H. Walters, and R. Wood-Baker, *Oral corticosteroids for stable chronic obstructive pulmonary disease (Review).* Cochrane Database Syst Rev, 2009(3): p. CD005374.
81. Worth, H., et al., *Budesonide added to formoterol contributes to improved exercise tolerance in patients with COPD.* Respir Med, 2010. **104**(10): p. 1450-9.
82. Wouters, E.F., et al., *[Withdrawal of fluticasone propionate from combined salmeterol/fluticasone treatment in patients with COPD causes immediate and sustained disease deterioration: a randomised controlled trial].* Rev Port Pneumol, 2005. **11**(6): p. 587-9.
83. Yang, I.A., et al., *Inhaled corticosteroids for stable chronic obstructive pulmonary disease.* Cochrane Database Syst Rev, 2007(2): p. CD002991.
84. Yennurajalingam, S., et al., *Reduction of cancer-related fatigue with dexamethasone: a double-blind, randomized, placebo-controlled trial in patients with advanced cancer.* J Clin Oncol, 2013. **31**(25): p. 3076-82.
85. Zhang, H., et al., *Prednisone adding to usual care treatment for refractory decompensated congestive heart failure.* International Heart Journal, 2008. **49**(5): p. 587-95.
86. Bausewein, C., et al., *Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases.* Cochrane Database Syst Rev, 2008(2): p. CD005623.
87. Bausewein, C., et al., *Effectiveness of a hand-held fan for breathlessness: a randomised phase II trial.* BMC Palliative Care, 2010. **9**: p. 22.
88. Galbraith, S., et al., *Does the use of a handheld fan improve chronic dyspnea? A randomized, controlled, crossover trial.* Journal of Pain & Symptom Management, 2010. **39**(5): p. 831-8.
89. Cranston, J.M., A. Crockett, and D. Currow, *Oxygen therapy for dyspnoea in adults.* Cochrane Database Syst Rev, 2008(3): p. CD004769.
90. Uronis, H., et al., *Symptomatic oxygen for non-hypoxaemic chronic obstructive pulmonary disease.* Cochrane Database Syst Rev, 2011(6): p. CD006429.
91. Uronis, H.E., et al., *Oxygen for relief of dyspnoea in mildly- or non-hypoxaemic patients with cancer: a systematic review and meta-analysis.* Br J Cancer, 2008. **98**(2): p. 294-9.
92. Merskey, H., *Classification of chronic pain: description of chronic pain syndromes and definition of pain terms.* Pain 1986. **Suppl.**(3): p. 1.
93. Ventafridda, V., et al., *A validation study of the WHO method for cancer pain relief.* Cancer, 1987. **59**(4): p. 850-6.
94. Deandrea, S., et al., *Prevalence of undertreatment in cancer pain. A review of published literature.* Ann Oncol, 2008. **19**(12): p. 1985-91.
95. Chow, E., et al., *Update on the systematic review of palliative radiotherapy trials for bone metastases.* Clin Oncol (R Coll Radiol), 2012. **24**(2): p. 112-24.
96. Lutz, S., et al., *Palliative radiotherapy for bone metastases: an ASTRO evidence-based guideline.* Int J Radiat Oncol Biol Phys, 2011. **79**(4): p. 965-76.
97. Rades, D., et al., *Evaluation of five radiation schedules and prognostic factors for metastatic spinal cord compression.* J Clin Oncol, 2005. **23**(15): p. 3366-75.
98. Leppert, W. and M. Majkowicz, *The impact of tramadol and dihydrocodeine treatment on quality of life of patients with cancer pain.* International Journal of Clinical Practice, 2010. **64**(12): p. 1681-7.
99. Tassinari, D., et al., *The second step of the analgesic ladder and oral tramadol in the treatment of mild to moderate cancer pain: a systematic review.* Palliat Med, 2011. **25**(5): p. 410-23.

100. Caraceni, A., A. Pigni, and C. Brunelli, *Is oral morphine still the first choice opioid for moderate to severe cancer pain? A systematic review within the European Palliative Care Research Collaborative guidelines project.* Palliat Med, 2011. **25**(5): p. 402-9.
101. King, S.J., et al., *A systematic review of oxycodone in the management of cancer pain.* Palliat Med, 2011. **25**(5): p. 454-70.
102. Mercadante, S., et al., *Morphine versus oxycodone in pancreatic cancer pain: a randomized controlled study.* Clinical Journal of Pain, 2010. **26**(9): p. 794-7.
103. Pigni, A., C. Brunelli, and A. Caraceni, *The role of hydromorphone in cancer pain treatment: a systematic review.* Palliat Med, 2011. **25**(5): p. 471-7.
104. Cherny, N., *Is oral methadone better than placebo or other oral/transdermal opioids in the management of pain?* Palliat Med, 2011. **25**(5): p. 488-93.
105. Klepstad, P., S. Kaasa, and P.C. Borchgrevink, *Starting step III opioids for moderate to severe pain in cancer patients: dose titration: a systematic review.* Palliat Med, 2011. **25**(5): p. 424-30.
106. Bruera, E., et al., *Methadone versus morphine as a first-line strong opioid for cancer pain: a randomized, double-blind study.* J Clin Oncol, 2004. **22**(1): p. 185-92.
107. Radbruch, L., et al., *Systematic review of the role of alternative application routes for opioid treatment for moderate to severe cancer pain: an EPCRC opioid guidelines project.* Palliat Med, 2011. **25**(5): p. 578-96.
108. Kurita, G.P., S. Kaasa, and P. Sjogren, *Spinal opioids in adult patients with cancer pain: a systematic review: a European Palliative Care Research Collaborative (EPCRC) opioid guidelines project.* Palliat Med, 2011. **25**(5): p. 560-77.
109. Lauretti, G.R., et al., *Epidural methadone results in dose-dependent analgesia in cancer pain, further enhanced by epidural dexamethasone.* British Journal of Cancer, 2013. **108**(2): p. 259-64.
110. Dale, O., K. Moksnes, and S. Kaasa, *European Palliative Care Research Collaborative pain guidelines: opioid switching to improve analgesia or reduce side effects. A systematic review.* Palliat Med, 2011. **25**(5): p. 494-503.
111. Moksnes, K., et al., *How to switch from morphine or oxycodone to methadone in cancer patients? a randomised clinical phase II trial.* European Journal of Cancer, 2011. **47**(16): p. 2463-70.
112. Mercadante, S. and A. Caraceni, *Conversion ratios for opioid switching in the treatment of cancer pain: a systematic review.* Palliat Med, 2011. **25**(5): p. 504-15.
113. Laugsand, E.A., S. Kaasa, and P. Klepstad, *Management of opioid-induced nausea and vomiting in cancer patients: systematic review and evidence-based recommendations.* Palliat Med, 2011. **25**(5): p. 442-53.
114. Candy, B., et al., *Laxatives or methylnaltrexone for the management of constipation in palliative care patients.* Cochrane Database Syst Rev, 2011(1): p. CD003448.
115. Stone, P. and O. Minton, *European Palliative Care Research collaborative pain guidelines. Central side-effects management: what is the evidence to support best practice in the management of sedation, cognitive impairment and myoclonus?* Palliat Med, 2011. **25**(5): p. 431-41.
116. Duarte Souza, J.F., et al., *Adjunct dipyrone in association with oral morphine for cancer-related pain: the sooner the better.* Supportive Care in Cancer, 2007. **15**(11): p. 1319-23.
117. Rodriguez, M., et al., *Efficacy and tolerance of oral dipyrone versus oral morphine for cancer pain.* European Journal of Cancer, 1994. **30A**(5): p. 584-7.
118. Yalcin, S., et al., *Ketorolac tromethamine in cancer pain.* Acta Oncologica, 1997. **36**(2): p. 231-2.
119. Yalcin, S., et al., *A comparison of two nonsteroidal antiinflammatory drugs (diflunisal versus dipyrone) in the treatment of moderate to severe cancer pain: a randomized crossover study.* American Journal of Clinical Oncology, 1998. **21**(2): p. 185-8.
120. Nabal, M., et al., *The role of paracetamol and nonsteroidal anti-inflammatory drugs in addition to WHO Step III opioids in the control of pain in advanced cancer. A systematic review of the literature.* Palliat Med, 2011. **26**(4): p. 305-12.
121. Bennett, M.I., *Effectiveness of antiepileptic or antidepressant drugs when added to opioids for cancer pain: systematic review.* Palliat Med, 2011. **25**(5): p. 553-9.
122. Mishra, S., et al., *A comparative efficacy of amitriptyline, gabapentin, and pregabalin in neuropathic cancer pain: a prospective randomized double-blind placebo-controlled study.* American Journal of Hospice & Palliative Medicine, 2012. **29**(3): p. 177-82.

123. Zeppetella, G., *Opioids for the management of breakthrough cancer pain in adults: a systematic review undertaken as part of an EPCRC opioid guidelines project.* Palliat Med, 2011. **25**(5): p. 516-24.
124. Zeppetella, G. and A.N. Davies, *Opioids for the management of breakthrough pain in cancer patients.* Cochrane Database Syst Rev, 2013. **10**: p. CD004311.
125. DGNM and DGVS *S2k-Leitlinie Chronische Obstipation: Definition, Pathophysiologie, Diagnostik und Therapie.* 2013.
126. Lembo, A. and M. Camilleri, *Chronic constipation.* N Engl J Med, 2003. **349**(14): p. 1360-8.
127. Bader, S., M. Weber, and G. Becker, *Is the pharmacological treatment of constipation in palliative care evidence based? : a systematic literature review.* Schmerz, 2012. **26**(5): p. 568-86.
128. Larkin, P.J., et al., *The management of constipation in palliative care: clinical practice recommendations.* Palliat Med, 2008. **22**(7): p. 796-807.
129. Solano, J.P., B. Gomes, and I.J. Higginson, *A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease.* J Pain Symptom Manage, 2006. **31**(1): p. 58-69.
130. Twycross, R.G. and J.M.V. Harcourt, *The use of laxatives at a palliative care centre.* Pall Med, 1991. **5**(1): p. 27-33.
131. Sykes, N.P., *The relationship between opioid use and laxative use in terminally ill cancer patients.* Palliat Med, 1998. **12**(5): p. 375-82.
132. Anthony, T., et al., *Report of the clinical protocol committee: development of randomized trials for malignant bowel obstruction.* J Pain Symptom Manage, 2007. **34**(1 Suppl): p. S49-59.
133. Zorn, M., et al., *Malignant bowel obstruction.* Z Gastroenterol, 2010. **48**(2): p. 264-73.
134. Dilling, H., W. Mombour, and M.H. Schmidt. Internationale Klassifikation psychischer Störungen. ICD-10 V (F) Klinisch-diagnostische Leitlinien, ed. Huber. Vol. 9. 2014, Bern.
135. Rayner, L., et al. *The Management of Depression in Palliative Care: European Clinical Guidelines*. 2010.
136. Deutsche Gesellschaft für Psychiatrie Psychotherapie und Nervenheilkunde, *S3-Leitlinie/Nationale VersorgungsLeitlinie Unipolare Depression*, in http://www.awmf.org/leitlinien/detail/ll/nvl-005.html2009, DGPPN, BÄK, KBV, AWMF, AkdÄ, BPtK, BApK, DAGSHG, DEGAM, DGPM, DGPs, DGRW: Berlin, Düsseldorf.
137. Block, S.D., *Assessing and managing depression in the terminally ill patient. ACP-ASIM End-of-Life Care Consensus Panel. American College of Physicians - American Society of Internal Medicine.* Ann Intern Med, 2000. **132**(3): p. 209-18.
138. Mitchell, A.J., *Are one or two simple questions sufficient to detect depression in cancer and palliative care? A Bayesian meta-analysis.* Br J Cancer, 2008. **98**(12): p. 1934-43.
139. Mitchell, A.J., et al., *Meta-analysis of screening and case finding tools for depression in cancer: evidence based recommendations for clinical practice on behalf of the Depression in Cancer Care consensus group.* J Affect Disord, 2012. **140**(2): p. 149-60.
140. Mitchell, A.J., N. Meader, and P. Symonds, *Diagnostic validity of the Hospital Anxiety and Depression Scale (HADS) in cancer and palliative settings: a meta-analysis.* J Affect Disord, 2010. **126**(3): p. 335-48.
141. Breitbart, W., *Do antidepressants reduce the effectiveness of tamoxifen?* Psychooncology, 2011. **20**(1): p. 1-4.
142. Chochinov, H.M. and B.J. Cann, *Interventions to enhance the spiritual aspects of dying.* J Palliat Med, 2005. **8 Suppl 1**: p. S103-15.
143. Lee, V., et al., *Meaning-making and psychological adjustment to cancer: development of an intervention and pilot results.* Oncol Nurs Forum, 2006. **33**(2): p. 291-302.
144. O'Mahony, S., et al., *Desire for hastened death, cancer pain and depression: report of a longitudinal observational study.* J Pain Symptom Manage, 2005. **29**(5): p. 446-57.
145. Dy, S.M., et al., *Evidence-based recommendations for cancer fatigue, anorexia, depression, and dyspnea.* J Clin Oncol, 2008. **26**(23): p. 3886-95.
146. DGPPN, et al., *S3-Leitlinie/Nationale Versorgungsleitlinie Unipolare Depression*, 2009, DGRW: Berlin-Düsseldorf 2009.
147. Rayner, L., et al., *Antidepressants for depression in physically ill people.* Cochrane Database Syst Rev, 2010(3): p. CD007503.
148. Rayner, L., et al., *Antidepressants for the treatment of depression in palliative care: systematic review and meta-analysis.* Palliat Med, 2011. **25**(1): p. 36-51.
149. Ujeyl, M. and B. Muller-Oerlinghausen, *[Antidepressants for treatment of depression in palliative patients : a systematic literature review].* Schmerz, 2012. **26**(5): p. 523-36.

150. Benkert, O. and H. Hippius, *Kompendium der Psychiatrischen Pharmakotherapie.* Vol. 9. 2013, Berlin: Springer.
151. Desmarais, J.E. and K.J. Looper, *Interactions between tamoxifen and antidepressants via cytochrome P450 2D6.* J Clin Psychiatry, 2009. **70**(12): p. 1688-97.
152. Kelly, C.M., et al., *Selective serotonin reuptake inhibitors and breast cancer mortality in women receiving tamoxifen: a population based cohort study.* BMJ, 2010. **340**: p. c693.
153. Abbasowa, L., L.V. Kessing, and M. Vinberg, *Psychostimulants in moderate to severe affective disorder: A systematic review of randomized controlled trials.* Nord J Psychiatry, 2013.
154. Candy, M., et al., *Psychostimulants for depression.* Cochrane Database Syst Rev, 2008(2): p. CD006722.
155. Gaspar, M.W., M., *Kommunikation in der Palliativmedizin.* Z Palliativmed, 2010.
156. Baile, W.F., et al., *SPIKES-A six-step protocol for delivering bad news: application to the patient with cancer.* Oncologist, 2000. **5**(4): p. 302-11.
157. Frick, E., et al., *A clinical interview assessing cancer patients' spiritual needs and preferences.* Eur J Cancer Care (Engl), 2006. **15**(3): p. 238-43.
158. Puchalski, C. and A.L. Romer, *Taking a spiritual history allows clinicians to understand patients more fully.* J Palliat Med, 2000. **3**(1): p. 129-37.
159. Weber, S., Frick, E., *Zur Bedeutung der Spiritualität von Patienten und Betreuern in der Onkologie*, in *Manual Psychoonkologie*, F. Sellschopp, Gruber, Pouget-Schors, Vollmer, Theml, Vordermaier, Fegg, Editor 2002, Zuckschwerdt: München, Wien, New York. p. 106-109.
160. Fineberg, I.C., M. Kawashima, and S.M. Asch, *Communication with families facing life-threatening illness: a research-based model for family conferences.* J Palliat Med, 2011. **14**(4): p. 421-7.
161. Clayton, J.M., et al., *Discussing end-of-life issues with terminally ill cancer patients and their carers: a qualitative study.* Support Care Cancer, 2005. **13**(8): p. 589-99.
162. Lautrette, A., et al., *End-of-life family conferences: rooted in the evidence.* Crit Care Med, 2006. **34**(11 Suppl): p. S364-72.
163. Witkowski, A. and M.E. Carlsson, *Support group programme for relatives of terminally ill cancer patients.* Support Care Cancer, 2004. **12**(3): p. 168-75.
164. Romer G, B.C., Möller B, *Kinder krebskranker Eltern: Manual zur kindzentrierten Familienberatung nach dem COSIP-Konzept* 2013, Göttingen: Hogrefe.
165. *Gesundheit - Todesursachen in Deutschland 2012*, in *https://www.destatis.de/DE/Publikationen/Thematisch/Gesundheit/Todesursachen/Todesursachen2120400127004.pdf?__blob=publicationFile*2013, Statistisches Bundesamt,: Wiesbaden.
166. RKI and GEKID *Krebs in Deutschland 2007/2008.* Beiträge zur Gesundheitsberichterstattung, 2012. **8**.
167. Nauck, F., E. Klaschik, and C. Ostgathe, *Symptom control during the last three days of life.* Eur J Pall Care, 2000. **7**(3): p. 81-84.
168. Kennedy, C., et al., *Diagnosing dying: an integrative literature review.* BMJ Support Palliat Care, 2014. **4**(3): p. 263-270.
169. Boettger, S. and W. Breitbart, *An open trial of aripiprazole for the treatment of delirium in hospitalized cancer patients.* Palliat Support Care, 2011. **9**(4): p. 351-7.
170. Breitbart, W., et al., *A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients.* Am J Psychiatry, 1996. **153**(2): p. 231-7.
171. Breitbart, W., A. Tremblay, and C. Gibson, *An open trial of olanzapine for the treatment of delirium in hospitalized cancer patients.* Psychosomatics, 2002. **43**(3): p. 175-82.
172. Lin, C.J., et al., *An open trial comparing haloperidol with olanzapine for the treatment of delirium in palliative and hospice center cancer patients.* Journal of Internal Medicine of Taiwan, 2008. **19**(4): p. 346-354.
173. Likar, R., et al., *Efficacy of glycopyrronium bromide and scopolamine hydrobromide in patients with death rattle: a randomized controlled study.* Wien Klin Wochenschr, 2008. **120**(21-22): p. 679-83.
174. Pastrana, T., H. Reineke-Bracke, and F. Elsner, *Empfehlung bei Rasselatmung.* Der Schmerz, 2012. **26**(5): p. 600-608.
175. Wee, B. and R. Hillier, *Interventions for noisy breathing in patients near to death.* Cochrane Database Syst Rev, 2008(1): p. CD005177.
176. Cherny, N.I. and L. Radbruch, *European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care.* Palliat Med, 2009. **23**(7): p. 581-93.
177. Alt-Epping, B., et al., *Sedation in palliative medicine: Guidelines for the use of sedation in palliative care : European Association for Palliative Care (EAPC).* Schmerz, 2010. **24**(4): p. 342-54.

178. Papavasiliou, E.E., S. Payne, and S. Brearley, *Current debates on end-of-life sedation: an international expert elicitation study.* Support Care Cancer, 2014.
179. Bruera, E., et al., *Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial.* J Clin Oncol, 2013. **31**(1): p. 111-8.
180. Nakajima, N., Y. Hata, and K. Kusumuto, *A clinical study on the influence of hydration volume on the signs of terminally ill cancer patients with abdominal malignancies.* J Palliat Med, 2013. **16**(2): p. 185-9.
181. Raijmakers, N.J.H., et al., *Artificial nutrition and hydration in the last week of life in cancer patients. A systematic literature review of practices and effects.* Annals of Oncology, 2011. **22**(7): p. 1478-86.
182. Bundesärztekammer, *Grundsätze der Bundesärztekammer zur ärztlichen Sterbebegleitung.* Deutsches Ärzteblatt, 2011. **108**(7): p. A 346-A348.
183. Bundesärztekammer, *Empfehlungen der Bundesärztekammer und der Zentralen Ethikkommission bei der Bundesärztekammer zum Umgang mit Vorsorgevollmacht und Patientenverfügung in der ärztlichen Praxis.* Deutsches Ärzteblatt, 2010. **18**(107): p. A877-A882.
184. Cohen, M.Z., et al., *The meaning of parenteral hydration to family caregivers and patients with advanced cancer receiving hospice care.* J Pain Symptom Manage, 2012. **43**(5): p. 855-65.
185. Del Rio, M.I., et al., *Hydration and nutrition at the end of life: a systematic review of emotional impact, perceptions, and decision-making among patients, family, and health care staff.* Psychooncology, 2012. **21**(9): p. 913-21.
186. RKI and GEKID, *Krebs in Deutschland 2009/2010*, in *Beiträge zur Gesundheitsberichterstattung des Bundes*2013, Robert Koch-Institut, Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V.: Berlin.
187. WHO, *Global Atlas of Palliative Care at the End of Life*, 2014, Worldwide Palliative Care Alliance: London.
188. WHO, *Palliative care.* Geneva, 2007.
189. Stockler, M.R., et al., *Disarming the guarded prognosis: predicting survival in newly referred patients with incurable cancer.* Br J Cancer, 2006. **94**(2): p. 208-12.
190. ICSI, *Health care guidelines: palliative care- 3d edition*, 2009, Institute for Clinical Systems Improvement.
191. Moss, A.H., et al., *Prognostic significance of the "surprise" question in cancer patients.* J Palliat Med, 2010. **13**(7): p. 837-40.
192. Eagar, K., et al., *An Australian casemix classification for palliative care: lessons and policy implications of a national study.* Palliat Med, 2004. **18**(3): p. 227-33.
193. Stiel, S., et al., *[Validation of the new version of the minimal documentation system (MIDOS) for patients in palliative care : the German version of the edmonton symptom assessment scale (ESAS)].* Schmerz, 2010. **24**(6): p. 596-604.
194. Bruera, E., et al., *The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients.* J Palliat Care, 1991. **7**(2): p. 6-9.
195. Bausewein, C., et al., *The use of two common palliative outcome measures in clinical care and research: a systematic review of POS and STAS.* Palliat Med, 2011. **25**(4): p. 304-13.
196. Hearn, J. and I.J. Higginson, *Development and validation of a core outcome measure for palliative care: the palliative care outcome scale. Palliative Care Core Audit Project Advisory Group.* Qual Health Care, 1999. **8**(4): p. 219-27.
197. Mehnert, A., et al., *Die deutsche Version des NCCN Distress-Thermometers.* Z Psychosom Med Psychother, 2006. **54**(3): p. 213-223.
198. Braun, M., et al., *The burden of spousal caregiving: a preliminary psychometric evaluation of the German version of the Zarit burden interview.* Aging Ment Health, 2010. **14**(2): p. 159-67.
199. Abernethy, A.P., et al., *The Australia-modified Karnofsky Performance Status (AKPS) scale: a revised scale for contemporary palliative care clinical practice [ISRCTN81117481].* BMC Palliat Care, 2005. **4**: p. 7.
200. Oken, M.M., et al., *Toxicity and response criteria of the Eastern Cooperative Oncology Group.* Am J Clin Oncol, 1982. **5**(6): p. 649-55.
201. Katz, S., et al., *Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function.* JAMA, 1963. **185**: p. 914-9.
202. Mahoney, F.I. and D.W. Barthel, *Functional Evaluation: The Barthel Index.* Md State Med J, 1965. **14**: p. 61-5.
203. Gomes, B., et al., *Effectiveness and cost-effectiveness of home palliative care services for adults with advanced illness and their caregivers.* Cochrane Database Syst Rev, 2013. **6**: p. CD007760.

204. Ahlner-Elmqvist, M., et al., *Place of death: hospital-based advanced home care versus conventional care. A prospective study in palliative cancer care.* Palliat Med, 2004. **18**(7): p. 585-93.
205. Brumley, R., et al., *Increased satisfaction with care and lower costs: results of a randomized trial of in-home palliative care.* J Am Geriatr Soc, 2007. **55**(7): p. 993-1000.
206. Cummings, J.E., et al., *Cost-effectiveness of Veterans Administration hospital-based home care. A randomized clinical trial.* Arch Intern Med, 1990. **150**(6): p. 1274-80.
207. Gade, G., et al., *Impact of an inpatient palliative care team: a randomized control trial.* J Palliat Med, 2008. **11**(2): p. 180-90.
208. Jordhoy, M.S., et al., *A palliative-care intervention and death at home: a cluster randomised trial.* Lancet, 2000. **356**(9233): p. 888-93.
209. Rabow, M.W., et al., *The comprehensive care team: a controlled trial of outpatient palliative medicine consultation.* Archives of Internal Medicine, 2004. **164**(1): p. 83-91.
210. Temel, J.S., et al., *Early palliative care for patients with metastatic non-small-cell lung cancer.* N Engl J Med, 2010. **363**(8): p. 733-42.
211. Hanks, G.W., et al., *The imPaCT study: a randomised controlled trial to evaluate a hospital palliative care team.* Br J Cancer, 2002. **87**(7): p. 733-9.
212. Jack, B., et al., *Improving cancer patients' pain: the impact of the hospital specialist palliative care team.* Eur J Cancer Care (Engl), 2006. **15**(5): p. 476-80.
213. DGP, *Positionspapier der AG Stationäre Versorgung zur aktuellen Entwicklung von Qualität, Umsetzung und Abbildbarkeit krankenhausbasierter Palliativversorgung im Vergütungssystem* 2011, Deutsche Gesellschaft für Palliativmedizin.
214. Bakitas, M., et al., *Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: the Project ENABLE II randomized controlled trial.* JAMA, 2009. **302**(7): p. 741-9.
215. Ventafridda, V., et al., *The importance of a home care program for patients with advanced cancer pain.* Tumori, 1985. **71**(5): p. 449-54.
216. McCorkle, R., et al., *A randomized clinical trial of home nursing care for lung cancer patients.* Cancer, 1989. **64**(6): p. 1375-82.
217. Ventafridda, V., et al., *Comparison of home and hospital care of advanced cancer patients.* Tumori, 1989. **75**(6): p. 619-25.
218. Candy, B., et al., *Hospice care delivered at home, in nursing homes and in dedicated hospice facilities: A systematic review of quantitative and qualitative evidence.* Int J Nurs Stud, 2011. **48**(1): p. 121-33.