German Guideline Program in Oncology (GGPO)

Extended S3 Guideline

Palliative care for patients with incurable cancer

Short version 2.2 – September 2020
AWMF- Registration number: 128/001OL

Guideline (Short Version)

DKG KREBSGESELLSCHAFT · Deutsche Krebshilfe HELFEN. FORSCHEN. INFORMIEREN. · AWMF

This is new!
This has changed!

Important New Features in the Extended 2019 Version of the Guideline

A. **Eight new chapters** have been written as part of the second development phase of the guideline (2016-2019) and added to the seven original chapters:

- Defining Goals of Care and Criteria for Clinical Decision-making
- Fatigue
- Sleep-related Illnesses/Nocturnal Restlessness
- Nausea and Vomiting (not Tumour Therapy-related)
- Malignant Bowel Obstruction (MBO)
- Malignant Wounds
- Anxiety
- The Desire to Die

B. In the seven chapters written during the first development phase in 2011-2015, all recommendations were **checked to ensure that they were up-to-date, and updated if necessary** (chapters on organisation of palliative care, communication, breathlessness, cancer pain, constipation, depression, dying phase). For this purpose, a systematic search for prioritised topics and a survey of the experts involved was conducted. As part of the updating process, the recommendations listed below have been revised. In some recommendations, only the level of evidence was changed on the basis of new study data (marked with a #).

- Recommendations 4.4., 4.5., 4.6. and 4.7. (Principles of Palliative Care)
- Recommendations 5.1.# and 5.2.# (Organisation of Palliative Care - Time of Palliative Care Integration)
- Recommendations 5.8.# and 5.9.# (Organisation of Palliative Care - Assessment of Patient Needs and Determining Complexity)
- Recommendation 8.2. (Breathlessness - Assessment)
- Recommendation 8.17. (Breathlessness - Steroids (Glucocorticoids))
- Recommendation 9.5.# (Cancer pain - WHO Step III First-choice Opioids)
- Recommendation 9.28 (Cancer pain - Treatment of Opioid-related Constipation)
- Recommendation 13.1. (Constipation - Assessment/Diagnosis of Constipation)
- Recommendation 13.7. (Constipation - Pharmacological Treatment)
- Recommendation 17.9. (Depression – The Principles of Treatment)
- Recommendations 17.12. and 17.14. (Depression - Treatment of Mild, Moderate or Severe Depression)
- Recommendations 17.18.# and 17.19. (Depression – Non-pharmacological Measures)
- Recommendation 19.1.# (The Dying Phase – Diagnosing Dying)
- Recommendation 19.17. (The Dying Phase – Delirium in the Dying Phase)
- Recommendation 19.24. (The Dying Phase – Dry Mouth (Xerostomia))
- Recommendations 19.33. and 19.36. (The Dying Phase – Medication and Measures in the Dying Phase/Withdrawal of Medication and Measures in the Dying Phase)

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Preface

The goal of palliative care is to improve and maintain quality of life for both the 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 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 in healthcare. This area of medicine has received considerable socio-political support, which is likely due to the demographic 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.

This extended guideline brings together the seven updated topic areas from the first development phase (2011-2015) - the organisation of palliative care, communication, breathlessness, cancer pain, constipation, depression, the dying phase – and the following eight new topics from the second development phase (2016-2019) - nausea and vomiting (not cancer therapy-related), malignant bowel obstruction (MBO), sleep related disorders/nocturnal restlessness, malignant wounds, fatigue, anxiety, goals of care and criteria for decision making, and caring for patients with a desire to die. Thus for the first time, a comprehensive palliative care guideline is available in Germany, which complies with the highest quality standards (S3-level, evidence and consensus based)[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

[1] The „S3-level" (Step 3-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

for Palliative Care (EAPC) [1, 2] etc.) The guideline 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.

The guideline clearly shows how, in addition to decades of experience, there is now also a considerable amount of evidence available from studies in palliative care – more than one third 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 extended guideline is the result of a joint effort. 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 express our deep gratitude to all involved in the development, as this was mainly on a voluntary basis. We also express our special thanks to the Guideline Program in Oncology (DKG, AWMF, DKH[4]) which made this guideline possible through continuous 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

Professor Dr Steffen Simon
Project Leader

Professor Dr Lukas Radbruch
DGP President

This guideline is unrelated to specific cancer entities and part of the German Guideline Program in Oncology (GGPO). With regard to the following topics we refer to the guidelines of the GGPO that already exist or are in preparation:

- S3 Guidelines on different cancer entities
- S3 Guideline “Psycho-oncological Diagnosis, Consultation and Treatment”
- S3 Guideline “Supportive Care in Cancer Patients”
- S3 Guideline “Complementary Medicine in the Treatment of Cancer Patients”

[3] The Leopoldina or German National Academy of Sciences 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 Program 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

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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 Program in Oncology.

1.4. Contact

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1.5. Citation

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1.6. Special Notice

Due to the fact that medicine is subject to a process of continuous development, all information, in particular 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, professionals are asked to consult the patient information 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.

Some recommendations on drugs in this guideline are off-label, i.e. they are recommended outside their licensed indication. Off-label-use medications are marked with an asterisk (*) below. Their clinical application requires the provision of detailed information to the patient and a careful risk-benefit analysis with regard to drug safety, costs and liability law aspects.

For reasons of better readability, the simultaneous use of male and female language forms is avoided. All personal designations apply equally to both sexes.

1.7. Objectives of the Guideline Program for Oncology

With the German Guideline Program 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 implementation 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 patient care. In this way, active implementation

and evaluation programmes are an important element of promoting the German Guideline Program in Oncology. The aim of the programme is to establish a professional basis and a medium-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 quality indicators from guidelines in the certification of tumour centres.

1.8. Further Documents Relating to this Guideline

The content of this short version is based on the full version of the S3 Guideline on 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.

1.9. Guideline Group Composition

1.9.1. Coordination and Editing

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

Guideline Office: Dr Anne Pralong (2011-2019), Verena Geffe M.A. (2011-2015, 2018), Gloria Hanke M.Sc. (2015-2016), Dr Kerstin Kremeike (2017), Dr Susanne König (2017-2018), Center for Palliative Medicine, University Hospital of Cologne

Editing: The coordination group, the leader of the working groups (steering group) as well as some members of the working groups were involved in editing the guideline.

1.9.2. Professional Societies and Authors Involved

- Academy for Ethics in Medicine (AEM) - Professor Dr Alfred Simon (2011-2019), Linda Hüllbrock (2011-2015), Dr Gerald Neitzke (2016-2019)
- Conference of Oncology and Paediatric Oncology Nurses within the German Cancer Society# (KOK) - Ulrike Ritterbusch (2011-2015), Kerstin Paradies (2011-2015)
- Department of Further Professions within the German Association for Palliative Medicine# - Professor Dr Martin Fegg (2011-2015)
- Department of Nursing within the German Association for Palliative Medicine# - Thomas Montag (2011-2015), Elisabeth Krull (2016-2019)
- Department for Psychology within the German Association for Palliative Medicine# - Urs Münch (2016-2019)
- Evangelical Church in Germany (EKD) - Professor Dr Traugott Roser (2011-2019)
- Frauenselbsthilfe nach Krebs e.V., a self-help association for cancer survivors (FSH) - Sabine Kirton (2011-2019)
- German Association for Logopedics (DBL) - Ricki Nusser-Müller-Busch (2011-2019) Dr Ruth Nobis-Bosch (2011-2015), Dr Ilona Rubi-Fessen (2016-2019)
- German Association for Palliative Medicine (DGP) - Professor Dr Gerhild Becker (2011-2015), Professor Dr Lukas Radbruch (2016-2019)
- German Association for Physiotherapy (ZVK) - Dr Beate Kranz-Opgen-Rhein (2011-2015), Andrea Heinks (2011-2015), Reina Tholen (2016-2019)
- German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) - Professor Dr Vjera Holthoff (2011-2019), Professor Dr Barbara Schneider (2016-2019)
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- German Association of Occupational Therapists (DVE) - Carsten Schulze (2011-2019)
- German Association of Psychosocial Oncology (dapo) - Dr Thomas Schopperth (2011-2017), Ruth Hirth (June 2017–2019)
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- German College of General Practitioners and Family Physicians (DEGAM) - Dr Peter Engeser (2011-2015), Professor Dr Nils Schneider (2011-2019), PD Dr Markus Bleckwenn (2016-2019), Professor Dr Klaus Weckbecker (2016-2019)
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- German Pain Society - Professor Dr Winfried Meißner (2011-2015), Dr Stefan Wirz (2011-2019), Dr Michael Schenk (2016-2019)
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- German Sleep Society (DGSM) - Dr Helmut Frohnhofen (2016-2019)
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- German Society for General and Visceral Surgery (DGAV) - Professor Dr Pompiliu Piso (2011-2015), Professor Dr Stefan Fichtner-Feigl (2011-2015), Professor Dr Jörg-Peter Ritz (2016-2019)
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- German Society of Neurology (DGN) - Professor Dr Raymond Voltz (2011-2019), Dr Jan Rémi (2016-2019)
- German Society of Neurosurgery (DGNC) - Professor Dr Roland Goldbrunner (2011-2015), Professor Dr Jürgen Hampl (2016-2019)
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- German Society of Radiation Oncology (DEGRO) - Professor Dr Birgit van Oorschot (2011-2019), Professor Dr Dirk Rades (2011-2015)
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- German Society of Surgery (DGCH) - Professor Dr Stefan Mönig (2011-2015), Professor Dr Stefan Fichtner-Feigl (2011-2015), Professor Dr Wolfgang Schwenk (2016-2019)
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- The German Society of Hospital Pharmacists (ADKA) – Dr Constanze Rémi (2011-2019), Dr Stefan Amann (2011-2015), Alina Marheinke (2016-2019)
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- Working group for Ethics within the German Association for Palliative Medicine (AG Ethik) - Professor Dr Martin Weber (2011-2015), Professor Dr Bernd Alt-Epping (2016-2019)
- Working group for Gynaecological Oncology within the German Cancer Society# (AG AGO) - Professor Dr Volkmar Müller (2016-2019), Professor Dr Jalid Sehouli (2016-2019)
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- Working group for Supportive Care within the German Cancer Society# (AG SMO), Dr Timo Behlendorf (2016-2019), Dr Markus Horneber (2016-2019)

- Working group for Urologic Oncology within the German Cancer Society[#] (AUO) - Dr Chris Protzel (2011-2019)
- Working group on Ear, Nose and Throat Medicine, Oral and Maxillofacial Oncology within the German Cancer Society (AHMO), Professor Dr Barbara Wollenberg (2016-2019)
- Working group Guidelines within the German Association for Palliative Medicine (AG Leitlinien) - Professor Dr Claudia Bausewein (2011-2015), PD Dr Steffen Simon (2016-2019)
- Working group Medical Oncology within the German Cancer Society (AIO) - Dr Ulrich Wedding (2011-2019)

([#]own translation)

In addition to the elected representatives there were 84 experts involved in the development of the guideline who had no voting rights:

Dr Elisabeth Albrecht, Dr Christopher Böhlke, Dr Susanne Ditz, Professor Dr Michael Ewers, Dr Steffen Eychmüller, Professor Dr Thomas Frieling, Dr Sabine Gabrijel, Dr Jan Gärtner, Manfred Gaspar, Dr Christiane Gog, Dr Heidrun Golla, Katja Goudinoudis, Jan Gramm, Dr Birgit Haberland, Michaela Hach, Dr Ute Helm, Professor Dr Peter Herschbach, Inga Hoffmann-Tischner, Franziska Hupke, Dr Elisabeth Jentschke, Professor Dr Frank Jessen, Ute Jungkunz, Dr Jürgen in der Schmitten, Stephanie Jeger, Dr Thomas Jehser, Dr Martin Kamprad, Dr Marianne Kloke, Dr Klaus Kobert, Dr Julia Köpp, Professor Dr Helen Kohlen, Dr Kerstin Kremeike, Dr Tanja Krones, Norbert Krumm, Dr Philipp Lenz, Dr Professor Dr Volker Lipp, Professor Dr Stefan Lorenzl, Vera Lux, Heiner Melching, Dr Elke Müller, Dr Gabriele Müller-Mundt, Professor Dr Friedemann Nauck, Michael Nehls, Wiebke Nehls, Dr Martin Neukirchen, Peter Nieland, Georg Nübling, Professor Dr Günter Ollenschläger, Professor Dr Gerhard Pott[#], Kerstin Protz, Professor Dr Karl Reif, Prof. Hartmut Remmers, Margot Renner, Monika Riepe, Dr Susanne Riha, Dr Roman Rolke, Dr Susanne Roller, Vanessa Romotzky, Dr Justina Rozeboom, Dr Jens Ulrich Rüffer, Professor Dr Rainer Sabatowski, Dr Christian Scheurlen, Dr Jan Schildmann, Dr Christine Schiessl, Professor Dr Barbara Schneider, Dr Christian Schulz, Waldemar Siemens, Dr Uwe Sperling, Dr Andreas Stähli, Professor Dr Ulrike Stamer, Dr Martin Steins, Dr Imke Strohscheer, Professor Dr Michael Thomas, Barbara Uebach, Dr Mariam Ujeyl[#], Dr Andreas Uschok, Dr Annette Vasel-Biergans, Stefanie Volsek, Dr Andreas von Aretin, Professor Dr Andreas von Leupoldt, Professor Dr Maria Wasner, Professor Dr Eva Winkler, Professor Dr Jürgen Wolf, Dr Birgit Weihrauch, Dr Heidi Wurst, Dr Thomas Zander

([#]withdrew during the course of the guideline preparation)

1.9.3. Patient Involvement

The guideline was developed with the direct involvement of two patient representatives. Ms Hilde Schulte (first development phase) and - during the subsequent development - Ms Sabine Kirton from “Frauenselbsthilfe nach Krebs e.V.” (Women's self-help after cancer) (first and second development phase) and Ms. Irmgard Nass-Griegoleit from the Women's Health Coalition e.V. (first development phase) were involved in the preparation of the guideline and took part in the consensus conferences with their own voting rights.

1.9.4. Methodological Support

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

- Professor Dr Ina Kopp (AWMF), Marburg,
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- Dr Monika Nothacker MPH (AWMF), Berlin

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

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

1.9.5. Guidelines Group Contractors

- Development of the quality indicators: Dr Simone Wesselmann MBA, German Cancer Society, Certification area
- Preparation of the patient guideline: Lydia Bothe und Corinna Schaefer, ÄZQ (Agency for Quality in Medicine, Berlin), Berlin

1.10. 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)
CCT	Controlled Clinical Trial
CHMG	Cochrane Haematological Malignancies Group
COPD	Chronic Obstructive Pulmonary Disease
CNS	Central Nervous System
CPAP	Continuous Positive Airway Pressure
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)
EAPC	European Association of Palliative Care

Abbreviation	Explanation
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)
GoR	Grade of Recommendation
HPS	Häusliche Pflegeskala (Home care scale)
i.v.	Intravenous
ICD	Implanted Cardioverter-Defibrillator
ICD-10	International Statistical Classification of Diseases
IPOS	Integrated Palliative care Outcome Scale

Abbreviation	Explanation
LoE	Level of Evidence
MIDOS	Minimales Dokumentationssystem (German version of the Edmonton Symptom Assessment Scale, ESAS)
NaSSA	Noradrenergic and Specific Serotonergic Antidepressant
NDMG	National Disease Management Guideline (Nationale Versorgungsleitlinie)
NRS	Numeric Rating Scale
NSAID	Nonsteroidal anti-inflammatory drugs
OTFC	Oral Transmucosal Fentanyl Citrate
p.o.	per os (oral administration)
p.r.	per rectum (rectal 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

Abbreviation	Explanation
S3	Step 3
s.c.	Subcutaneous
s.l.	Sublingual
SAPV	Spezialisierte Ambulante Palliativversorgung (Specialised Home Palliative Care)
SGB	Sozialgesetzbuch (German Social Security Code)
SIGN	Scottish Intercollegiate Guidelines Network
SPV	Spezialisierte PalliativVersorgung (Specialist Palliative Care)
SSNRI	Selective Serotonin-Noradrenalin-Reuptake-Inhibitor
SSPV	Spezialisierte Stationäre Palliativversorgung (Specialist in-Patient Palliative Care)
SSRI	Selective Serotonin Reuptake Inhibitor
ST	Statement
TTS	Transdermal Therapeutic System
TCA	Tricyclic antidepressant
VAS	Visual Analogue Scale
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 needs of those affected (see chapter Organisation of Palliative Care),
- treating the common symptoms and problems according to current scientific evidence and clinical expertise (see chapters Breathlessness, Cancer pain, Fatigue, Sleep-related Illnesses/Nocturnal Restlessness, Nausea and Vomiting (not Tumour Therapy-related), Constipation, Malignant Bowel Obstruction (MBO), Malignant Wounds, Anxiety and Depression),
- enabling conversations with patients and their families to be held and goals of care to be set together (see chapter Communication and Defining Goals of Care and Criteria for Clinical Decision-making)
- the conversations with people with desires to die can be conducted empathetically and dealing with them in an appropriate and helpful manner is made possible (see chapter The Desire to Die),
- ensuring that support in the dying phase can be appropriately and optimally given (see 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, supportive care and complementary medicine, we also refer to the corresponding S3-guidelines ([4, 5]; Guideline Complementary Medicine, under preparation).

2.1.2. Addressees

Target Patient Group

The target patient group for this guideline is adult patients with incurable cancer for whom the primary goal of care is improving quality of life (see definition of Quality of life in the Glossary). 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 with 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 medical specialist groups and non-physician care providers in the health care system, who treat and care for patients with incurable cancer and who were involved in creating this guideline. In addition, this guideline serves as information for all other specialist groups.

2.1.3. Period of Validity and Updating Procedure

The S3-guideline is deemed valid until the next update. The next update is planned in five years, in 2024. 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:

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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 Program 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 grading 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 Levels Grading System

The German Guideline Program in Oncology methodology requires the guideline authors to allocate recommendation levels in accordance with a formal process of consensus. In accordance with this, structured consensus conferences were held by the AWMF [6]. In the course of these processes, elected representatives (see the section Professional Societies and Authors Involved) came to an agreement on the recommendation levels by voting.

In the guideline, the evidence level (see the section SIGN Evidence Grading System) of the underlying studies is given for all evidence-based statements and recommendations, for which the strength of the recommendation (recommendation level) is also provided.

With regard to the strength of the recommendation, the guideline differentiates between three recommendation 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	shall
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 (shall/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 Program 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 by the coordinators and evaluated according to defined criteria based on the AWMF recommendations (see methodological report, chapter 8). 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 tabular form (see methodological report, chapter 13.1).

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, consultations were held with the mandate holders concerned and the restriction was communicated and implemented, e.g. if a mandate holder was not allowed to vote on certain recommendations because of a potential conflict of interest.

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 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 [7, 8]. 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* [9]. 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 [10]. 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 [11, 12].

FAMILY CARERS

(Synonym: relatives, loved ones)

People who, through family or another close social relationship (as an individual relationship between two people or systemically as "feeling as if one belongs to a system of relationships"), belong to the close environment of the patient, such as children, parents, friends or neighbours.

INCURABILITY

Incurability is not a uniformly defined term. In this guideline, the term is used in disease situations in which there is no relevant probability of being able to cure and overcome the oncological disease with a tumour-specific therapy. Criteria for incurability are therefore:

- the progression tendency of the natural, untreated course of the disease,
- the extent and probability of treatment being able to influence the course of the disease,
- the availability of the treatment options in question and
- the individual willingness of those affected to accept corresponding treatment offers.

This results in a considerable variance in the time of the courses of incurable cancers from months to many years.

Disease situations in which the probability of a cure is low but not completely impossible (e.g. locally advanced but not remote metastatic cancers, or situations with only a few isolated, fully resectable metastases, so-called "oligometastasis") in normative-evaluative terms can lead to categorisation as both curable and incurable. In these cases, the principles of palliative care laid down in this guideline should be applied.

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 the 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 [13]. 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 him/herself 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 physical, psychological, social and everyday aspects of well-being and functional capacity. 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 Sections 39 und 42 German Social Security Code (Sozialgesetzbuch, 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 ("Supportive Therapie bei onkologischen PatientInnen" - Langversion 1.1, 2017) [5], 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 transparent 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 [14, 15].

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 *shall* 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 *shall* 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. Perceive the patients in their cultural, ideological and religious identity; 4. Determine realistic goals of care; 5. Be informed about organisational forms of palliative care; 6. Create conditions which respect the patient's privacy. [Modified 2019]		EC	
4.5.	The following principles *shall* 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. Use preventive measures and 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. [Modified 2019]		EC	
4.6.	If there are any questions regarding drug application, the expertise of a pharmacist *should* be obtained.		EC	

No.	Recommendations/Statements	GoR	LoE	Sources
	[New 2019]			
4.7.	The patient's wishes are to be considered in every phase of the treatment, including the dying phase. If the patient is not able to express himself/herself, 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. [Modified 2019]	EC (Statement)		
4.8.	The following principles *shall* 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 of care; 3. Be informed about specific support offers for family carers.	EC		
4.9.	The following principles *shall* 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 undertake professional development; 4. Create suitable basic conditions through people in leadership positions.	EC		
4.10.	Criteria for the quality of palliative care *shall* include patient-reported outcomes (PRO).	EC		

5. Organisation of Palliative Care

Working Group Leaders: Bernd Oliver Maier, Raymond Voltz

5.1. 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 offers to the needs of both the 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 2014 was 1,908 per 100,000 residents, the mortality was 275 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 [16]. 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 [17].

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 expertise, 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 Figure 1).

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 divided into three or even four tiers (see WHO [18], 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 an insight of the situation in Germany.

5.2. Clinical Pathway for Patients and Family Carers

The clinical pathway for patients with terminal cancer and their family carers (Figure 1) 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 sections.

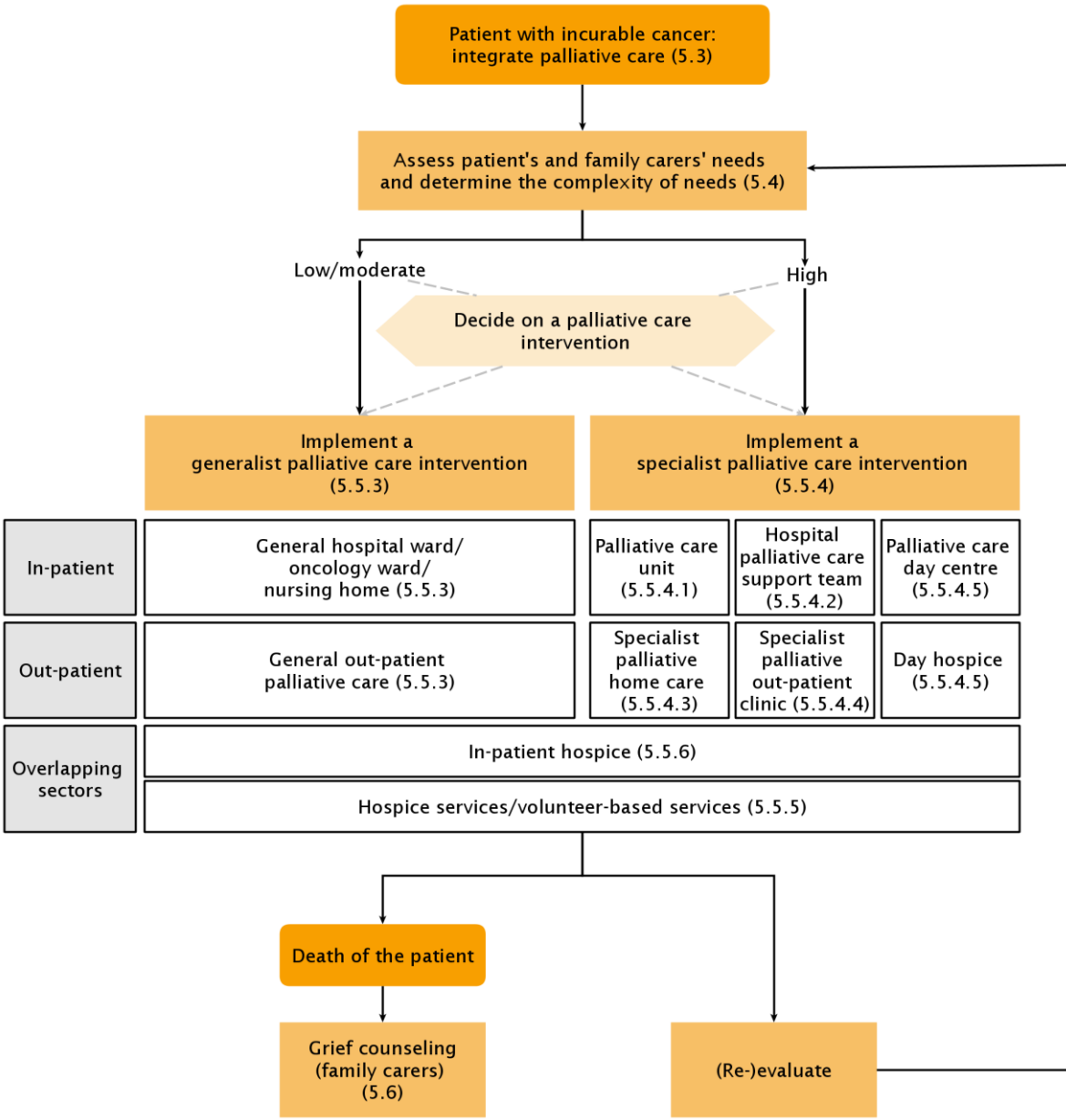


Figure 1: Clinical pathway for patients and family carers

5.3. Integration of Palliative Care

5.3.1. Time of Palliative Care Integration

No.	Recommendations	GoR	LoE	Sources
5.1.	All patients with cancer *shall* have access to information on palliative care, regardless of what disease stage they are in.		EC	
5.2.	All patients *shall* be offered palliative care following the diagnosis of incurable cancer, regardless of whether cancer-specific therapy is being implemented. [Modified 2019]	A	1-	[19-26]

The assessment that a cancer is "incurable" is based on prognostic probabilities (see Glossary). These statistical findings are always associated with a prognostic uncertainty in isolated cases, which means that every case has to be individually assessed [27]. 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?" [28, 29]. 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.

5.3.2. Integration of Oncological Services and Palliative Care

No.	Recommendations	GoR	LoE	Sources
5.3.	Specialist palliative care *shall* be integrated into oncological decision-making processes, e.g. by means of participation in interdisciplinary tumour conferences.		EC	
5.4.	Patients with incurable cancer who are treated within the context of specialised palliative medicine (palliative ward, specialist palliative home care, e.g. SAPV) *should* have access to oncological counselling. [New 2019]		EC	

5.4. Assessment of Patient Needs and Determining Complexity

No.	Recommendations	GoR	LoE	Sources
5.5.	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 *shall* be assessed regularly and when there is a change in the clinical situation.	EC		
5.6.	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		
5.7.	In patients with incurable cancer, the complexity of the situation *shall* 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		
5.8.	Patients *should* be offered a needs assessment by an SPC team after the diagnosis of incurable advanced cancer. [New 2019]	A	3	[19-26]
5.9.	Patients with incurable cancer and a highly complex situation *shall* receive specialist palliative care. [Modified 2019]	A	3	[22, 24, 25]

	Dissenting opinion of DEGAM on recommendations 5.8 and 5.9
	In recommendations 5.8 and 5.9, DEGAM is in favour of a "should" (recommendation level B), since the deployment of the SPC team in standard care should be reserved for complex situations.

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 either the category low/moderate or high. The complexity is determined by many different factors – the factors specified in Table 3 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 results 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** [30]. 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) [30] (see Table 3).

Table 3: 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) [31] (German version of the Edmonton Symptom Assessment Scale, ESAS), Edmonton Symptom Assessment System (ESAS/revised version ESAS-r) [31, 32], Palliative Care Outcome Scale (POS) [33, 34], Distress-Thermometer and problem list [35]
2. Distress of family carers	e.g. German version of the Zarit Burden Interview (G-ZBI) [36], 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) [37], Eastern Cooperative Oncology Group (ECOG) [38], Activities of Daily Living (ADL) [39], Barthel Index [40]
4. Phase of illness:	**Description**
a) stable	Symptoms under control, patient needs satisfied by care plan, stable family situation
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.

5.5. Deciding on a Palliative Care Intervention

5.5.1. Differentiation between Generalist and Specialist Palliative Care

Generalist Palliative Care

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 (e.g. general practitioners, oncologists).
- 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 section Generalist Palliative Care, the tasks and possibilities of generalist palliative care will be defined and described

Specialist Palliative Care

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 the German Social Security Code (Sozialgesetzbuch, SGB V (§ 37b, § 132d)), as well as the guidelines from the "Gemeinsamen Bundesausschusses" (Joint Federal Committee[1]) 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 (Operationen- und Prozedurenschlüssel - Operation and Procedure Classification System) 8-982 and 8-98e.

Indicators for assigning a health care service to the category of specialist palliative care are (see also section Specialist Palliative Care):

- 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.

[1] 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.

- 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 [41].
- 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 section In-patient Hospice) and the hospice service or voluntary work (see section Hospice Services/Volunteer-based Services). Thus, they are addressed following the sections on generalist (Generalist Palliative Care) and specialist palliative care (Specialist Palliative Care) in an individual chapter.

5.5.2. 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 07.2019). 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:

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)

5.5.3. Generalist Palliative Care

No.	Recommendations	GoR	LoE	Sources
5.10.	Everyone who is affected by incurable cancer *shall* have access to generalist palliative care.	EC		

No.	Recommendations	GoR	LoE	Sources
5.11.	Everyone involved in the care of patients with incurable cancer *shall* be able to assess palliative care needs and recognise need for palliative action in order to initiate palliative care.		EC	
5.12.	Generalist palliative care of a patient with incurable cancer *shall* 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 goals of care • Coordinating care • Involving specialist palliative care, if indicated		EC	
5.13.	Every physician involved in generalist palliative care of a patient with incurable cancer *shall* be able to assess the indication for specialist palliative care and integrate this into the treatment based on the patient's needs.		EC	
5.14.	Everyone involved in generalist palliative care of a patient with incurable cancer *shall* attain a basic qualification in palliative care, which has been undertaken by means of a training course or further education and is regularly renewed.		EC	

5.5.4. Specialist Palliative Care

No.	Recommendations	GoR	LoE	Sources
5.15.	A specialist palliative care core team *shall* consist of members from at least three professional groups (physician, nursing profession and other professional groups). Of these at least the physician and nurse *shall* possess a specialist palliative care qualification.	A	1-	[42-48]
5.16.	Members of the specialist palliative care core team *should* primarily or exclusively work in specialist palliative care.		EC	

5.5.4.1. Palliative Care Unit

No.	Recommendations	GoR	LoE	Sources
5.17.	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.		ST (EC)	

No.	Recommendations	GoR	LoE	Sources
5.18.	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 goals of care • Complex medical or nursing care • Home care is overstrained or uncertain	0	4[1]	-
5.19.	A palliative care unit *shall* 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 goals of care 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 • Caring for the patient during the dying phase • Rituals of saying goodbye and remembering • Arranging grief counseling	A	4	-
5.20.	Treatment and care on a palliative unit *shall* be provided by an independent, specialised, qualified and multi-professional team.	A	4	-
5.21.	The palliative care unit *shall* act as an independently organised and spatially separated unit.	A	4	-
5.22.	Treatment on a palliative care unit *should* be provided in an appropriate setting such as providing single rooms, overnight stay opportunities for family carers, homelike communal meeting areas and access to outdoor areas.	B	4	-
5.23.	To ensure qualified treatment on a palliative care unit, a medical and nursing service with a specialised palliative care qualification *shall* be made available 24 hours a day and 7 days a week.	A	4	-
5.24.	The team on a palliative care unit *shall* carry out the following measures to ensure process quality:	A	4	-

[1] 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
	• Individual treatment planning • Regular evaluation of goals of care • 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.			

5.5.4.2. Hospital Palliative Care Support Team

No.	Recommendations	GoR	LoE	Sources
5.25.	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.	ST (EC)		
5.26.	Every hospital that treats patients with incurable cancer *shall* provide a palliative care support team.	0	4[1]	-
5.27.	Patients with incurable cancer *shall* be offered a contact to a palliative care support team during a hospital stay.	A	1+	[45, 49, 50]
5.28.	A hospital palliative care support team *shall* 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 goals of care 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	A	4	-

[1] 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
	• Supporting members of the main care team			
5.29.	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	-
5.30.	Consultation and shared treatment by the hospital palliative care support team *shall* take place in close coordination with the main care team.	A	4	-
5.31.	The hospital palliative care support team *should* carry out the following measures to ensure process quality: • Individual treatment planning • Regular evaluation of goals of care • Regular evaluation of performed treatment measures • Exchange between referrers and those continuing the treatment, as well as coordination between in-patient and outpatient 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 [51]. 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 short term consulting activity in the narrow sense. Therefore, this guideline forgoes using the often-used term "palliative care consult".

5.5.4.3. Specialist Palliative Home Care

No.	Recommendations	GoR	LoE	Sources
5.32.	This guideline distinguishes between "specialist palliative home care" and "SAPV":	ST (EC)		

No.	Recommendations	GoR	LoE	Sources
	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 ("Sozialgesetzbuch", German Social Security Code) V.			
5.33.	Specialist palliative home care *shall* complement already existing health care services if the latter 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[1]	-
5.34.	Specialist palliative home care *shall* 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 goals of care 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-	[41, 43, 52, 53]
5.35.	Specialist palliative home care *shall* be available round-the-clock.	A	4	-
5.36.	The specialist palliative home care team *shall* work as an independent and multi-professional team (physician, nurse and another professional group).	A	1-	[42-46, 54, 55]
5.37.	A specialist palliative home care team *shall* carry out the following measures to ensure process quality: • Individual treatment planning • Regular evaluation of goals of care • Regular evaluation of performed treatment measures	A	4	-

[1] 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
	• 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.			
5.38.	Specialist palliative home care *shall* 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	-

In the context of this guideline, the abbreviation "SAPV" (Spezialisierte Ambulante Palliativ-Versorgung) refers to the home care entitlement stated by law. In turn, the term "specialist palliative home care" ("ambulante spezialisierte 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).

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 of the German Social Security Code (Sozialgesetzbuch, 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).

5.5.4.4. Specialist Palliative Out-patient Clinic

No.	Recommendations	GoR	LoE	Sources
5.39.	A palliative out-patient clinic is an integral part of specialist ambulatory palliative care.	ST (EC)		
5.40.	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+	[47, 48]
5.41.	A palliative out-patient clinic *shall* provide the following components when caring for patients with incurable cancer to improve quality of life:	A	1+	[47, 48]

No.	Recommendations	GoR	LoE	Sources
	• 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 goals of care 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			
5.42.	Consultation and shared treatment in the palliative out-patient clinic *shall* take place in close coordination with the main health care provider or the main care team.	A	1+	[47, 48]

A palliative out-patient clinic is a facility for out-patients, which offers 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.

5.5.4.5. Palliative Day-care Centre and Day Hospice

No.	Recommendation	GoR	LoE	Sources
5.43.	The palliative day-care centre and the day hospice are specialist offers for out-patients with incurable cancer and limited life-expectancy.		ST (EC)	

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 provides a day care service to out-patients.

5.5.5. In-patient Hospice

No.	Recommendations	GoR	LoE	Sources
5.44.	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 (“Sozialgesetzbuch”, German Social Security Code) V and the general agreement in connection with these.		ST (EC)	

No.	Recommendations	GoR	LoE	Sources
5.45.	Palliative care treatment and hospice care in an in-patient hospice *shall* 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[1]	-
5.46.	An in-patient hospice *shall* 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, 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 counselling	A	4	-
5.47.	Palliative and hospice care *shall* be provided by a qualified multiprofessional 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	-
5.48.	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	-
5.49.	If necessary, specialist palliative home care *shall* be consulted.	A	4	-
5.50.	An in-patient hospice *shall* 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 *shall* have a comfortable-familiar character with communal meeting areas and areas to enable privacy.	A	4	-

[1] 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.

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 of the German Social Security Code (Sozialgesetzbuch, 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.

5.5.6. Hospice Services/Volunteer-based Services

No.	Recommendation	GoR	LoE	Sources
5.51.	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	

5.5.7. Family Carers

See also section Communication with Family Carers

No.	Recommendations	GoR	LoE	Sources
5.52.	Family carers of patients with incurable cancer *shall*, 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[1]	-
5.53.	Family carers of patients with incurable cancer *shall* 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+	[56]

[1] 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
5.54.	Family carers of patients with incurable cancer *shall* be informed of available support offers such as self-help groups and training for family carers.	EC		

5.6. Grief and Bereavement Counseling

No.	Recommendations	GoR	LoE	Sources
5.55.	Facilities, which care for and treat dying people, *shall* develop a culturally sensitive way of saying goodbye and grieving, specific to their own facility, which enables a dignified farewell for patients, family carers and members of staff.	A	4[(1)]	-
5.56.	Patients with incurable cancer and their family carers *shall* have access to information on grief counselling at all stages of the illness.	A	4	-
5.57.	If desired, family carers of patients with incurable cancer *should* be informed of the offer of qualified grief counselling, also following the patient's death.	B	4	-

When and by whom information concerning grief services and counselling should be provided is shown in Table 4.

Table 4: Grief counselling 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 counselling 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 counselling in one-on-one discussions or groups	• Patients • Family carers	Qualified grief counsellor, 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 counselling in one-to-one settings or groups • Identification of possible emergence of complicated grief	• Family carers • Team of carers	Qualified grief counsellor, e.g. from hospice care, pastoral care or psycho-oncologists

Time/trigger point	Offer/intervention	Addressees	Person responsible
In cases of already diagnosed or suspicion of complicated grief	Psychotherapeutic grief counselling in one-to-one settings or in a group setting	Family carers with complicated grief reactions	Qualified psychotherapists, psychologists, psychiatrists

6. Communication

Working Group Leaders: Martin Weber, Joachim Weis

6.1. 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." [57]. 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 addressed in the fourth section. This section will highlight the specific aspects of discussions with family carers, such as family meetings, and also 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.

Overall, the recommendations in this chapter are consistent with the main statements of the ASCO guidelines on communication in oncological care, particularly on communication at the end of life [59].

6.2. The Principles of Patient-centred Communication

No.	Recommendations	GoR	LoE	Sources
6.1.	In order to ensure patient-centred communication with patients with incurable cancer, health care providers *shall* • 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	
6.2.	When communicating with patients with incurable cancer and various cultural and religious backgrounds, health care providers *shall* take the personal, cultural and religiously linked principles and values into account.		EC	
6.3.	In cases of impaired communication of the patient with incurable cancer, non-verbal and technical possibilities for the improvement of communication *shall* be offered.		EC	
6.4.	All health care providers who care for patients with incurable cancer *shall* train and develop their communicative competencies through suitable further training. They *should* regularly reflect on their communicative competences e.g. through supervision/intervision.		EC	

6.3. Conversations about Serious Changes in the Course of a Disease

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

No.	Recommendations	GoR	LoE	Sources
6.7.	Information *shall* be gradually conveyed with regular reassurance as to whether and to what extent the patient has understood. Furthermore, the patient *shall* be explicitly encouraged to ask questions.		EC	
6.8.	Emotional experience and spiritual needs *shall* 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 [58]. 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 informational 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 [59-61]. 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?

6.4. Raising the Issue of Dying and Death

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

6.5. Communication with Family Carers

No.	Recommendations	GoR	LoE	Sources
6.10.	Family carers *shall* be appreciated in their role as providers of support and as affected persons. They *shall* be asked about their needs and – if necessary – encouraged to accept offers of support.		EC	
6.11.	Family meetings *shall* 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 goals of care; • if diverging opinions arise in the family in the course of palliative care. The facilitator of the family meeting *shall* bring up various points of view and encourage all those involved to take part in the communication.		EC	
6.12.	If the patient agrees, family carers *shall* 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 *shall* be respected and communication about underlying fears shall be offered.		EC	
6.13.	The needs of parents with incurable cancer regarding information, family meetings and if necessary further support with respect to interaction with children *shall* be identified. The affected parents with incurable cancer *shall* 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 cancer *shall* be involved in communication about the disease in all phases of treatment in an age appropriate manner and in accordance with their needs.		EC	
6.14.	Underage children as family of patients with incurable cancer *shall* 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) [62]. 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 [63-65].

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 [66]. 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 opportunities to introduce support on-site.

6.6. Advance Care Planning (ACP)

No.	Recommendations	GoR	LoE	Sources
6.15.	The topics of discussions in Advance Care Planning *shall* 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	
6.16.	Patients with incurable cancer *shall* be offered Advance Care Planning.		EC	
6.17.	Facilitating communication about Advance Care Planning *shall* be offered early on and repeated in the case of considerable changes in the state of health and prognosis.		EC	
6.18.	Conversations on Advance Care Planning *should* be supported by informative written material and content and outcomes *should* be documented.		EC	
6.19.	With the patient’s consent, family carers and, if appropriate, the health care proxy agent/legal representative *shall* 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 – anticipatory care planning” was chosen in the original German version because it best encompasses all the aspects of ACP. The terminology used in Germany, "Behandlung im Voraus planen (BVP) - Planning treatment in advance (PTA)" describes a concept for the

realisation of effective living wills, which includes a discussion process and the inclusion of relevant regional health care structures. However, PTA requires the involvement of a qualified or certified facilitator. Paragraph 132 (g) of the Social Security Code V (SGB V) uses the term "health care planning for the last phase of life" only for people in care facilities and is therefore also too narrow in terms of its definition for this guideline. Finally, the term “umfassende Versorgungsplanung – comprehensive care planning” integrates a wide variety of issues, which should be discussed at the end of life but is further removed from the English term, Advanced Care Planning.

7. Defining Goals of Care and Criteria for Clinical Decision-making

Working Group Leaders: Bernd Alt-Epping, Alfred Simon

7.1. Introduction

No.	Recommendations	GoR	LoE	Sources
7.1.	The recommendations and statements in this chapter do not apply only to patients with incurable cancer. The limitation to this patient group is due to the context of this guideline.		EC (statement)	

Within the context of incurable cancer and a limited survival time prognosis, a large number of decisions have to be met, which relate not only to medical-therapeutic, nursing and care-related aspects of life, but also to ethical-normative ones: Should further diagnostics be carried out or therapy directed against the tumour disease? What should happen if a complication occurs? Who should express my consent or rejection of medical interventions on my behalf if I cannot give my consent myself? Where would I like to die? What should happen to my body after my death? and many more.

Against the palliative care background of finiteness and the quality of life, even the decision on the start, continuation or termination of a medical intervention implies to a large extent the consideration of individual values relating to patients, family carers and the therapeutic environment. It is therefore correct to present the processes and criteria underlying a treatment decision as well as decision-making aids and their underlying evidence in a guideline for incurable cancer patients.

When caring for patients with "incurable" cancer, it should be taken into account that patients often find themselves in a situation, in which it is unclear whether their disease is "incurable" or "curable" (in the sense of a persistent complete remission). For example, patients with curatively treatable haematological neoplasias have a significant probability of healing, but at the same time also a high probability of dying from complications in cases where the underlying disease is cured. Or there are cases where the treatment is carried out with a "curative" intention but the probability of a cure is low. This may apply, for example, to patients with solid tumours in locally advanced stages or to patients with limited remote metastasis of the underlying disease ("oligometastasis").

Even if these patients are not considered a priori to be "incurable", the decision-making processes and criteria presented below also apply to these patients with an uncertain prognosis. The principles of clinical decision-making are ultimately applicable to all areas of medicine; the limitation to patients with incurable cancer presented below is due solely to the context of this guideline.

For the communication processes that accompany this decision-making process, see the chapter on Communication, in particular the sections The Principles of Patient-centred Communication and Conversations about Serious Changes in the Course of a Disease.

7.2. Fundamental Aspects of the Clinical Decision-making Process

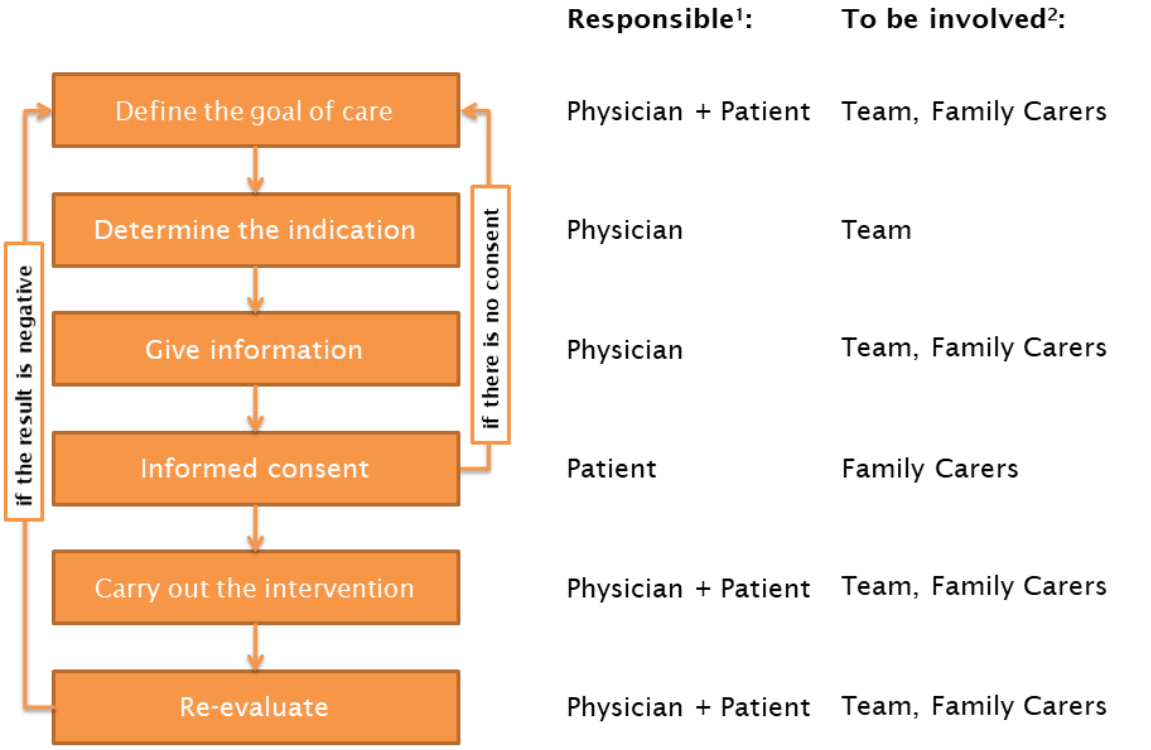
No.	Recommendations	GoR	LoE	Sources
7.2.	Defining goals of care and deciding on the start, continuation or termination of medical interventions for patients with incurable cancer *shall* be carried out within the framework of a participatory clinical decision-making process, i.e. with the active participation of the patient.		EC	
7.3.	Family carers and other trusted persons of a patient with incurable cancer *shall* be involved in the clinical decision-making process to the extent that this is desired by the patient.		EC	
7.4.	Decisions about the medical intervention at the end of life *should* be made and documented at an early stage of the disease - also in anticipation.		EC	
7.5.	Ethics consultation *should* be provided in difficult or controversial decision-making situations associated with the treatment of patients with incurable cancer.		EC	

7.3. Defining Goals of Care

No.	Recommendations	GoR	LoE	Sources
7.6.	When goals of care of patients with incurable cancer are defined, the current stage of the disease, the available treatment options and the patient's wishes, values and goals *shall* be taken into account.		EC	
7.7.	Goals of care associated with the treatment of patients with incurable cancer *shall* be regularly reviewed and adapted to the current stage of the disease and treatment situation and/or to the changed wishes, values and goals of the patient.		EC	
7.8.	When caring for patients with incurable cancer who pursue unrealistic goals of care, a medical intervention *can* be rejected by the physician with reference to the questionable medical indication. If there is no indication, the intervention *shall* be rejected.		EC	

7.4. Deciding on the Start, Continuation or Termination of Medical Interventions

No.	Recommendations	GoR	LoE	Sources
7.9.	The key criteria in deciding on the start, continuation or termination of a medical intervention are the medical indication and the patient's consent.	EC (statement)		
7.10.	In the treatment of patients with incurable cancer, the indication *shall* be determined with regard to the defined goal of care and take into account both the achievability of the goal of care and the possible benefits and risks of the medical intervention for the patient.	EC		
7.11.	Consent to the implementation of a medical intervention assumes that the patient with incurable cancer who is capable of giving consent is appropriately informed about the planned intervention, its possible benefits and risks and possible alternatives.	EC (statement)		
7.12.	The consent to a medical intervention may be revoked at any time by the patient with incurable cancer.	EC (statement)		
Principles 4.7.	The will of the patient must be complied with in every phase of treatment, including the dying phase. If the patient is not able to express himself/herself, 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.	EC (statement)		
7.13.	In the case of a patient with incurable cancer who is not capable of giving consent, in addition to the health care proxy agent, close relatives and other people trusted by the patient *shall* also be involved in deciding on the start, continuation or termination of a medical intervention.	EC		
7.14.	During the course of treatment, regular assessments *shall* be carried out to determine if the medical indication and the consent of the patient with incurable cancer still exist for the specific medical interventions and, if necessary, whether the therapy plan should be adapted or the goal of care changed.	EC		



[1] If there are substantiated doubts as to the patient's ability to give consent, his or her health care proxy agent (by means of a written power of attorney for personal we-fare or a legal representative) is also to be consulted. The proxy agent's task is to support the patient in the decision-making process and to represent him/her if necessary.
[2] If medically meaningful or desired by the patient.

Figure 2: Decision tree for deciding on a medical intervention and carrying it out

7.5. Special Situations

No.	Recommendations	GoR	LoE	Sources
7.15.	Particularly in cases of prognostic uncertainty, the criteria underlying the indication and treatment decision *should* be explicitly formulated and documented.		EC	
7.16.	In patients with incurable cancer, cultural aspects *should* be communicated in a sensitive manner and taken into account when defining the goal of care and making the treatment decision.		EC	

7.6. Decision-making Tools

No.	Recommendations	GoR	LoE	Sources
7.17.	For patients with incurable cancer, decision-making aids (e.g. in the form of brochures, videos, internet programmes or decision boards) *can* be used to support joint clinical decision-making and the Advance Care Planning.	1-	0	[69-86]

8. Breathlessness

Working Group Leaders: Claudia Bausewein, Helgo Magnussen (2011-2015), David Heigener (2016-2019 for the update)

8.1. 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” [67, 68]. 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) [69]. An international group of experts has proposed to use the term "chronic breathlessness syndrome" for patients with refractory breathlessness [70]. 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 [71]. Patients with continuous breathlessness complain of uninterrupted distress due to breathlessness which, albeit, typically varies significantly in its intensity [72]. 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). An episode can be caused by one or more triggers [73, 74].

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% [75]. The highest prevalence was shown in patients with lung cancer (74.3%). These results correlate with data from other countries [76-78]. Cancer patients with pulmonary, pleural or mediastinal affections suffer breathlessness more frequently and more severely [77, 79]. Breathlessness will increase in its frequency and severity over the course of the illness [76, 80, 81].

Breathlessness is not only a distressing symptom for patients but also for their family carers [82, 83]. In comparison to other symptoms, breathlessness causes the highest levels of distress [84]. Patients often describe significant restrictions in their physical abilities, which can lead to social isolation among other things [85]. Breathlessness is closely related to anxiety and panic [67, 68, 72, 86]. There appears to be a connection between anxiety/panic and breathlessness, in that breathlessness causes anxiety and in

turn anxiety/panic worsens breathlessness [87]. Patients describe this as a vicious circle, which often leads to acute emergencies, hospital admissions and need of help [87, 88].

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

8.2. Assessment

No.	Recommendations	GoR	LoE	Sources
8.1.	Breathlessness *shall* be assessed by the patient's subjective experience, e.g. as part of an evaluation of several symptoms.		EC	
8.2.	When undertaking a comprehensive assessment of breathlessness (incl. episodic 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 [Modified 2019]		EC	
8.3.	A repeated assessment of breathlessness before, during and following a symptomatic therapy *shall* be part of the evaluation.		EC	
8.4.	For incurable cancer patients with breathlessness and considerable cognitive or physical restrictions, the assessment of breathlessness *shall* be carried out by others (family carers or health care team).		EC	
8.5.	Potentially treatable causes of breathlessness *shall* be identified.		EC	
8.6.	Where causal treatment of breathlessness is possible, it *shall* be carried out before or parallel to a symptomatic treatment. In this case the following *shall* be taken into consideration: • Consideration of medical indication • Burden and benefit for the patient • Patient's wishes		EC	

A symptomatic treatment shall either precede or occur simultaneously with optimal treatment of the underlying condition and excluding treatable causes. This requires a close cooperation with relevant specialists (e.g. oncology, pulmonology, radiotherapy). In cancer patients, the following potentially reversible causes are often responsible for breathlessness (see Table 5).

Table 5: 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

8.3. Non-pharmacological measures

No.	Recommendations	GoR	LoE	Sources
8.7.	In patients with incurable cancer and breathlessness, non-pharmacological measures for the relief of breathlessness *shall* be used, e.g. informing the patient about the symptom of breathlessness, calming or relaxation, breathing exercises or cooling of the face.	EC		
8.8.	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-	[89-91]
8.9.	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-	[89]

8.4. Opioids

No.	Recommendations	GoR	LoE	Sources
8.10.	Oral[1] or parenteral opioids* *shall* be administered to patients with incurable cancer and breathlessness for the symptomatic relief of breathlessness. [Reviewed 2019, new literature added]	A	1+	[92-109]
8.11.	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	[110]
8.12.	There is no evidence that a correct treatment of breathlessness with opioids leads to clinically relevant respiratory depression. [Reviewed 2019, new literature added]	ST	1+	[92-96, 98, 101-107, 111]

* Off-label use

Opioids are the only group of drugs with sufficient study evidence with regard to the symptomatic relief of breathlessness [114, 117]. In view of this, morphine was licensed for this indication in Australia for the first time worldwide (see Australian Register of Therapeutic Goods (ARTG) www.ebs.tga.gov.au, approval of morphine sulphate pentahydrate 10 to 20 mg).

With pre-existing renal impairment and opioid therapy, increased vigilance is required (see Table 6) [112]. However, pre-existing renal impairment must not lead to a delayed administration of opioids for symptomatic treatment of breathlessness [110]. 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 7). 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 [110, 112-114].

Table 6: 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 [110, 112])

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 a reduction in 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.

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

Level of renal insufficiency	Use of opioids
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 7: 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 [110, 112, 114])

Opioid	Active metabolites with renal excretion	Removed by dialysis?[1]	Safe and effective use in dialysis patients?[2]
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

[1] 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.

[2] 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 on dialysis is a generalization and can vary from patient to patient. The classification is based predominantly on case reports and clinical experience.

8.5. Other drugs

8.5.1. Benzodiazepines

No.	Recommendations	GoR	LoE	Sources
8.13.	Benzodiazepines* *can* be administered for the relief of breathlessness if treatment with opioids is not effective. [Reviewed 2019, new literature added]	0	1+	[115, 116]
8.14.	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-	[106, 117]

* Off-label use

8.5.2. Phenothiazines

No.	Recommendations	GoR	LoE	Sources
8.15.	Phenothiazines* *should not* be administered to patients with incurable cancer for the relief of breathlessness.	B	1-	[118-121]

* Off-label use

8.5.3. Antidepressants, buspirone

No.	Recommendations	GoR	LoE	Sources
8.16.	Antidepressants* or buspirone* *should not* be administered to patients with incurable cancer for the relief of breathlessness.	B	1-	[122-129]

* Off-label use

8.5.4. Steroids (Glucocorticoids)

No.	Recommendations	GoR	LoE	Sources
8.17.	Steroids* *can* be administered to patients with incurable cancer for the relief of breathlessness. [Reviewed 2019, new literature added]	0	1+	[130-148]

* Off-label use

8.6. Oxygen

No.	Recommendation	GoR	LoE	Sources
8.18.	Oxygen *should not* be administered to non-hypoxaemic patients with incurable cancer for the relief of breathlessness.	B	1+	[69, 149-151]

9. Cancer pain

Working Group leaders: Winfried Meißner, Lukas Radbruch

9.1. 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" [152]. 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 [9].

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 [113]. (As soon as the EAPC guideline is updated, the update will also be included in this S3-guideline; correct as of: early 2019). 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 section Metamizole). 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.

The WHO has developed evidence-based guidelines for the pharmacological and radiotherapeutic treatment of tumour pain in adolescents and adults and published them on the occasion of World Cancer Day in February 2019 (www.who.int/ncds/management/palliative-care/cancer-pain-guidelines/en/). Compared to the last version of the WHO guidelines on tumour pain treatment dated 1998, the new guidelines are formulated differently in some points. For example, the WHO pain-relief ladder can only be found in the appendix, while the guidelines no longer distinguish between WHO-II and WHO-III opioids. In addition to morphine, hydromorphone and oxycodone are recommended. For the discontinuation of opioid therapy, non-retarded or retarded forms of administration can be selected according to the recommendations, but in all cases the long-term medication should be supplemented with a fast-acting as-needed medication. The recommendations correspond to those set out in this guideline.

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 [153]. 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 [154]. 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 [155-157]. 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.

9.2. Pain Assessment

No.	Recommendations	GoR	LoE	Sources
9.1.	Pain history and a pain related clinical examination *shall* be part of every diagnosis of pain.		EC	
9.2.	Where possible the assessment of pain intensity *shall* 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	
9.3.	In patients with incurable cancer and pain, as well as cognitive and physical impairment, the assessment of pain intensity *shall* be made by family carers or the health care team.		EC	

9.3. Application of Various Opioids

9.3.1. WHO Step II Opioids

No.	Recommendations	GoR	LoE	Sources
9.4.	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 opioids given orally or low doses of a step III opioid *should* additionally be administered.	B	1-	[113, 158, 159]

9.3.2. WHO Step III First-choice Opioids

No.	Recommendations	GoR	LoE	Sources
9.5.	In patients with moderate to severe cancer pain step III opioids *shall* be used. [Modified 2019]	A	1-	[160]
9.6.	Morphine, oxycodone or hydromorphone *can* be used as the first choice step III opioid for moderate to severe cancer pain. [Reviewed 2019, new literature added]	0	1-	[113, 161-165]

9.3.3. Levomethadone in Cancer Pain Treatment

No.	Recommendations	GoR	LoE	Sources
9.7.	In patients with moderate to severe cancer pain, levomethadone *can* be used as a step III opioid of first or later choice.	0	1-	[113, 166]

No.	Recommendations	GoR	LoE	Sources
9.8.	Levomethadone *shall* be used only by experienced doctors due to a complex pharmacokinetic profile with an unpredictably long half-life.	A	1-	[113, 166]

In the original English guideline, the recommendations are based on methadone and not levomethadone. In Germany, methadone (as a racemate) is only licenced 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.

9.4. Opioid Titration

No.	Recommendations	GoR	LoE	Sources
9.9.	In patients with cancer pain, immediate-release and slow release oral formulations of morphine, oxycodone and hydromorphone *can* be used for dose titration.	0	1-	[113, 167]
9.10.	In patients with cancer pain, titration schedules for immediate- and slow-release formulations *should* be supplemented with oral[1] immediate-release opioids given as needed.	B	1-	[113, 167]

9.5. Routes of Administration

9.5.1. The Role of Transdermal Opioids

No.	Recommendations	GoR	LoE	Sources
9.11.	Transdermal fentanyl and buprenorphine *can* be alternatives to oral opioids as the preferred step III opioid for some patients with cancer pain. [Reviewed 2019, new literature added]	0	1-	[113, 162, 168]
9.12.	For patients with cancer pain unable to swallow, transdermal opioids *can* be given as an effective, non-invasive means of opioid delivery.	0	1-	[113, 169]

[1] 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.

9.5.2. Alternative Systematic Routes of Opioid Administration

No.	Recommendations	GoR	LoE	Sources
9.13.	The subcutaneous route for administering morphine and hydromorphone *shall* be the first-choice alternative for patients unable to receive opioids by oral[1] or transdermal routes.	A	1+	[113, 170]
9.14.	In patients with cancer pain, intravenous infusion shall 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+	[113, 170]
9.15.	In patients with cancer pain, intravenous administration *shall* be used for opioid titration when rapid pain control is needed.	A	1+	[113, 170]
9.16.	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	[113, 170]
9.17.	Techniques for patient-controlled analgesia can be adopted for subcutaneous and intravenous opioid infusions in patients.	0	3	[113, 170]
9.18.	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	[113, 170]
9.19.	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	[113, 170]

9.5.3. Spinal Administration of Opioids

No.	Recommendations	GoR	LoE	Sources
9.20.	Spinal (epidural or intrathecal) administration of opioid analgesics in combination with local anaesthetics or clonidine* *can* be given to 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-	[113, 171, 172]

* Off-label use

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

9.6. Opioid Switching

No.	Recommendation	GoR	LoE	Sources
9.21.	In patients receiving step III opioids who do not achieve adequate analgesia and have side-effects that are severe, unmanageable, or both, the current opioid *can* be switched to an alternative opioid.	0	3	[113, 173, 174]

9.6.1. Relative Opioid Analgesic Potencies

No.	Recommendations	GoR	LoE	Sources
9.22.	When switching from one opioid drug to another, dose conversion ratios *should* be used.	B	1-	[113, 175]
9.23.	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-	[113, 175]

Conversion ratios are shown in Table 8 together with the strength of the recommendation on the basis of current evidence.

Table 8: 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(1)	75:1	weak
Oral morphine to TD fentanyl(2)	100:1	strong

TD = transdermal. (1) Example: 60 mg oral morphine to 35 µg/h TD buprenorphine (equal to 0.8 mg per 24 h). (2) 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.

9.7. Prophylaxis and Treatment of Side Effects

9.7.1. Treatment of Opioid-related Nausea and Emesis

No.	Recommendations	GoR	LoE	Sources
9.24.	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-	[113, 176]

* Off-label use

9.7.2. Treatment of Opioid-related Constipation

See also section

Opioid-related Constipation in the chapter Constipation

No.	Recommendations	GoR	LoE	Sources
9.25.	Laxatives *shall* be routinely prescribed for the management or prophylaxis of opioid-induced constipation. [Reviewed 2019, new literature added]	A	1+	[113, 177, 178]
9.26.	No evidence suggests that one laxative agent *should* be recommended over others. [Reviewed 2019, new literature added]	ST	1+	[113, 177, 178]
9.27.	A combination of laxatives with different modes of action *can* be administered in resistant constipation. [Reviewed 2019, new literature added]	0	1+	[113, 177, 178]
9.28.	In the case of opioid-related constipation, the administration of peripherally-acting μ-opioid receptor antagonists (PAMORA), such as methylnaltrexone, naldemedin, naloxegol or the combination of oxycodone with the opioid antagonist naloxone, *should* be considered if conventional laxatives are not effective enough. [Modified 2019]	A	1+	[113, 177-187]

9.7.3. Treatment of Opioid-related CNS Symptoms

No.	Recommendations	GoR	LoE	Sources
9.29.	Methylphenidate* *can* be used to improve opioid-induced sedation but the threshold between desirable and undesirable effects is narrow.	0	1-	[113, 188]

No.	Recommendations	GoR	LoE	Sources
9.30.	In patients with opioid-related neurotoxic effects (delirium, hallucinations, myoclonus and hyperalgesia), dose reduction or opioid switching *can* be performed.	0	1-	[113, 188]

* Off-label use

9.8. Use of Opioids in Patients with Renal Failure

No.	Recommendations	GoR	LoE	Sources
9.31.	In patients with severe impairment of renal function (glomerular filtration rate < 30 mL/min) opioids *should* be used with caution.	B	3	[110, 113]
9.32.	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	[110, 113]
9.33.	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	[110, 113]

9.9. Non-opioids

9.9.1. Metamizole

No.	Recommendation	GoR	LoE	Sources
9.34.	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. [Reviewed 2019, new literature added]	0	1-	[189-193]

9.9.2. NSAIDs and Paracetamol as Supplement to Step III Opioids

No.	Recommendations	GoR	LoE	Sources
9.35.	NSAIDs *can* be added to step III opioids to improve analgesia or reduce the opioid dose required to achieve analgesia. [Reviewed 2019, new literature added]	0	1-	[113, 193, 194]

No.	Recommendations	GoR	LoE	Sources
9.36.	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-	[113, 194]
9.37.	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-	[113, 194]

9.10. Role of Adjuvant Drugs for Neuropathic Pain (Antidepressants and Anticonvulsants)

No.	Recommendation	GoR	LoE	Sources
9.38.	Amitriptyline, gabapentin or pregabalin *shall* 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+	[113, 195, 196]

9.11. Opioids for Pain Exacerbation and Breakthrough Pain

No.	Recommendations	GoR	LoE	Sources
9.39.	Pain exacerbations resulting from uncontrolled background cancer pain *shall* be treated with additional doses of immediate-release oral[1] opioids.	A	1+	[113, 197, 198]
9.40.	In cases of pain exacerbations resulting from uncontrolled background cancer pain an appropriate titration of around-the-clock opioid therapy *shall* always precede the recourse to potent rescue opioid analgesics.	A	1+	[113, 197]
9.41.	In patients with cancer, breakthrough pain (e.g. incident pain) *shall* be managed with oral[4], immediate-release opioids or with transmucosal[2] fentanyl preparations.	A	1+	[113, 197, 198]

[1] 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.

[2] The “transmucosal” pharmaceutical form includes the following administration routes: buccal, sublingual or intranasal.

No.	Recommendations	GoR	LoE	Sources
9.42.	In some cases of breaththrough pain, the transmucosal fentanyl preparations *should* be favoured over immediate-release oral opioids because of more-rapid onset of action and shorter duration of effect.	B	1-	[113, 197, 198]
9.43.	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 a triggering event.	B	1+	[113, 197, 198]

10. Fatigue

Working Group leaders: Pia Heußner, Lukas Radbruch

10.1. Introduction

The European Association for Palliative Care (EAPC) describes fatigue as “a subjective feeling of tiredness, weakness or lack of energy” [219]. Cancer-related fatigue is defined by the National Comprehensive Cancer Network (NCCN) as "a distressing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" [220]. Glaus emphasizes the qualitative differences between everyday and cancer-related fatigue, which affects the body (physically), the emotions (affectively) and the cognitive functions (mentally), lasts for several weeks and is only partially relieved, if at all, by rest or sleep [221]. Tiredness in healthy individuals is a physiological regulator that responds to physical or psychological exertions [222] and can be perceived as pleasant and normal, and remedied by rest [221].

With a prevalence of 70-90% [223-231], fatigue is the most common symptom in patients with cancer and a frequent side effect of cancer treatment [232, 233]. However, the prevalence and influence of fatigue are often not recognised [223, 232]. Fatigue can occur in a primary and secondary form. Primary fatigue syndrome is interpreted as a part of inflammatory tumour syndrome, so that frequent coincidence with primary anorexia-cachexia syndrome and depression is observed. While primary fatigue is thought to be associated with high cytokine levels, the secondary form is triggered by cancer or treatment-related symptoms or co-morbidities. As a hypothesis for the development of primary fatigue, animal studies indicate the degradation of striated musculature by a reflex circuit with vagal afferent stimulation [234]. In most patients, several symptoms will contribute to the development of secondary fatigue during the course of the disease [235]. For example, peripheral energy depletion as a consequence of decreased food intake has been postulated to be the cause of fatigue [234, 236]. However, it remains unclear to what extent the lack of energy of patients with fatigue is primarily due to the accompanying cachexia. Other symptoms and co-morbidities, such as anaemia, fever, infections, depression or electrolyte and hormone imbalances, can also further deplete the patient’s energy resources and thereby increase the feeling of energy deficiency and fatigue [237, 238]. Similarly, new immune-modulating therapies, with new mechanisms such as checkpoint inhibitors, can contribute to the development of fatigue [239]. For instance, hypomagnesaemia resulting from the administration of cetuximab, a monoclonal antibody of the epithelial growth factor receptor (EGFR), has been identified as a cause of secondary fatigue [240, 241]. Many of the drugs used in palliative care to control symptoms, such as opioids, benzodiazepines, antidepressants or anti-convulsants, can also increase fatigue due to their sedative effect.

The recommendations presented here are based on the EAPC guidelines on pharmacological and non-pharmacological treatment options for fatigue [219]. The guidelines of the NCCN with a focus on non-pharmacological interventions for patients with cancer (not only in palliative care setting) have been taken into account as far as possible [220]. When there was no evidence available from cancer patients in palliative stage, studies on the treatment of fatigue in cancer patients who did not receive palliative care or in patients with other life-limiting diseases in palliative care were considered. Exhaustion syndromes without any association with a cancer disease, such as the Chronic Fatigue Syndrome or fibromyalgia, are not taken into consideration. We also refer to the S3-Fatigue Guideline, which makes recommendations for the general patient population

[242], and to the S3 Guideline Psycho-oncological Diagnosis, Consultation and Treatment ("S3-Leitlinie Psychoonkologische Diagnostik, Beratung und Behandlung") with recommendations for the treatment of cancer patients [4].

10.2. Differential Diagnosis

No.	Recommendation	GoR	LoE	Sources
10.1.	In patients with incurable cancer and fatigue, a differential diagnosis *shall* be made to determine whether the symptoms result from a treatable cause (e.g. depression or drug side effects).		EC	

Table 9: Laboratory parameters for potentially treatable differential diagnoses of fatigue

Co-morbidities	Parameters
Anaemia	Haemoglobin
	Transferrin, ferritin, iron
	Erythropoietin
Electrolytes	Calcium (and albumin), magnesium, phosphate
Organic dysfunctions	Creatinine, urea, bilirubin, cholinesterase
Hypothyroidism	TSH, free T3 and T4
Infection	C-reactive protein, procalcitonin
Hormones	ACTH, cortisol, free testosterone
	Melatonin
Vitamin deficiency	Vitamin B1, vitamin B6, vitamin B12

10.3. Assessment

No.	Recommendation	GoR	LoE	Sources
10.2.	Screening for fatigue in patients with incurable cancer *should* include questions on weakness and tiredness such as "Do you feel unusually tired and/or weak?" or "How tired are you? How weak are you?".		EC	
10.3.	Validated multi-dimensional questionnaires *can* be used as part of the assessment for patients with incurable cancer and complex issues.		EC	

No.	Recommendation	GoR	LoE	Sources
10.4.	The assessment of fatigue in patients with incurable cancer *shall* take place at the beginning and be repeated throughout the course of the disease.		EC	

In patients with moderate to high-intensity fatigue or subjective impairment due to fatigue, further information from the medical history (Figure 3), the clinical examination or laboratory tests (see Table 9) are required in order to identify potentially treatable causes of fatigue.

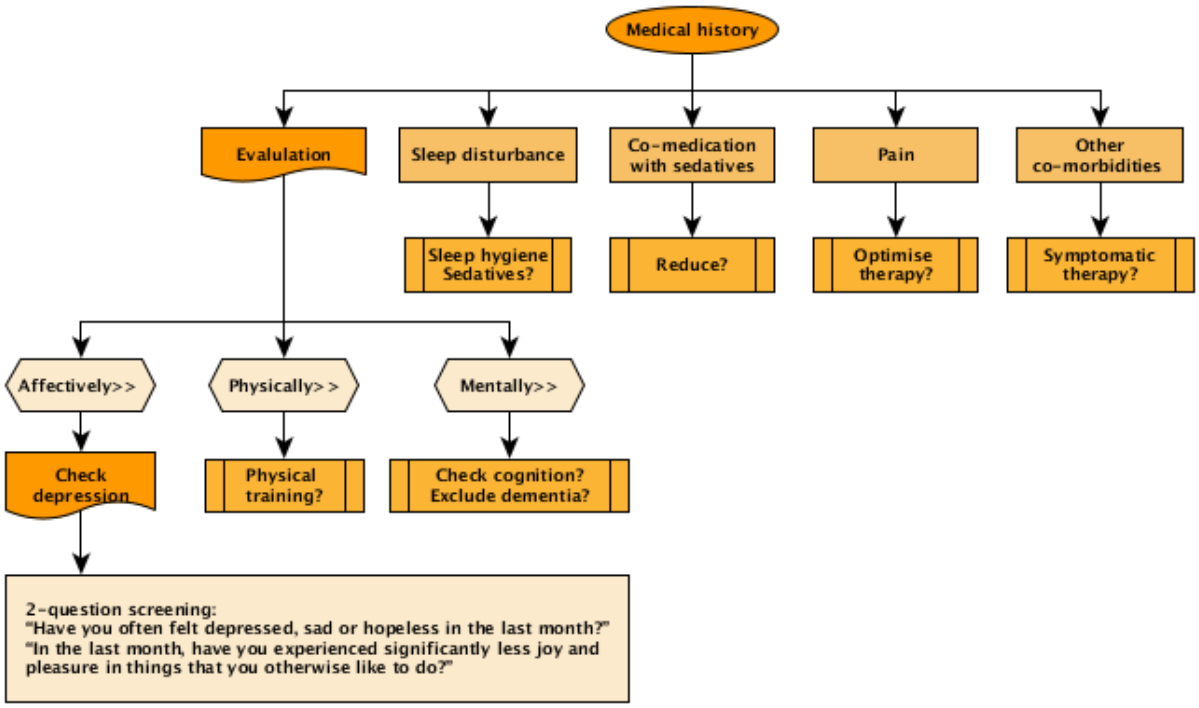


Figure 3: Assessment of fatigue: anamnesis and consequent causal therapy approaches [1]

10.4. Attitudes, strategies and treatment options

No.	Recommendation	GoR	LoE	Sources
10.5.	Specific information and therapeutic support *shall* be offered to patients with incurable cancer who are burdened or impaired by fatigue.		EC	
10.6.	Potential causes of fatigue *should* be treated in patients with incurable cancer and fatigue.		EC	

No.	Recommendation	GoR	LoE	Sources
10.7.	Erythropoietin *should not* be used for the treatment of fatigue in patients with incurable cancer due to the unfavourable risk-benefit balance.		EC	
10.8.	In the last few days or weeks of the patient's life the indication for the treatment of fatigue *should* be reviewed in order to avoid stress caused by this treatment.			

In patients with secondary fatigue, treatment of the underlying causes should be initiated (see Figure 4). Some causes of secondary fatigue, such as anaemia, depression, infection, dehydration, undernourishment, hypercalcaemia, hypomagnesaemia or the sedative side effect of opioids or other medications, can be treated. Fatigue can be alleviated with the effective treatment of such causes.

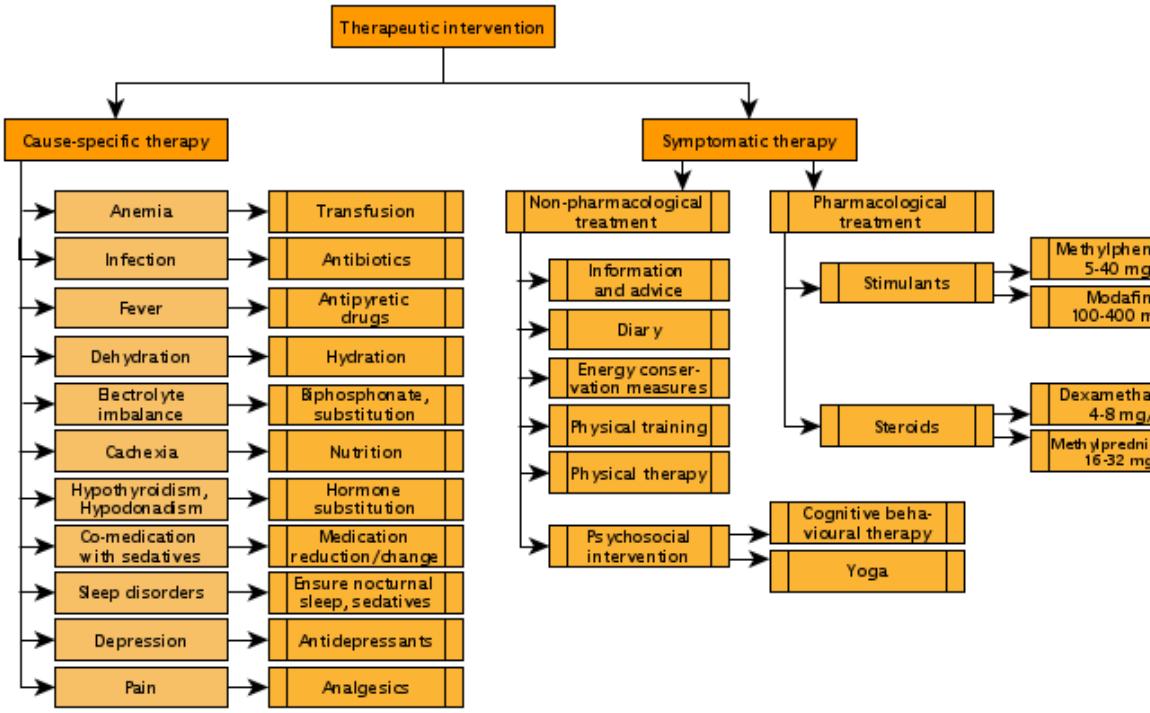


Figure 4: Therapy options for primary and secondary fatigue [1]

10.5. Symptomatic Non-pharmacological Measures

No.	Recommendations	GoR	LoE	Sources
10.9.	Patients with incurable cancer and cancer-related fatigue *should* do regular aerobic endurance and strength training.	B	1-	[243, 244]; Mochamat et al.
10.10.	Psycho-educational procedures, particularly cognitive behavioural therapies, *should* be offered to patients with incurable cancer and fatigue.	B	1-	Mochamat et al.; [245, 246]
10.11.	Counselling on strategies for energy management and an energy-adapted daily structure *should* be offered to patients with incurable cancer and fatigue.	B	1-	[245]

10.6. Symptomatic Pharmacological Treatment

No.	Recommendations	GoR	LoE	Sources
10.12.	A therapy trial with methylphenidate* or modafinil* *can* be considered for patients with incurable cancer and fatigue.	0	1-	[233]
10.13.	A therapy trial with corticosteroids* *can* be considered for patients with incurable cancer and fatigue.	0	1-	[233]
10.14.	A therapy trial with corticosteroids* in patients with incurable cancer and fatigue *should* be limited in terms of duration due to the potential side effects.	B	4	[233]

* Off-label use

11. Sleep-related Illnesses/Nocturnal Restlessness

Working Group leaders: Jan Rémi, Johannes Rosenbruch

11.1. Introduction

Sleep is required for relaxation, the processing of emotions and learning. Human beings spend about a third of their lives asleep. Adequate sleep in terms of quality and quantity is important for wakefulness during the day, physical and mental performance, well-being and quality of life, among other things. In serious illnesses such as incurable cancer when the patient is permanently bedridden, physical and psychological stress, pain or restlessness, both sleep and wakefulness can be disturbed and thereby lose their important functions.

Persistent insomnia is associated with a higher risk of developing anxiety or depression and is an important factor in the quality of life of patients with incurable cancer [247]. Disturbed sleep places a burden on patients in the form of the inability to fall asleep or to sleep through the night, early waking, unwanted behaviour patterns during sleep or in the form of restless sleep with increased daytime tiredness [248]. In patients with incurable cancer, sleep disorders are a stressful symptom on the one hand, while on the other hand they occur more frequently due to the underlying diseases or accompanying symptoms and are often associated with situational stress, advanced age and the intake of medications. For bedridden patients in particular, the bed becomes a living environment and is no longer reserved for sleep only. Conversely, the reduced physical activity results in further sleep disturbances.

Sleep disorders can lead to the aggravation of other symptoms: for example, delirium occurs more often in conjunction with sleep disorders in both the domestic and in-patient setting [249, 250]. Pain and breathlessness, however, also increase with sleep disorders [251]. Disturbed sleep can be associated with an increased desire to die [252, 253]. Adequate sleep, on the other hand, can increase pain tolerance, and patients without sleep disorders have significantly lower rates of depression and less fatigue [254].

Sleep disorders and daytime tiredness are distinct from fatigue, although these concepts are not always strictly distinguishable in practice (see Table 10). Regularly disturbed sleep results in the intensification of fatigue syndrome, whereby fatigue during the day can cause the quality of nocturnal sleep to decline [255]. The terms fatigue and daytime tiredness are often used interchangeably. However, fatigue in the narrower sense is defined as faster exhaustion or reduced resilience and the subjective feeling of fatigue, weakness or a lack of energy. Daytime tiredness (DT) is the feeling of having to fall asleep, while daytime sleepiness (DS) in the narrower sense is the tendency to need to fall asleep too often during the day [256, 257]. Both can be an expression of fatigue. The treatment of fatigue and sleep disorders is often complementary and both entities have to be considered in the differential diagnosis (see chapter Fatigue).

Table 10: Definition of sleep-related complaints and related terms

Term	Definition	Burden on patients
Sleep disorder	Disturbance of sleep in the narrower sense.	Insomnia, resulting daytime tiredness or unusual behaviour (sleepwalking) lead to complaints.

Term	Definition	Burden on patients
Daytime sleepiness (DS)	Reduction of central nervous activation with urge to fall asleep and actual falling asleep. Also known as the urge to fall asleep. Measurable through vigilance tests.	DS can reduce participation in everyday life, can limit the driving abiliy.
Daytime tiredness (DT)	A general term used to describe the reduction in psychological and physical performance as a consequence of stress.	DT is a normal experience of every human being, provided that it does not cause any restrictions in everyday life. If this results in restrictions, or if compensation mechanisms have been exhausted, it can be pathological.
Fatigue	Subjective perception of physical and/or mental exhaustion. This occurs without stress or is disproportionately strong compared to the stress level.	Fatigue reduces participation in everyday life and the ability to perceive participation as pleasant and not as a burden.

Sleep disorders are many and varied. Statements made by patients saying that their sleep is disturbed are not to be equated with a diagnosis of classic insomnia. Disturbed sleep can occur in the form of insomnia with an actual lack of sleep. However, the core symptom is often a disturbance to the sense of well-being during the day, so that the path to the diagnosis is often first reached by, for example, the complaint of daytime tiredness. The International Classification of Sleep Disorders (ICSD-3, www.aasmnet.org) shows the diversity of the disorders. This divides sleep disorders into seven main groups: insomnia (sleeplessness), sleep-related breathing disorders, hypersomnias of central origin, circadian rhythm disorders, parasomnias (undesirable behaviour patterns while sleeping), sleep-related movement disorders (such as restless legs syndrome) and other sleep disorders. All disorders can occur in patients with incurable cancer; their respective significance varies depending on the palliative context.

Overall, sleep disorders are very common in palliative care patients (up to 100% of patients depending on the setting), especially in patients with incurable cancer [258], although their significance for the patient has to be recorded individually. The prevalence differs, sometimes considerably, due to the different assessment instruments. In patients with incurable cancer, sleep disorders are often disregarded and reported too rarely, as they are not sufficiently taken into account or perceived along with the other symptoms [259-264]. For the frequency of sleep disorders see Table 11. Insomnia sleep disorders are a well described symptom area in cancer patients, although the study situation is still relatively small in non-cancer palliative patients [254, 265]. The causes are many and varied and can be subdivided into psychological (emotional stress, nocturnal restlessness) and physical (pain, breathlessness, etc.) causes [265-267]. Chronic pain frequently results in insomnia [268, 269]. Sleep disorders are a burden not only for patients, but also for their family carers [270, 271] and can in turn lead to sleep disorders in the carers [272].

Table 11: Frequency of sleep disturbances

Sleep disturbance/ prevalence according to situation	Patients with incurable cancer	Dying phase	Patients with depression	Total population
Insomnia	30-100% [258, 264]	Very common [258]	16-20% [273]	Approx. 10% [274]
Sleep-related breathing disorders (AHI = Apnoea/Hypopnoea Index)	Unknown	Unknown	Unknown, SRRD patients have a 1.8-fold risk of depression [275]	Men 3-7%; Women 2-5%; AHI >5 at 20%; AHI >15 at 6% [276]
Hypersomnia (high level of daytime tiredness without other cause)	Unknown	Unknown	Up to 50% of narcolepsy patients have depression before diagnosis [277]	<0.1% [278, 279]
Sleep-related movement disorders, restless legs syndrome (RLS)	1-50% [280, 281]	Unknown	Depression is more common in RLS. RLS in depression no data [282]	Requiring treatment 2.4-3.5% [283, 284]
Parasomnias (unwanted behaviour patterns during sleep)	Unknown	Unknown	Unknown	Children up to 17%; Adults up to 4% [285]
Circadian rythm disorders	Unknown	Unknown	Increased, extent unknown [286]	Intrinsically rare (<1%); Extrinsic (shift work, jet lag) frequent (>20%)

The diagnosis and therapy of sleep disorders is pragmatically described in detail in the S3 Guideline of the German Society for Sleep Medicine (DGSM) “Nonrestorative Sleep” in its 2009 version [287]. This guideline is currently being revised, with individual chapters such as sleep-related respiratory disorders and insomnia having already been published [256, 288]. The present chapter of the S3 Guideline on Palliative Care does not replace the guideline on “Nonrestorative Sleep”, but is intended to complement it with regard to the specific requirements and situations in the palliative setting. Therefore, the general, non-palliative medical principles are only briefly presented in an overview, with the focus lying on the special conditions of sleep disorders in patients with incurable cancer and in the palliative situation.

11.2. Symptom Identification and Assessment

No.	Recommendation	GoR	LoE	Sources
11.1.	In the assessment of symptoms in patients with incurable cancer, the patient *shall* be asked about sleep disorders and daytime tiredness/daytime sleepiness.		EC	
11.2.	Questionnaires for symptom assessment in patients with incurable cancer *should* include sleep disorders.		EC	

The medical history should take into account that sleep disorders can occur in the three dimensions of subjectively disturbed sleep (e.g. insomnia), sleep disorders (parasomnias) and increased daytime tiredness/daytime sleepiness (see Table 12).

Table 12: Typical symptoms of sleep disorders in patients with incurable cancer

Symptom	Possible causes	Assessment
Sleeplessness/"insomnia"	Concerns about illness, depression, anxiety, pain, breathlessness, nocturnal disturbances (e.g. care measures), substance abuse, medications	(Third-party) medical history, actigraphy (activity measurement)
Daytime tiredness/ daytime sleepiness	Nonrestorative night sleep (sleep apnoea, restless legs syndrome (RLS), sleep deprivation, side effects of medication, depression, tumours, chemotherapy)	Third-party medical history, Epworth Sleepiness Scale
Sleep-related breathing pauses	Sleep apnoea syndrome, opioid or benzodiazepine effect, head and neck cancers, lung diseases, heart failure, dying phase	Third-party medical history directly for breathing pauses, medical history and third-party medical history for the resulting daytime tiredness/daytime sleepiness
Restless legs complaints	RLS, neuropathy, peripheral artery disease, rheumatic diseases, myopathies, medications	Medical history
Disruption of the daily rhythm	Lack of daily structure, nocturnal disturbances (e.g. care measures), lack of time information (e.g. light), delirium	Medical history, third-party medical history
Parasomnias (undesirable behaviour patterns out of a state of sleep)	Parasomnias can pre-exist (e.g. sleepwalking), possibly triggered by psychotropic drugs, anti-cholinergics	Medical history, third-party medical history

If questionnaires are used for general symptom assessment, the use of questionnaires that also screen sleep disorders is recommended (see Table 13).

Table 13: Questionnaires that also cover sleep disorders (selection)

Questionnaire	Sleep contents	Data collection	Literature	Language
Edmonton Symptom Assessment System Revised (ESAS-r)	Tiredness (NRS)	Patient	[260]	English, modified German version: MIDOS [44]
Brief Pain Inventory	Sleep disorders due to pain	Patient	[259]	Englisch, German
IPOS	Fatigue	Patients/professionals/family carers	[289]	Englisch, German
M.D. Anderson Symptom Inventory (MDASI)	Sleep disorder	Patient	[290]	Englsh, German (only linguistically validated)

11.3. Diagnosis and Differential Diagnosis

No.	Recommendation	GoR	LoE	Sources
11.3.	The use of diagnostic methods beyond the medical history (e.g. patient-based questionnaires or sleep laboratory) *should* be critically evaluated in patients with incurable cancer with regard to their therapeutic consequences.		EC	
11.4.	When taking the medical history of sleep disorders, a psychosocial, spiritual and somatic medical history with the assessment of all currently administered drugs *shall* be performed.		EC	
11.5.	In patients with incurable cancer and sleep disorders, a differential diagnosis *shall* be performed to determine whether the symptoms are due to a treatable or modifiable cause (e.g. pain, anxiety, side effects of medication, respiratory or movement disorders, dry mouth).			

11.3.1. Insomnias

Insomnias are one of the most important groups of sleep disorders. The patient typically reports problems falling asleep and sleeping through the night. The diagnosis is made by means of the medical history, sleep questionnaires and sleep diaries (S3 Guideline on "Nonrestorative sleep" of the German Sleep Society (DGSM) [288]). In patients with incurable cancer, the medical history has priority. It includes a comprehensive psychosocial (e.g. anxiety, depression, sadness), spiritual (e.g. feelings of guilt, fear of death) and somatic medical history with a record of all medications (see Table 14).

Table 14: Insomnia-promoting substances

Substances that promote insomnia	
Alcohol	Other intoxicants

Substances that promote insomnia	
Stimulants (coffee, amphetamines)	Diuretics
Blood pressure medications (beta-blockers)	Anti-asthmatics (theophylline, sympathomimetics)
Antibiotics (gyrase inhibitors)	Activating antidepressants
Steroids (esp. evening intake)	Anti-dementia drugs

11.3.2. Sleep-related Breathing Disorders

Sleep-related Breathing Disorders (SRBD) are characterised by disorders of physiological breathing during sleep due to apnoeas and hypopnoeas. The breathing pauses are associated with hypoxia, with hypercapnia and acidosis, and neurophysiologically with arousals during sleep, but have to be distinguished from changing patterns related to the dying phase. The typical symptoms of a sleep-related respiratory disorder (SRRD) are an exacerbated form of daytime fatigue. Assessment instruments for SRRD are presented in Table 15.

Table 15: Questionnaires for Sleep-related Breathing Disorders (SRBD)

Questionnaire	Description
Epworth Sleepiness Scale	Records daytime sleepiness as a central symptom of SRBD [291]
STOP-BANG questionnaire	Screening tool for SRBD [292] (http://www.stopbang.ca/osa/screening.php)
Berlin questionnaire	Detailed questionnaire for sleep apnoea [293]

11.3.3. Restless Legs Syndrome (RLS)

Restless legs syndrome is a clinical diagnosis. The core symptom is unpleasant restlessness in the legs (the arms may also affected, however less frequently). The symptoms occur mainly at rest, are pronounced in the evening and at night and improve as soon as the patient moves.

11.3.4. Parasomnias

Parasomnias are disorders during sleep in which involuntary and unwanted behaviour patterns occur. Typical examples are sleepwalking, night terrors, REM sleep behaviour disorder and nightmares [287].

11.3.5. Circadian (Day-night) Rhythm Disorders

No.	Recommendation	GoR	LoE	Sources
11.6.	In the medical history, the patient *should* be asked about any shift/reversal of the day-night rhythm.		EC	

11.4. Framework Requirements and Treatment Principles

No.	Recommendation	GoR	LoE	Sources
11.7.	The expectations regarding sleep *shall* be addressed.		EC	
11.8.	In the selection of non-pharmacological and pharmacological intervention for sleep disorders in patients with incurable cancer, both the stage of the disease and the severity of the symptoms *shall* be considered.		EC	
11.9.	All medical interventions, which potentially represent a burden with respect to the sleep of the patient with incurable cancer, *should* be critically evaluated for their benefit in the overall context.		EC	
11.10.	In the case of psychosocial and spiritual causes of sleep disorders (e.g. anxiety, depression, sadness, feelings of guilt, fear of death), patients with incurable cancer *shall* be offered conversations and/or therapeutic interventions.		EC	

11.5. Non-pharmacological Measures

No.	Recommendation	GoR	LoE	Sources
11.11.	The sleep hygiene of patients with incurable cancer *shall* be evaluated and optimised in the case of nocturnal complaints.		EC	
11.12.	The distinction between day and night *should* be made easier for the patient by means of a clear daily structure.		EC	
11.13.	Stimulus control *can* be used in patients with incurable cancer to improve sleep quality.		EC	
11.14.	Cognitive behavioural therapy for insomnia *can* be performed in patients with incurable cancer.	0	2++	[288]
11.15.	Relaxation techniques such as autogenic training and progressive muscle relaxation *can* be used to treat insomnia in patients with incurable cancer.		EC	
11.16.	A high daytime light exposure *can* be used to improve the day-night rhythm in particular and well-being in general.		EC	
11.17.	CPAP therapy *can* be used for patients with incurable cancer and obstructive sleep apnoea.	0	2-	[256]

The general prerequisites for good sleep are summarised under the term of **sleep hygiene** (see Table 16) [288, 294]. Not every practice is supported by evidence, but compliance with these practices is generally regarded as conducive.

Table 16: Practices for good sleep hygiene [288]

Measures
No caffeinated drinks after lunch
Avoid alcohol as much as possible and do not use it to help you fall asleep.
Regular physical activity
Reduction of activity before sleeping
Introduction of a personal sleep ritual
Pleasant atmosphere in the bedroom, appropriate room temperature and humidity
No repeated time checks at night (alarm clock, wristwatch, smartphone)
No use of smartphone or notebook in bed
No salty drinks or food before going to bed

Stimulus control is a behavioural therapy based on classic conditioning. This is suitable for the treatment of insomnia disorders. The stimulus of "lying in bed" should be associated with "sleeping" behaviour [295]. For patients who are not bedridden, the following methods may be considered (see Table 17):

Table 17: Stimulus control methods (where feasible)

Methods
Patients should only go to bed if they are clearly tired in terms of sleep readiness.
In bed patients should only sleep.
If they do not fall asleep within 10 minutes, patients should get up and go back to bed only when they are very tired. This step can and should be repeated if falling asleep is still not possible.
Patients should have fixed bed times.
Patients should always get up at the same time every morning.
Patients should not stay in bed longer if the night was bad.
Patients should not sleep during the day.

11.6. Pharmacological Treatment

No.	Recommendation	GoR	LoE	Sources
11.18.	The pharmacological treatment of sleep disorders *shall* be cause-specific.		EC	
11.19.	When sedatives are used for other indications, their effects on sleep *should* be used in case of concomitant insomnia.		EC	

11.6.1. Pharmacological Treatment of Insomnias

11.6.1.1. Treatment Principles

No.	Recommendation	GoR	LoE	Sources
11.20.	The common period of short-term pharmacological treatment (3-4 weeks) of insomnias *can* be extended in patients with incurable cancer.		EC	

11.6.1.2. Recommendations and Data for Patients with Incurable Cancer

No.	Recommendation	GoR	LoE	Sources
11.21.	Zopiclone and zolpidem *should* be preferred for the short-term treatment of insomnias in patients with incurable cancer, and sedative antidepressants over the medium-term.	B	4	-

11.6.1.2.1. Z-Substances (Zopiclone and Zolpidem)

No.	Recommendation	GoR	LoE	Sources
11.22.	In patients with incurable cancer, zopiclone and zolpidem *should* be used for the short-term treatment of insomnia.	B	1-	[296]

The Z-substances zopiclone and zolpidem act on the benzodiazepine receptor. They have some dependence potential, but a lower addiction potential than pure benzodiazepines. The main difference with most pure benzodiazepines is their significantly shorter half-life (see Table 18).

Table 18: Z-substances and benzodiazepines for the treatment of insomnia

Active substance and dose (mg)	Half-life (h)	Insomnia approval	Comment	Instructions for application
Z-SUBSTANCES				

Active substance and dose (mg)	Half-life (h)	Insomnia approval	Comment	Instructions for application
Zolpidem 5-10	2-4	Yes	No active metabolites, most prescribed hypnotic, dosage >10 mg, narcotic	All Z-substances and benzodiazepines are only licensed for the short-term treatment (3-4 weeks) of insomnias. Prescribe the smallest pack size. Evaluate carefully the indication. Define therapy duration before start. Reduce doses early. Avoid in the case of a history of addiction.
Zopiclone 3.75-7.5	5-6	Yes	Typical side effect: bitter or metallic taste	
BENZODIAZEPINES[1]				
Triazolam 0.125-0.25	2-5	Yes	Dosage >0.25 mg, narcotic	
Lormetazepam 0.5-1	12	Yes	Half-life in older patients up to >20 h	
Temazepam 10-20	5-13	Yes	Dosage >20 mg, narcotic	
Oxazepam 10-20	8-12	Yes	Metabolite of diazepam, no active metabolites itself	
Nitrazepam 5-10	15-30	Yes	Drowsiness and fatigue possible, little influence on REM sleep	
Diazepam* 5-10	24-48	No	Half-life of active metabolites 50-80 h, availability also i.v. and p.r.	
Clonazepam* 0.25-2	30-40	No	Use in epilepsy and parasomnias	

* Off-label use

[1] Lorazepam is used for anxiolysis and in the treatment of epileptic seizures. Lorazepam is not the first-choice drug for insomnia and is therefore not referred to in this table.

11.6.1.2.2. Sedative Antidepressants

No.	Recommendation	GoR	LoE	Sources
11.23.	a) Sedative antidepressants *can* be used for the short-term pharmacological treatment of insomnia. b) Sedative antidepressants *should* be used for the medium-term pharmacological treatment of insomnia.	0/B	1-	[297-300]

Antidepressants have also become a widespread substance group for the treatment of insomnias not associated with depression in the general population when non-pharmacological measures are not sufficiently effective (see Table 19). Typically, lower dosages are used for insomnia treatment than for the treatment of depression. For some substances, the sleep-promoting effect is even no longer significant at higher doses (e.g. mirtazapine). These are preferred over the benzodiazepines for the exclusive treatment of insomnia because of their lack of dependency potential and drowsiness and fatigue.

Table 19: Sedative antidepressants

Active substance and dose (mg)	Half-life (h)	Comment
Doxepin 3-100	8-24	Licensed for sleep disorders associated with depression; side effects: anti-cholinergic effects; ECG changes; phototoxic reactions possible
Agomelatine* 25-50	1-2	Effect on melatonin and histamine receptors. Possible circadian resynchronisation
Trazodone* 25-100	5-8	No anti-cholinergic side effects, no weight gain; QTc prolongation; in combination, serotonergic syndrome can occur
Amitriptyline 25-100	10-28	Adjuvant pain therapy; effective in specific headache therapy; anti-cholinergic side effects; QTc prolongation; degraded via CYP3A4
Trimipramine 50-100	24 (15-40)	Licensed for sleep disorders associated with depression; anti-cholinergic side effects; adjuvant pain therapy; leukopenia; weight gain
Mirtazapine* 7.5	20-40	Sleep-inducing effect above all in the low dose range. Side effects: occurrence of RLS symptom. Increase in appetite (possibly intended in the case of patients with incurable cancer)
* Off-label use		

11.6.1.2.3. Benzodiazepines

No.	Recommendation	GoR	LoE	Sources
11.24.	For the treatment of insomnia, benzodiazepines *should* be selected only where other indications for their application also exist.	B	4	[301-303]

In patients with incurable cancer, benzodiazepines may play a more important role because other symptoms such as anxiety might be treated concomitantly; however, the synergistic effect has not been studied. The half-lives of the benzodiazepines can vary considerably (see Table 18). This should be considered during the selection process and attention should be paid to side effects on the following day, such as fatigue, unsteady gait or impaired driving ability.

11.6.1.2.4. Sedative Anti-psychotics

No.	Recommendation	GoR	LoE	Sources
11.25.	In patients with incurable cancer, sedative anti-psychotics *can* be used to treat insomnia if other therapies are not possible or if they can be used synergistically for other symptoms.	0	3	[304]

Anti-psychotics are not recommended for the treatment of isolated sleep disorders in the general population. However, in cancer patients and elderly patients at risk of developing delirium, they can help with prevention. If there is another indication for the administration of a neuroleptic drug, a sedating neuroleptic drug could be chosen if sleep disturbance is also present (see Table 20).

Table 20: Sedative anti-psychotics

Active substance and dose (mg)	Half-life (h)	Comment
Melperone 10-100	6-8	Licensed for insomnia. Extrapyramidal symptoms (EPS, dyskinesias) rare; available as a syrup
Pipamperone 40-120	17-22	Licensed for insomnia. Delirium treatment; no anti-cholinergic side effects; more EPS than melperone; available as a syrup
Prothipendyl* 40-120	2-3	Clear first-pass effect, therefore i.v. and i.m. lower doses; blood pressure reduction; dry mouth; available as drops
Quetiapine* 12.5-150	7(-12)	Potent neuroleptic at higher dosages. Unretarded use is better for a sleep-inducing effect, very low EPS risk; orthostasis; degradation via CYP3A4; available as a syrup
Chlorprothixene* 15-90	8-12	For the therapy of mania; to be used only with special caution in cases of depression; anti-cholinergic side effects
Levomepromazine* 2.5-5	15-30	Long half-life, therefore, tends to have a rather general calming effect, risk of drowsiness. Available as an i.v. solution and as drops
Olanzapine* 5-10	32-52	Potent neuroleptic. Long half-life, therefore, tends to have a rather general calming effect, risk of drowsiness. Available as an orally disintegrating tablet and as drops.
* Off-label use		

11.6.1.2.5. Melatonin

No.	Recommendation	GoR	LoE	Sources
11.26.	For the treatment of insomnia, melatonin *can* be administred after application of other substance classes.	0	1+	[305-307]

11.6.2. Pharmacological Treatment of Restless Legs Syndrome

No.	Recommendation	GoR	LoE	Sources
11.27.	The pharmacological treatment of restless legs syndrome *should* make use of synergistic effects of other symptom-oriented treatments.	EC		

11.6.3. Special Aspects

No.	Recommendation	GoR	LoE	Sources
11.28.	Intermittent sedation (parenteral or sedatives with a long half-life) *should not* be used as a treatment for sleep disorders unless it is within the context of other symptom therapies.		EC	

See also section Medication and Measures in the Dying Phase/Withdrawal of Medication and Measures in the Dying Phase in the chapter on the dying phase.

12. Nausea and Vomiting (not Tumour Therapy-related)

Working Group leaders: Gesine Benze, Bernd Oliver Maier

12.1. Introduction

Nausea and vomiting are two independent symptoms, but one is often accompanied by the other.

In this guideline, we use nausea synonymously with the feeling of having to vomit, and vomiting for the process itself, which results in the ejection of stomach or bowel contents through the mouth. The main somatic consequences associated with vomiting may be inappetence, malnutrition, dehydration, electrolyte disorders and mucous membrane damage. Furthermore, it is more difficult or maybe impossible to take medication orally. For patients, nausea and vomiting have a significant impact on their quality of life [317, 318].

This guideline describes nausea and vomiting not induced by tumour therapy, in palliative care patients with oncological disease.

Nausea and vomiting can also be induced by tumour-specific therapies such as chemotherapy, immunotherapy and radiotherapy. The evidence on this symptom complex, known in the literature as CINV (chemotherapy-induced nausea and vomiting), is good, with evidence-based guidelines having been implemented. In particular, we refer here to the S3 Guideline Supportive Care ("Supportive Therapie bei onkologischen PatientInnen" - Langversion 1.1, 2017) [2], in which tumour therapy-induced nausea and vomiting are specifically addressed. In practice, it has to be taken into account that in many cases a clear distinction between tumour therapy-related and not tumour therapy-related is often not possible. Therapy-related triggers indeed often coexist with potential disease-specific triggers. Some therapeutic approaches can be applied in both situations and may have positive effects.

Malignant intestinal obstruction as a special form of functional restriction of the gastrointestinal tract is usually accompanied by nausea and vomiting. The therapy of nausea and vomiting in the context of malignant bowel obstruction is discussed in a separate chapter of the guideline (see the chapter on Malignant Bowel Obstruction (MBO)), because of specific aspects of these symptoms and of their aetiology.

The aim of this chapter is to present recommendations, which are based on the evidence for anti-emetic therapy in patients with incurable cancers who require palliative care. These recommendations take into account the complex situation of severely ill patients. They aim to alleviate nausea and to reduce the frequency of vomiting by means of non-pharmacological and pharmacological interventions.

Epidemiology and pathogenesis

Many of the studies on nausea and vomiting address both symptoms, without any precise differentiation between the individual prevalence figures for nausea or vomiting. Values of approximately 10-70% for nausea in cancer patients at an advanced stage and approximately 10-40% for vomiting [231, 319-326] show the significance of the symptom complex.

There are many and varied causes leading to the development of the symptom complex of nausea and vomiting: toxic substances, metabolic, gastro-intestinal and central disorders, as well as a psychological genesis have been plausibly demonstrated. A multifactorial aetiology is the rule rather than an exception and a clear classification is often not possible.

In approximately 50% of the cases, the cause lies in organic and functional changes in the gastro-intestinal tract [327, 328].

Drugs or drug interactions are frequently the cause of nausea and vomiting. At the beginning of opioid application, for example, up to 40% of previously opioid-naive cancer patients suffer from nausea and vomiting as side effect [329]. With regard to the treatment of opioid-related nausea and vomiting, please see the chapter on Cancer pain.

Pathophysiology

Various anatomical structures play a role in the development of nausea and vomiting. In the central nervous system these are the chemoreceptor trigger zone in the area postrema on the floor of the IV ventricle, the vomiting centre in the brainstem, the cerebral cortex and the vestibular apparatus, peripheral vagal afferents and the gastro-intestinal tract [323, 330, 331]. Impulse transmission takes place via a large number of neurotransmitters and receptors, such as muscarinic acetylcholine (mACh), histamine (H_1), dopamine (D_2), serotonin ($5HT_2$, $5HT_3$, $5HT_4$) and neurokinin (NK_1) receptors [323].

Assessment and impact of the symptoms and therapeutic approaches

Often, the patient's subjective perception of the burden and the assessment of third parties differ. The invisibility of the feeling of nausea compared to the visual and olfactory presence of vomiting is considered to be a possible reason. As a consequence, the third parties tend to overestimate the impact of vomiting on the patient and to underestimate the effect of nausea. Nausea can have a greater negative impact on the quality of life than vomiting [332]. Vomiting and vomit trigger aversive reactions, such as a feeling of disgust among third parties. This can in turn result in people distancing themselves from the patient. It is not uncommon for feelings of helplessness or frustration to arise in the social environment. This social dimension and its effects on the planning of care and the emotional attachment of those affected must be taken into account when establishing goals of care.

Various non-pharmacological and pharmacological treatments are available. Due to the often multi-factorial aetiology and a discrepancy in the evaluation of the symptoms by the patient, family carers and health care providers, it can initially be challenging to reach a consensus on a realistic goal of care and an effective therapy.

Literature on the therapy of this two symptoms, which are associated with each other time and again in the palliative situation, does not consistently distinguish between the assessment of one or the other symptom. Therefore, taking into account the evidence available, a differentiation of the therapy effectiveness of the individual symptoms is only possible on a selective basis.

12.2. Assessment

No.	Recommendations	GoR	LoE	Sources
12.1.	Patients with incurable cancer *shall* be asked about the presence of nausea and vomiting during every symptom assessment as part of a systematic assessment of symptoms.		EC	
12.2.	The medical history for nausea and vomiting in patients with incurable cancer *should* assess the following aspects for each of the two symptoms: • Frequency, intensity and duration • Simultaneous occurrence of other symptoms • Temporal connection with food, fluid and drug intake • Intensity of the subjective symptom burden • Impairment of the oral intake of food, fluids and drugs • Triggering and modulating factors (including psychosocial stress) • Current medication history, including tumour-specific therapy • Effect of vomiting (Relief? Improvement in nausea?)		EC	
12.3.	The medical history of vomiting in patients with incurable cancer *should* also record the following aspects: • Appearance of the vomit • Amount of vomit • Smell of the vomit		EC	
12.4.	The significance of nausea and vomiting and their burden on third parties of a patient with incurable cancer *shall* be recorded.		EC	
12.5.	The extent of the physical examination, the instrumental and laboratory diagnostics relating to patients with nausea and vomiting and incurable cancer *shall* be weighted on the basis of proportionality against the clinical situation, disease phase and relevance to decisions.		EC	
12.6.	The intensity of the burden caused by nausea and vomiting in cognitively fit patients *shall* be evaluated by self-assessment, e.g. by means of a validated self-assessment tool that records several symptoms.		EC	
12.7.	The subjective burden of nausea and vomiting in patients with incurable cancer *should* be determined for rapid and frequent assessment using one-dimensional assessment tools (VAS/NRS) or within the framework of a several symptom assessment, e.g. with MIDOS/ESAS[1] or IPOS.	0	4	-

[1] MIDOS is the German version of the ESAS, the Edmonton Symptom Assessment Scale.

The medical history and diagnostics provide a clinically-relevant working hypothesis as the basis for the therapeutic decisions. It should be determined whether or not the cause is reversible and in which phase of life the patient is (see Figure 5).

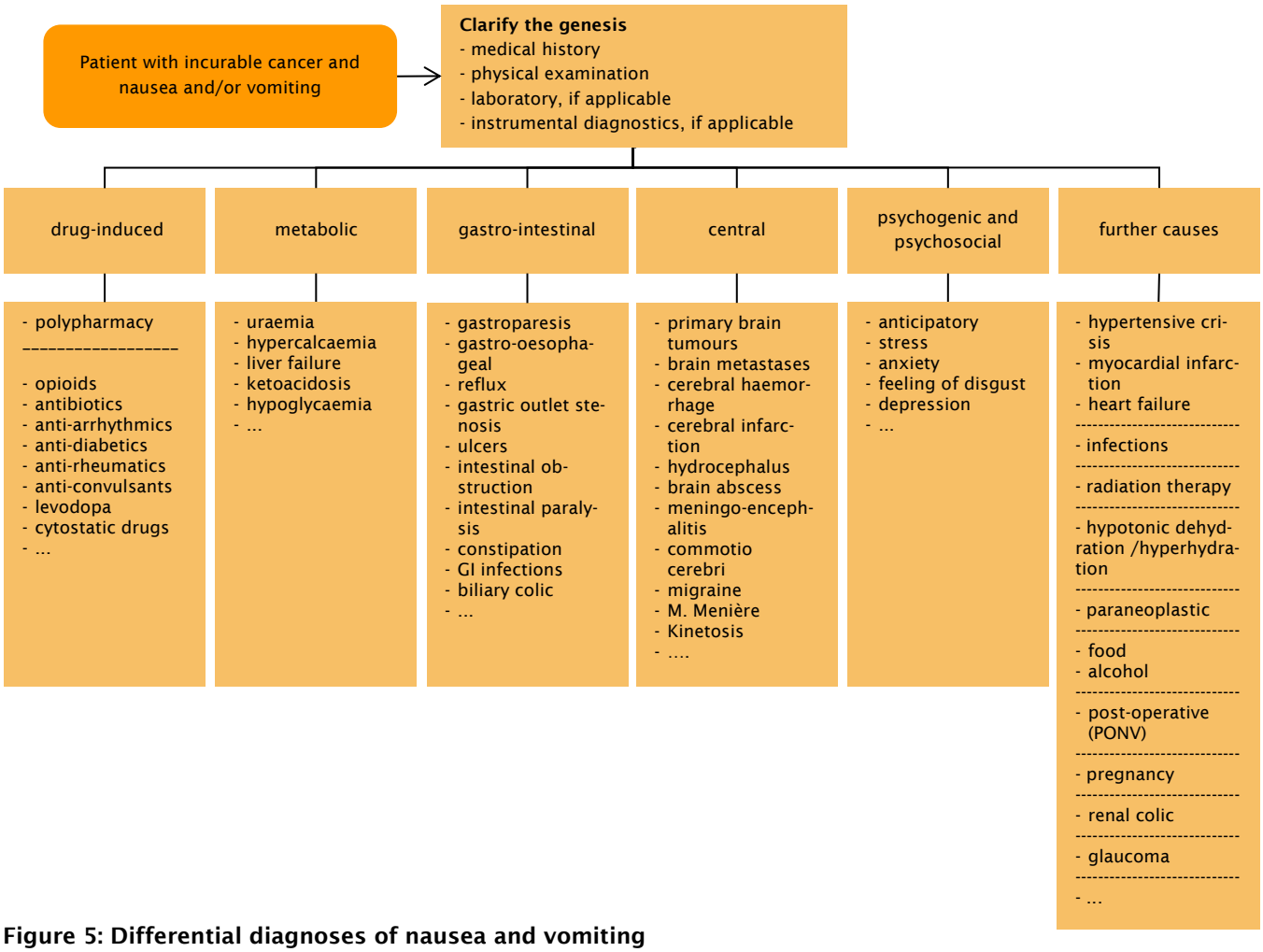


Figure 5: Differential diagnoses of nausea and vomiting

12.3. The Principles of Treatment

No.	Recommendations	GoR	LoE	Sources
12.8.	Patients with incurable cancer and their family carers *shall* be informed individually and in a situation-specific manner about the causes of nausea and vomiting.		EC	
12.9.	Patients with incurable cancer and their family carers *shall* be supported with the development of coping strategies.		EC	

12.10.	Aggravating factors for nausea and vomiting, in particular stress and a smell and/or taste perceived as unpleasant by the patient, *shall* be avoided.	EC

It is essential that the effectiveness of the measures used is evaluated by means of an appropriate symptom assessment (see Figure 6).

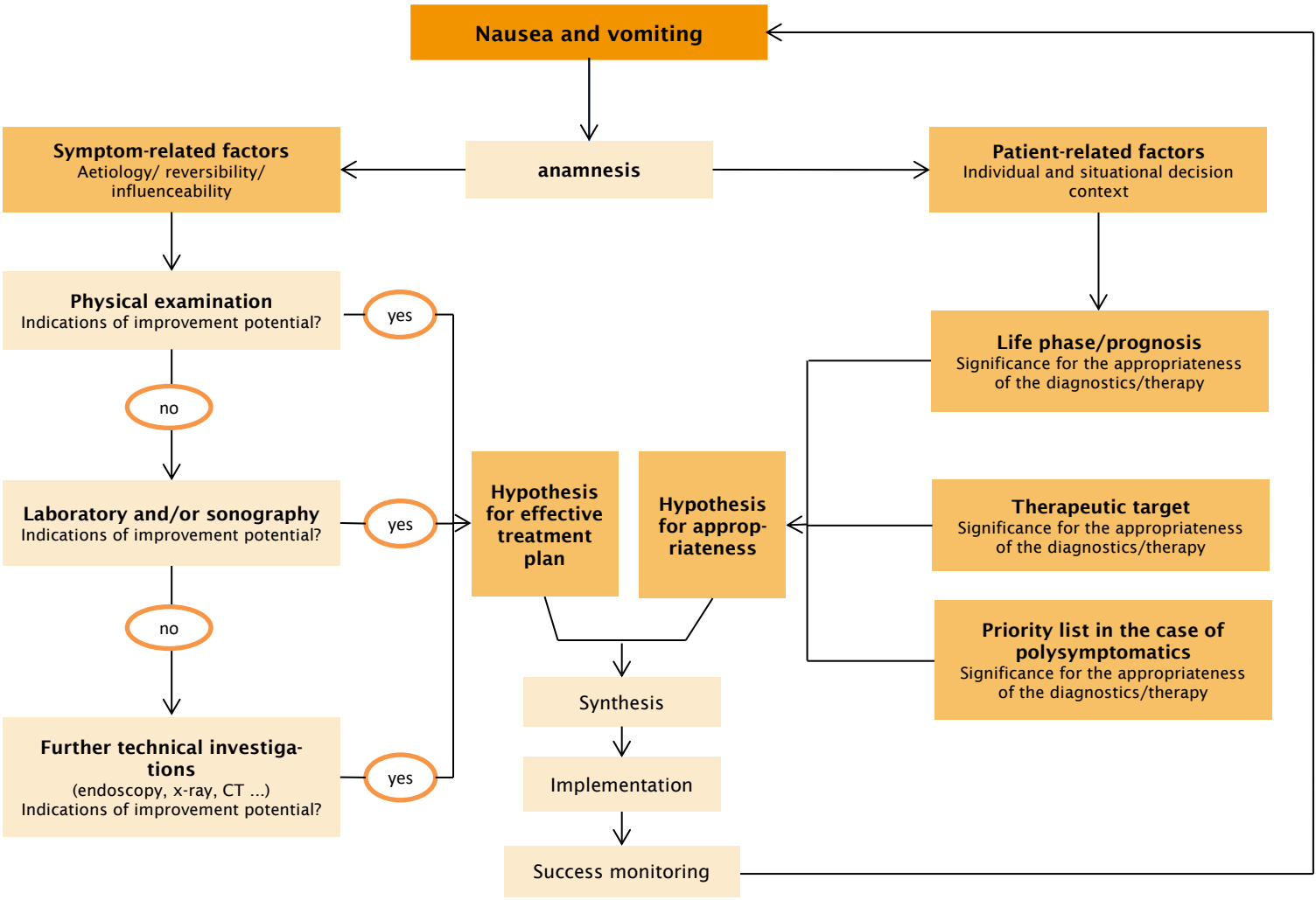


Figure 6: Establishing and re-evaluating a treatment plan considering its appropriateness

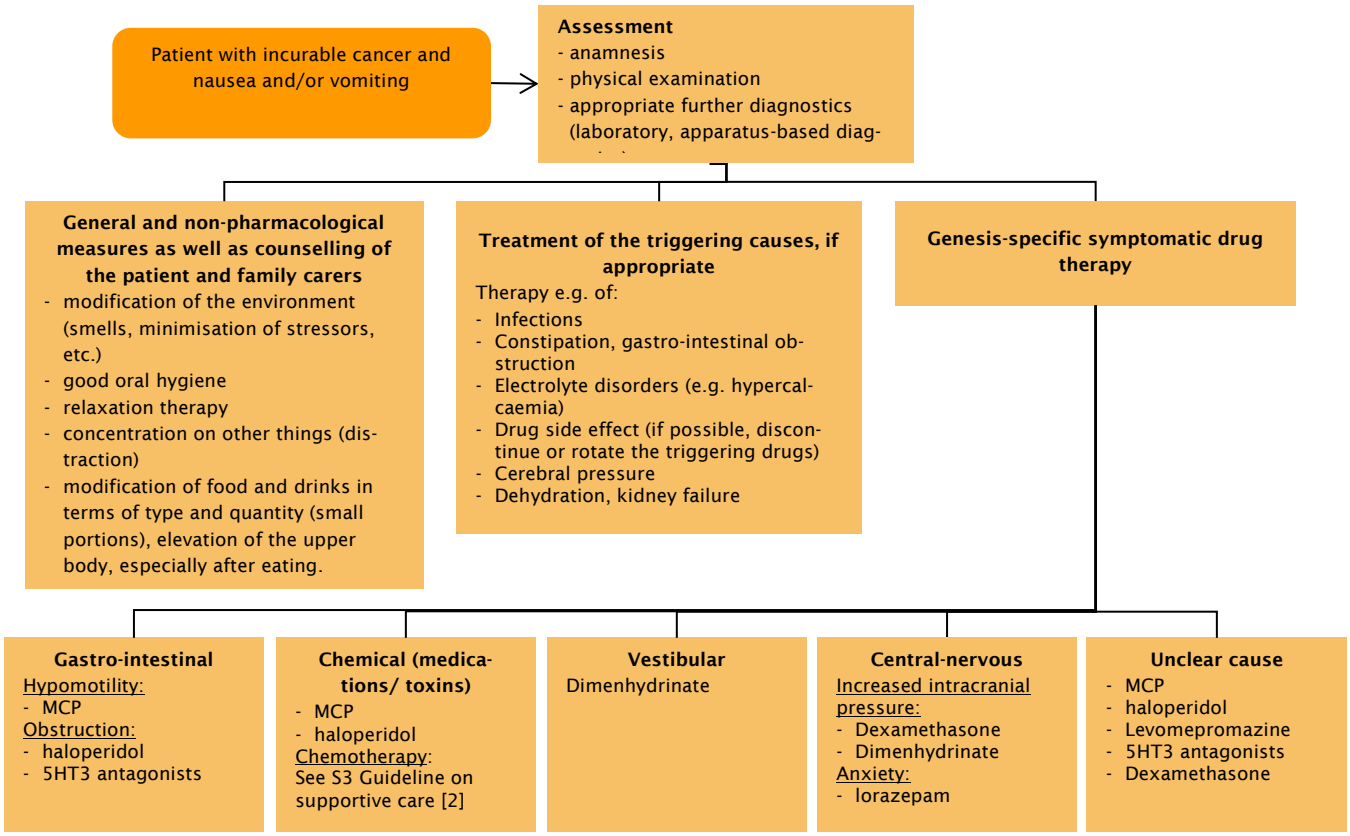


Figure 7: General, non-pharmacological and pharmacological measures for treating nausea and vomiting

12.4. Non-pharmacological Measures

No.	Recommendations	GoR	LoE	Sources
12.11.	After each case of vomiting, oral hygiene *shall* be offered to the patient and made possible.		EC	
12.12.	Food *should* be offered to the patient with nausea and vomiting and incurable cancer in small, appetising portions.		EC	
12.13.	In patients with incurable cancer and significantly reduced oral fluid and food intake due to nausea and vomiting with impending or actual exsiccosis, or nutrient deficiency, it *shall* be determined whether parenteral substitution is indicated, depending on the goal of care.		EC	
12.14.	Relaxation techniques *should* be offered to patients with incurable cancer, in order to alleviate nausea and vomiting regardless of the trigger.		EC	

12.15.	Behavioural therapeutic methods (e.g. systematic desensitisation) and hypnotherapeutic methods *should* be offered to patients with incurable cancer if there is evidence of mental causes.	EC
12.16.	If vomiting persists and cannot be controlled by other methods, a nasogastric drain tube *should* be offered to the patient with incurable cancer.	EC

12.5. Pharmacological Treatment

No.	Recommendations	GoR	LoE	Sources
12.17.	The anti-emetic *should* be selected on the basis of the aetiology for patients with incurable cancer and nausea and vomiting.	EC		
12.18.	In the case of patients with incurable cancer and nausea and vomiting, tests *shall* be carried out to determine whether drugs that cause nausea and vomiting can be discontinued, replaced or reduced.	EC		
12.19.	For patients with incurable cancer and persistent opioid-related nausea or vomiting despite corresponding anti-emetic therapy and an otherwise appropriate opioid dose, the type of opioid *can* be switched to another.	0	1-	[196, 333]
Pain 9.24.	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-	[113, 176]
12.20.	Anti-psychotics with a broad spectrum of action, such as levomepromazine*, *should* be used as a therapy to alleviate nausea and vomiting in patients with incurable cancer when the response to other anti-emetics is insufficient.	B	3	[334, 335]
12.21.	Anti-histamines, such as dimenhydrinate, *can* be used as anti-emetics in patients with nausea and vomiting and incurable cancer, especially when a vestibular or cerebral cause is likely.	0	4	-
12.22.	Dexamethasone* *should* be used to alleviate nausea and vomiting in patients with incurable cancer and increased brain pressure due to brain metastases.	B	1-	[336]
12.23.	$5HT_3$ receptor antagonists (setrone*) *can* also be used as a supplement to relieve nausea and vomiting in patients with incurable cancer outside the tumour therapy-induced genesis, when	0	1-	[337]

	dopamine antagonists, such as metoclopramide and haloperidol, are contra-indicated or their effect is insufficient.			
12.24.	If the response to the aetiology-based pharmacotherapy of nausea and vomiting is insufficient, cannabinoids* *can* be used as a reserve for patients with incurable cancer.	0	1+	[338, 339]
12.25.	In patients with incurable cancer, a combination of anti-emetics with different receptor affinities *should* be used if there is an insufficient response to individual substances used to alleviate nausea and vomiting.	B	4	-
12.26.	If vomiting persists in patients with incurable cancer, the drug *should* be administered parenterally.	EC		

* Off-label use

The drugs mentioned act on different receptors. Therefore it is helpful to consider the probable aetiology and the receptors involved when selecting the medication (see Table 21 and Table 22).

Table 21: Receptor affinity of anti-emetics (according to Rémi and Bausewein 2018) [340])

	D_2 receptor antagonist	H_1 receptor antagonist	Anti-muscarinic agent	$5HT_2$ receptor antagonist	$5HT_3$ receptor antagonist	NK_1 antagonist	$5HT_4$ receptor agonist	CB_1 agonist	GABA mimetic
Metoclopramide	++	–	–	–	+	-	++	-	-
Domperidone	++	_	-	-	-	-	-	-	-
Ondansetron, Granisetron	–	–	–	–	+++	-	–	-	-
Dimenhydrinate	–	++	++	–	–	-	–	-	-
Promethazine	+/++	++	++	–	–	-	–	-	-
Haloperidol	+++	–	–	–	–	-	–	-	-
Levomepromazine	++	+++	++	+++	–	-	–	-	-
Olanzapine	++	+	++	++	+		–	-	-
lorazepam	–	–	–	–	–	–	–	–	+++
Dronabinol, Nabilone	–	–	–	–	–	–	–	+++	–
Scopolamine hydrobromide	–	–	+++	–	–	-	–	-	-

	D_2 receptor antagonist	H_1 receptor antagonist	Anti-muscarinic agent	$5HT_2$ receptor antagonist	$5HT_3$ receptor antagonist	NK_1 antagonist	$5HT_4$ receptor agonist	CB_1 agonist	GABA mimetic
Aprepitant	–	–	–	–	–	+++	–	–	–

Affinity: +++ high, ++ moderate, + low, – slight or absent.

H = histamine, D = dopamine, HT = hydroxytryptamine, NK = neurokinin, CB = cannabinoid, GABA = γ-aminobutyric acid

Table 22: Drugs and dosages (adapted from Bausewein et al. [341])

Drug	Oral	Subcutaneous for 24 h	Other routes of administration
PROKINETIC AGENTS			
Metoclopramide	10 mg/8 h	30 mg*	10 mg/8 h *rectal, 10-30 mg/24 h i.v.
Domperidone	10-20 mg/6-8 h[1]	–	–
ANTIHISTAMINES			
Dimenhydrinate	50-100 mg/6-8 h*	62-372 mg*	150 mg/6-8 h*rectal, 31-62 mg/4 h i.v. (max. 372 mg/24 h i.v.)
ANTI-PSYCHOTICS			
Haloperidol*	0.5-1 mg at night and up to every 2 hours as required	s.c.* 2.5-5 mg/24 h and 1 mg up to once an hour as required; usual maximum dosage s.c.* 5 mg/24 h	(i.v. administration[2])
Levomepromazine*	1-5 mg in the evening 1-5 mg/12 h	1-2.5 mg[3]	–
Olanzapine*	1.25-2.5 mg at night, if necessary up to 5 mg		
ANTI-CHOLINERGICS			
Scopolamine*	–	–	1.54 mg/72 h transdermal
$5HT_3$ ANTAGONISTS			
Ondansetron*	8 mg/8-12 h	–	8 mg/8-12 h i.v.
Granisetron*	2 mg p.o./d	1 mg 1×/d*	1 mg i.v.

Drug	Oral	Subcutaneous for 24 h	Other routes of administration
STEROIDS			
Dexamethasone*	2-4 mg/d (up to 8 mg)	2-4 mg* (up to 8 mg)	2-4 mg/24 h i.v. (up to 8 mg)
CANNABINOIDS			
Dronabinol (e.g. Dronabinol drops)	2.5-40 mg/6-12 h		
BENZODIAZEPINES			
Lorazepam*	0.5-1.0 mg/8 h	–	–

* Off-label use (refers to the initial supplier's drug; approval status for generics is not usually considered) [342]. Subcutaneous administration is not permitted for metoclopramide, dimenhydrinate, haloperidol, levomepromazine, granisetron or dexamethasone. Permitted maximum daily doses are lower for metoclopramide (30 mg/d) and dimenhydrinate (400 mg/p.o., 450 mg/d rectal)

(1) Domperidone: The permitted level is 10 mg up to 3 times a day. The indication for rectal administration refers only to certain forms of nausea and vomiting.

(2) Haloperidol (i.v. administration analogous to the s.c. application): The approval for i.v. administration was withdrawn due to the increased risk of cardiac side effects. Within the context of palliative medicine, i.v. administration continues to be used, but should only be carried out after a strict risk-benefit assessment. Recent findings indicate that the i.v. administration of lower doses of haloperidol has no effect on the QT time (see also long version of the guideline).

(3) Levomepromazine: in the Prescribing Information for Neurocil®, subcutaneous application is explicitly advised against due to the risk of tissue damage. Since the preparation is also available as drops, this can be an alternative to s.c. administration.

13. Constipation

Working Group Leaders: Gerhild Becker, Martin Holtmann (2011-2015), Philipp Lenz (2016-2019 for the update)

13.1. Introduction

While constipation has traditionally 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 [199].

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 sub-types only hold limited significance [200].

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 [201, 202]. Approximately half of all patients complain about constipation on admittance to a palliative care unit [203]. In patients receiving opioids, the prevalence can increase to almost 90 % [204, 205]. Pathophysiologically speaking, immobility, a low-fibre diet, inflammatory oedema, 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 [206, 207]. Malignant gastro-intestinal obstruction (MBO) is understood to be the presence of a clinical and radiologically confirmed gastro-intestinal occlusion due to an incurable intra-abdominal tumour or intra-peritoneal metastasis [349, 350]. The obstruction may be complete or incomplete (see the chapter on Malignant Bowel Obstruction (MBO)).

13.2. Assessment/Diagnosis of Constipation

No.	Recommendations	GoR	LoE	Sources
13.1.	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 stool frequency and/or hard stool consistency *shall* be taken into account. [Modified 2019]		EC	
13.2.	In patients with incurable cancer, the assessment of constipation *shall* 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	
13.3.	In patients with incurable cancer, the amount of stool and frequency of defecation as well as the subjective impairment *shall* be documented for an early diagnosis of constipation.		EC	

13.3. Prophylaxis

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

13.4. Pharmacological Treatment

13.4.1. Constipation (Regardless of the Cause)

No.	Recommendations	GoR	LoE	Sources
13.6.	Osmotic and/or stimulant laxatives *shall* be used for the pharmacological mono- or combination therapy of constipation for patients with incurable cancer.	A	1-	[178, 201]
13.7.	Osmotic salts or magnesium hydroxide *should not* be administered to patients with incurable cancer and constipation. [Modified 2019]	B	1-	[201]

No.	Recommendations	GoR	LoE	Sources
13.8.	In respect to defecation disorders in patients with incurable cancer, rectal measures *should* be used.	B	1-	[201]
13.9.	Pharmacological treatment with prokinetic or secretagogue agents *can* be administered in patients with incurable cancer and constipation when conventional treatment fails.	0	1-	[201]

13.4.2. Opioid-related Constipation

See also section Treatment of Opioid-related Constipation, in the chapter on Cancer Pain, from which the recommendations given here were taken.

No.	Recommendations	GoR	LoE	Sources
Pain 9.25.	Laxatives *shall* be routinely prescribed for the management or prophylaxis of opioid-induced constipation. [Reviewed 2019, new literature added]	A	1+	[113, 177, 178]
Pain 9.26.	No evidence suggests that one laxative agent *should* be recommended over others. [Reviewed 2019, new literature added]	ST	1+	[113, 177, 178]
Pain 9.27.	A combination of laxatives with different modes of action *can* be administered in resistant constipation. [Reviewed 2019, new literature added]	0	1+	[113, 177, 178]
Pain 9.28.	In the case of opioid-related constipation, the administration of peripherally-acting mu-opioid receptor antagonists (PAMORA), such as methylnaltrexone, naldemedin, naloxegol or the combination of oxycodone with the opioid antagonist naloxone, *should* be considered if conventional laxatives are not effective enough. [Modified 2019]	A	1+	[199-207]

13.4.3. Step-wise Approach

No.	Recommendation	GoR	LoE	Sources
13.10.	In the prophylaxis and treatment of constipation a standardised approach in the form of a step-wise approach *should* be chosen (see Figure 8).		EC	

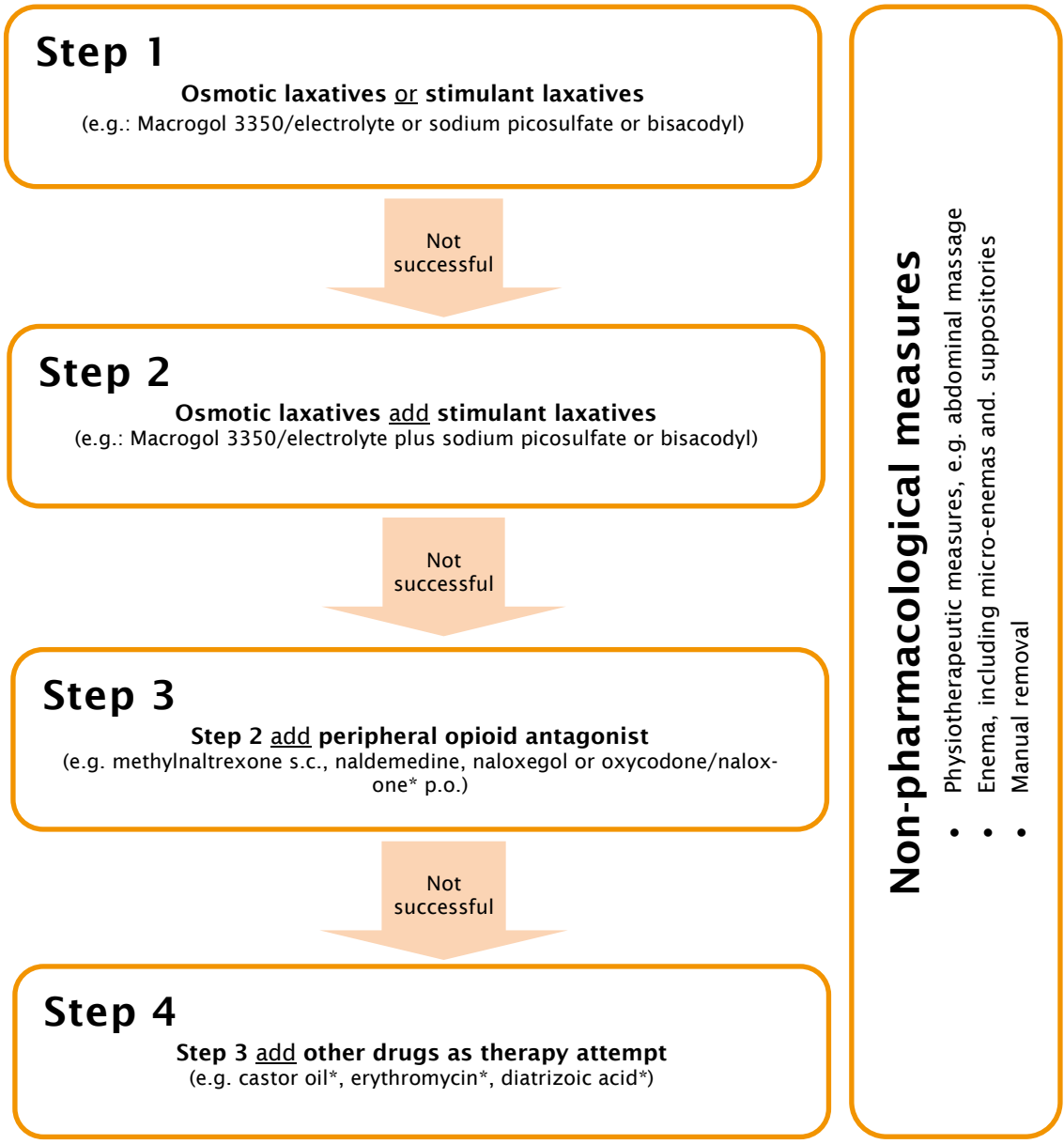


Figure 8: Step-wise approach for the treatment of constipation

* Off-label use

13.5. Non-pharmacological Measures

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

14. Malignant Bowel Obstruction (MBO)

Working Group Leaders: Claudia Bausewein, Robert Siegel

14.1. Introduction

Definition

Malignant bowel obstruction (MBO) is understood to be the presence of a clinical and radiologically confirmed gastro-intestinal occlusion due to an incurable intra-abdominal tumour or intra-peritoneal metastasis [349]. The obstruction may be complete or incomplete.

A paralytic ileus without obstruction must also be considered as a differential diagnosis in MBO, but this will not be discussed further here. However, it should be pointed out that the treatment of late-stage paralytic ileus does not differ significantly from the treatment of the MBO itself due to its similarity to MBO. Pronounced constipation, possibly with coproliths, can clinically display the signs of a gastro-intestinal obstruction, but must be distinguished from the later.

MBO and its clinical consequences cause among the most debilitating situations for patients with advanced tumour diseases. The prevalence of MBO is 10-28% in colorectal tumours and 20-50% in ovarian cancer [351]. Patients with cervical, prostate and bladder cancer also suffer from an increased risk of MBO. Approximately 60% of patients have primary disease of the small intestine, 33% have colon disease, while both intestinal segments are affected in more than 20% of patients [352].

Causes, Pathophysiology

The conceptual and pathophysiological background of malignant gastro-intestinal transit disorders is shown in Figure 9.

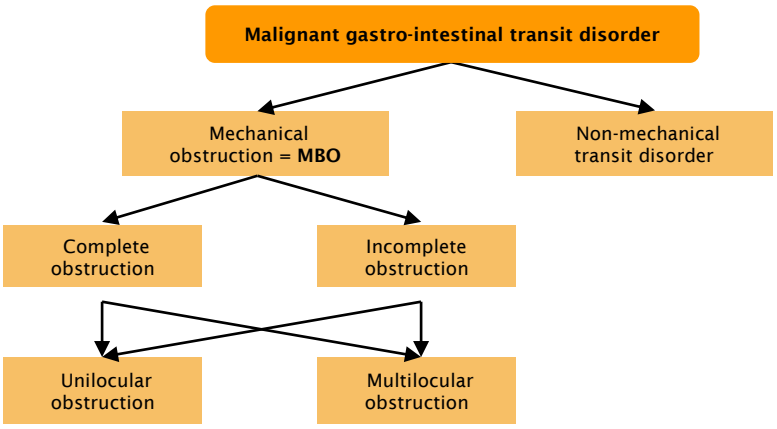


Figure 9: Differentiation of malignant gastro-intestinal transit disorders

The causes listed in Table 23 can lead to MBO.

Table 23: Causes of gastro-intestinal obstruction (adapted from Ripamonti et al. 2001 [352], Anthony et al. 2007 [349])

Causes and pathogenetic factors of gastro-intestinal obstruction
• Pressure on the intestinal lumen from the outside: Primary tumour, metastases, adhesions, radiogenic fibrosis • Intraluminal occlusion of the intestine • Tumour infiltration of the intestinal musculature and the resulting rigidity of the intestinal wall ("intestinal linitis plastica") • Motility disorders of the intestine, induced by tumour infiltration into the mesentery, the coeliac plexus or other nerve structures • Pronounced constipation due to potentially motility-inhibiting medications: opioids, anti-cholinergics

In most cases, MBO is based on a combination of different causes. As a rule, malignant bowel obstructions are caused by tumour recurrence or metastases in the mesentery and intestinal wall, mostly in the form of peritoneal carcinoma.

Intestinal obstructions of a non-malignant origin are not covered in this chapter. These include adhesions and adhesive bands after a previous operation. In the case of isolated or clearly localised causes, surgery may also be useful in patients with incurable cancer. Inflammatory intestinal diseases, adhesions and intestinal strictures as a late consequence of radiotherapy, especially in cervical and bladder carcinomas, are usually not unilocular and therefore rarely benefit from surgical therapy, with individual exceptions.

Symptoms

Patients with MBO often suffer from nausea and vomiting, pain and constipation. Continuous or colicky pain may be caused by the tumour, hepatomegaly or pronounced meteorism. Nausea and vomiting occur intermittently or continuously. The severity of the main symptoms of abdominal pain, vomiting and meteorism depends on the degree of the obstruction in the gastro-intestinal tract (see Table 24).

Table 24: Degree of the MBO and severity of the symptoms (according to Bausewein 2015 [353])

Localisation of the obstruction/ symptoms	Vomiting	Pain	Flatulence
Stomach outlet/ duodenum	+++ Mostly undigested food	+	0
Small intestine	+	++ colicky, epigastrium, umbilical	+
Colon	(++) Late symptom, up to fecal vomiting	+ para-umbilical, lower abdomen	+++

In the case of a complete obstruction, no or little stool is usually passed, but in the case of an incomplete occlusion, the patient may still have occasional bowel movement [354]. Wind is passed for as long as the obstruction is not complete. So-called pseudo-diarrhoea occurs when stool accumulates proximal to the constriction and is liquefied by bacterial

migration. This liquid stool can then pass through the constriction more easily and appears as suspected diarrhoea. Furthermore, patients complain of heartburn, a dry mouth, loss of appetite and weight loss.

It is often clinically difficult to distinguish whether the MBO is complete or incomplete. One indication can be the passing of wind, which is not present in the case of complete occlusions.

In most cases the symptoms of MBO develop slowly over days or weeks. As a rule, the MBO is not an emergency, as symptoms are very rarely acute. Obstructions can also exist intermittently, with the regression of symptoms from time to time and spontaneous regression possibly occurring even without therapy.

The complications of MBO include peritonitis, perforation and reflux, with the risk of aspiration. Furthermore, patients and their family carers are placed under high levels of psychological stress by the situation. In addition to symptom relief, questions of food and fluid intake, as well as in-home care, need to be clarified.

Even if the MBO does not represent a uniform clinical picture, the life prognosis for many patients, especially if only a purely symptomatic therapy is possible, is often limited to a few days or weeks. For this reason, advance care planning should also be considered not later than at the time when the MBO occurs in order to enable patients to clarify questions that they deem important.

14.2. Assessment and Diagnostics

14.2.1. Assessment

No.	Recommendations	GoR	LoE	Sources
14.1.	In patients with incurable cancer and suspected MBO, assessment of nausea, vomiting, bloating and abdominal pain, as well as changes in bowel movements *shall* be carried out in the form of a subjective assessment by the patient, e.g. within the framework of a multi-symptom survey.		EC	
14.2.	In patients with incurable cancer, an assessment of nausea, vomiting, bloating, abdominal pain and changes in bowel movements *shall* be carried out regularly before, during and after symptomatic MBO therapy.		EC	
14.3.	In patients with incurable cancer and suspected MBO, a careful medical history, in particular with all previous abdominal operations, interventions and radiation therapy treatments, the current dietary form and/or changes and medication, as well as a stool medical history *shall* be taken.		EC	
14.4.	Parallel to the initiation of a symptomatic therapy of the MBO in patients with incurable cancer, potentially treatable causes *shall* be determined.		EC	

14.2.2. Diagnostic Measures

No.	Recommendations	GoR	LoE	Sources
14.5.	Further diagnostic measures for the MBO *shall* be considered, depending on the clinical situation of the patient, existing systemic therapy options, potential operability and previous findings.		EC	
14.6.	Patients with incurable cancer and suspected MBO *should* undergo rectal digital exploration during the physical examination.		EC	
14.7.	A CT abdomen and pelvis scan *shall* be performed to clarify a possible MBO in patients with incurable cancer if surgical, systemic or interventional measures are being considered or if imaging is required for a diagnosis and decision-making with the patient.		EC	
14.8.	An ultrasound examination of the abdomen *can* be performed on patients with incurable cancer and a suspected MBO if the CT scan is not desired or not possible, or as part of the follow-up during treatment.		EC	
14.9.	If a surgical or interventional measure for the treatment of the MBO is being considered, a laboratory tests *shall* be carried out to assess the risk and record important parameters, such as the blood count, electrolytes, kidney and liver function parameters (including albumin and coagulation).		EC	

A CT scan of the abdomen and pelvis with intravenous contrast agent is the gold standard for the diagnosis of MBO [355], as it has a specificity and sensitivity of more than 90% [351, 356]. CT should only be performed if an intervention or operation is not refused and appears reasonable. If nausea and/or vomiting are present and there is suspicion of a severe obstruction proximal to the colon, no oral contrast agent should be administered [355]. Radiation exposure from CT examinations plays a subordinate role in the palliative situation.

An ultrasound examination of the abdomen by an experienced examiner is useful at the bedside if a CT examination has not been performed or as part of the progress assessment during therapy.

14.3. Strategies, Attitudes, Techniques

14.3.1. Information and Advance Care Planing

No.	Recommendations	GoR	LoE	Sources
14.10.	With patients with incurable cancer and MBO and their family carers, it shall be discussed at an early stage (i.e. as soon as the clinical symptoms are relevant for the patient) about the possible course of the disease, the therapy options and goals of care as well as the patient's wishes, and an appropriate treatment plan should be developed.		EC	

14.3.2. Nursing Measures

See also the chapter on Nausea and Vomiting (not Tumour Therapy-related).

No.	Recommendations	GoR	LoE	Sources
14.11.	In order to relieve a dry mouth in patients with incurable cancer and MBO, oral hygiene including lip moisturisation *shall* be offered and performed regularly and several times a day.		EC	
14.12.	In order to relieve a dry mouth in patients with incurable cancer and MBO, ice cubes to suck, crushed ice, frozen fruit pieces, sour sweets and/or chewing gum *should* be offered.		EC	
14.13.	In patients with incurable cancer and MBO-related vomiting, issues such as disgust and shame *should* be considered within the framework of the discussions.		EC	
14.14.	After each episode of vomiting, oral hygiene *shall* be offered to the patient and made possible.		EC	
14.15.	In patients with incurable cancer, MBO and meteorism, warm and moist tummy wraps and pads *can* be offered for relaxation.		EC	
14.16.	In patients with incurable cancer and an incomplete MBO, enemas *can* be offered as an accompanying therapy to pharmacological treatment in order to maintain or restore intestinal transit and/or draw away any gases that have formed.		EC	

14.3.3. Drug Application

No.	Recommendations	GoR	LoE	Sources
14.17.	In cases of persistent vomiting and resorption disorders in patients with incurable cancer and MBO, drugs *shall* be administered parenterally.		EC	

14.3.4. Oral and Parenteral Hydration and Nutrition

No.	Recommendations	GoR	LoE	Sources
14.18.	Patients with incurable cancer and MBO *should* be offered oral fluids.		EC	
14.19.	Patients with incurable cancer and MBO *can* be offered oral food.		EC	
14.20.	If electrolyte disorders and dehydration are present, infusions *shall* be administered for compensation purposes until a surgical or interventional treatment of the MBO has been decided upon.		EC	
14.21.	If there is no surgical or interventional treatment of the MBO and the therapy is purely symptomatic, parenteral hydration *can* be considered depending on the therapeutic goal.		EC	
14.22.	In patients with incurable cancer and MBO who have an expected survival time of a few weeks, parenteral nutrition *should* be critically considered.	B	3	[357-363]
14.23.	In patients with incurable cancer and MBO who have an expected survival time of several weeks or months, parenteral nutrition *shall* be considered.	A	3	[357-363]

The **parenteral hydration** in cases of gastro-intestinal obstruction is being controversially discussed. In cases of profuse vomiting due to severe gastro-duodenal occlusion, parenteral fluid administration may be indicated. As a rule, parenteral fluid is of little help in the treatment of a dry mouth and thirst, since both are mainly caused by the medication that is necessary to alleviate the symptoms and do not depend on hydration levels. Sizeable amounts of parenteral fluid can cause increased gastro-intestinal secretions and therefore more vomiting, making it necessary to weigh its use in terms of the resulting benefits and burden [354]. Parenteral fluid can be administered both intravenously and subcutaneously.

14.4. Surgical Procedures

14.4.1. Participatory Decision-making and Goals of Care

Participatory decision-making should define a specific goal of care that can be achieved by the surgical procedure. The focus is on clearly defined goals, such as the avoidance of vomiting, the resumption of oral food intake or improving or eliminating an enteral fistula or preventing or resolving a septic focus in the case of impending perforation or peritonitis due the MBO [364, 365]. General or non-specific objectives such as prolonging life or improving the quality of life should be avoided.

14.4.2. Interdisciplinary Decision-Making Involving Visceral Surgery

No.	Recommendations	GoR	LoE	Sources
14.24.	The recommendation in favour of or against surgical treatment of the MBO *shall* be multidisciplinary.		EC	

The recommendation for or against an operation should be multi-disciplinary, i.e. involving an experienced visceral surgeon, a palliative care physician, an anaesthetist and, if necessary, colleagues from other speciality.

14.4.3. Success Rate of a Surgical Intervention: Prognostic Factors and Prediction Estimates

Negative prognostic factors in patients with MBO have been identified in several retrospective studies and on the basis of registry data. In particular, ascites palpable tumour masses, advanced age, previous abdominal or pelvic radiation, hypalbuminaemia and leucocytosis have been described as prognostically unfavourable factors with regard to a successful surgical intervention [366-370].

14.4.4. Surgical Procedure

No.	Recommendations	GoR	LoE	Sources
14.25.	The surgical treatment of a patient with MBO *shall* be performed by a surgeon experienced in tumour surgery.		EC	
14.26.	In individual cases, the operation of an MBO *can* also be performed laparoscopically.		EC	

14.4.5. Peri-operative Management

No.	Recommendations	GoR	LoE	Sources
14.27.	Before surgical or interventional therapy, patients with incurable cancer and MBO *should* receive a transnasal gastric tube for decompression or removal of content of the stomach and small intestine.		EC	
14.28.	Before any operation on the MBO, pre-operative stoma marking *should* be carried out. Pre- and post-operative care *shall* be ensured by a stoma therapist.		EC	
14.29.	Symptomatic therapy *shall* be provided alongside any surgical or interventional therapy of the MBO.		EC	

14.4.6. Limitation of Therapy in the Case of Intra- and Post-operative Morbidity

No.	Recommendations	GoR	LoE	Sources
14.30.	Simultaneously with the decision for surgical treatment of the MBO, possible post-operative treatment limitations *shall* be discussed with the patient and their family carers.		EC	

14.5. Interventional Procedures

14.5.1. Endoscopic Procedures and Stents

No.	Recommendations	GoR	LoE	Sources
14.31.	In patients with incurable cancer and a tumour-induced obstruction in the stomach outlet and duodenum, an endoscopic stent *can* be used to alleviate the symptoms.		EC	
14.32.	In patients with incurable cancer and a life expectancy of a few months or in a poor general state (ECOG 3-4), an endoscopic procedure *can* be considered for an isolated obstruction in the area of the stomach or the gastroduodenal transition.		EC	
14.33.	In patients with incurable cancer and with a circumscribed, isolated obstruction of the colon or rectum, an endoscopic stent system *can* be considered, particularly in patients where surgery appears difficult due to co-morbidities.		EC	

14.34.	The indication for endoscopic stent placement in patients with incurable cancer and MBO *should* be drawn up in an interdisciplinary manner with the gastro-enterologist, who performs the endoscopy, and the visceral surgeon. The pre-operation discussion with the patient *should* also include the possible consequences of the failure of the endoscopic therapy or related complications.	EC

14.5.2. Nasogastric Drain Tube and Venting PEG

No.	Recommendations	GoR	LoE	Sources
14.35.	In patients with incurable cancer and MBO for whom surgery is no longer possible, a nasogastric tube *can* be temporarily inserted to relieve nausea and vomiting if the symptomatic therapy is not satisfactory.		EC	
14.36.	In patients with incurable cancer and MBO in whom a nasogastric tube provides relief from nausea and vomiting, the placement of a venting PEG tube *should* be considered.		EC	

14.6. Pharmacological Treatment

The focus of the pharmacological treatment is on alleviating nausea, vomiting and abdominal pain. In drug therapy, two different approaches have to be considered as a matter of principle [371]. If the aim is to restore transit (incomplete MBO), corticosteroids are used to reduce oedema in addition to prokinetic anti-emetics and laxatives. If the restoration of intestinal transit through the use of drugs is excluded (complete MBO), not only anti-emetics and analgesics are used, but also anti-secretory drugs in particular, which are intended to reduce intraluminal secretion [371].

14.6.1. Treatment of Nausea and Vomiting in MBO

See also the chapter on Nausea and Vomiting (not Tumour Therapy-related).

No.	Recommendations	GoR	LoE	Sources
14.37.	For the treatment of nausea and vomiting in patients with incurable cancer and **incomplete MBO**, prokinetics such as metoclopramide *should* be used for anti-emesis.	B	4	-
14.38.	For the treatment of nausea and vomiting in patients with incurable cancer and **complete MBO**, prokinetics such as metoclopramide *should not* be used for anti-emesis.	B	4	-

No.	Recommendations	GoR	LoE	Sources
14.39.	For the treatment of nausea and vomiting in patients with incurable cancer and **complete MBO**, anti-psychotics (e.g. haloperidol*, levomepromazine*, olanzapine*) or anti-histamines should be used alone or in combination for anti-emesis.	B	3 4	Anti-psychotics: [372] Antihistamines: -
14.40.	For the treatment of nausea and vomiting in patients with incurable cancer and **complete MBO**, $5HT^3$ antagonists* *can* be used for anti-emesis in combination with typical and atypical anti-psychotics and anti-histamines.	0	4	-
14.41.	Anti-cholinergics such as butylscopolamine* *can* be used to reduce gastro-intestinal secretion in patients with incurable cancer and MBO.	0	3	[371, 373]
14.42.	Anti-cholinergics and prokinetics *shall not* be given in combination to patients with incurable cancer and MBO.	0	4	-
14.43.	Somatostatin analogues* *can* be used to reduce gastro-intestinal secretion in patients with incurable cancer and MBO.	0	1+	[371, 373]
14.44.	Somatostatin analogues* *can* be used in patients with incurable cancer and MBO in combination with butylscopolamine* in order to reduce gastro-intestinal secretion.	0	4	-
14.45.	Ranitidine* or proton pump inhibitors* *can* be used to reduce secretion in patients with incurable cancer and MBO.	EC		
14.46.	Glucocorticoids* *can* be used as a therapy attempt at transit reopening for 5-10 days in patients with incurable cancer and MBO.	0	1+	[374]

* Off-label use

Both anti-emetics and secretion-inhibiting drugs, which do not possess a known anti-emetic effect, are used to treat nausea and vomiting (see Table 25).

Table 25: Treatment of nausea and vomiting in cases of gastro-intestinal obstruction (adapted from Bausewein et. al. [353])

Substance class	Drug	Dose	Remark
Prokinetic agent	Metoclopramide	30-40* mg/d s.c.*	Drug of choice when incomplete obstruction or functional disorders are suspected. Due to increased GI motility, pain and vomiting may be exacerbated. **Cave**: If a complete obstruction is present, discontinue the medication.
Anti-psychotics	Haloperidol*	2.5–10 mg/d s.c.* or i.v.*	Drug of choice in the case of complete obstruction and when no prokinetic anti-emetics can be used

Substance class	Drug	Dose	Remark
	Levomepromazine*	1-5 mg oral/s.c.* at night	Increase up to 25 mg/d possible, but rarely necessary
	Olanzapine*	2.5 mg as initial dose, if necessary 5–10 mg oral/s.l. daily	Cave in elderly and dementia patients due to the prolonged half-life and increased mortality risk
Anti-histamine	Dimenhydrinate	150 mg rectal 62–400 mg/d s.c.* or i.v.	Has a sedative effect
Setrone	Ondansetron*	8 mg oral or s.l./s.c.*/i.v. 2-3 times a day	Increases constipation
	Granisetron*	1-2 mg oral/s.c.*/i.v. once a day	Increases constipation; an increase of up to 9 mg per day is possible
Anti-cholinergic	Butylscopolamine*	40–80 mg/d s.c./i.v. Dosage increase up to 120 mg* possible	For the reduction of GI secretion, no own anti-emetic effect. Increase in mouth dryness and thirst possible
Somatostatin analogues	Octreotide*	Initial dose 100 µg every 12 hours, increase up to 750 µg/d possible, over that rarely any more effect	For reducing GI secretion, second-choice agent, as it is expensive
	Lanreotide*	60 mg deep s.c. in the outer upper quadrants of the buttocks every 3 months	If necessary, 120 mg every 4 weeks
H_2 blocker	Ranitidine*	50 mg 2-4 times daily or continuously 100 – 200 mg/24 h i.v.	
Proton pump inhibitors	Omeprazole*	40–80 mg/d i.v, s.c.*	
Corticosteroids	Dexamethasone*	8–12 mg/d s.c.*/i.v.	For a reduction in peri-tumourous oedema (possible restoration of transit) and anti-emesis, fewer mineralocorticoid side effects than methylprednisolone
* Off-label use			

14.6.2. Treatment of Abdominal Pain in MBO

No.	Recommendations	GoR	LoE	Sources
14.47.	In patients with incurable cancer and MBO, abdominal pain *shall* be treated with non-opioids (e.g. metamizole) and opioids.		EC	
14.48.	Butylscopolamine *should* be administered for the treatment of colicky abdominal pain in patients with incurable cancer and MBO.		EC	

14.49.	For the treatment of colicky abdominal pain in patients with incurable cancer and MBO, motility-enhancing drugs such as prokinetics and stimulant laxatives *should not* be administered.	EC

Patients with gastro-intestinal obstruction suffer from both continuous and colicky abdominal pain. Colicky pain can be an indication of the presence of a complete obstruction. Colicky pain usually responds well to spasmolytics such as butylscopolamine. Metamizole also has spasmolytic properties and is therefore particularly suitable as a non-opioid (see Table 26). NSAIDs are not used as non-opioids in MBO because they are not suitable due to their side effect (gastro-intestinal bleeding) and limited parenteral administration. Furthermore, pain therapy in patients with gastro-intestinal obstruction does not differ from other tumour pain, i.e. the WHO pain-relief ladder is used in the same way (see the chapter on Cancer pain).

Table 26: Drug therapy of intestinal colic (according to Bausewein 2015) [353])

Drug	Dose	Remark
Metamizole	1,000–4,000 mg/d s.c.* or i.v.	Additional spasmolytic component. Subcutaneous administration: do not administer as a single dose but as an infusion
Butylscopolamine (anti-cholinergic)	40–80 mg/d s.c./i.v.	Simultaneous reduction in GI secretion. Increase in mouth dryness and thirst possible
Morphine (or other level III opioids)	10–20 mg/d s. c. or titrate	In opioid-naive patients or according to the previously prescribed oral dose
* Off-label use		

14.6.3. Therapy of Constipation in MBO

No.	Recommendations	GoR	LoE	Sources
14.50.	Patients with incurable cancer and **incomplete MBO** *should* receive stimulating laxatives and large enemas only under close monitoring.		EC	
14.51.	Patients with incurable cancer and **incomplete MBO** *can* be given softening laxatives.		EC	
14.52.	Patients with incurable cancer and a **complete MBO** *should not* receive stimulating laxatives or large enemas.		EC	

For further information on laxatives see the chapter on Constipation; for nursing interventions see the section Nursing Measures of this chapter.

15. Malignant Wounds

Working Group Leaders: Axel Doll, Elisabeth Krull

15.1. Introduction

The recommendations in this chapter relate to the symptom-oriented treatment, care and support for patients with malignant wounds, as well as the support for their family carers. A malignant wound, or fungating wound, is defined by the British Columbia Cancer Agency as a malignant lesion of the skin "the result of cancerous cells infiltrating the skin and its supporting blood and lymph vessels causing loss in vascularity leading to tissue death. The lesion may be a result of a primary cancer or a metastasis to the skin from a local tumour or from a tumour in a distant site" [375]. The European Oncology Nursing Society also describes malignant cutaneous wounds as the "Infiltration of the tumour or the metastasis into the skin and the afferent blood and lymph vessels" [376, 377].

There are few reliable data available on the prevalence of malignant wounds. The available literature describes a prevalence of between 6.6% and 14.5% among all cancer patients [378-380]. Malignant wounds can occur in all regions of the body: breast (49.3%), neck (20.9%), thorax (17.6%), extremities (16.6%), genitals (16.6%), head (13.5%) or other regions, e.g. armpit (1.7%) [380].

Depending on the patient's general condition, the stage of the disease and the expected remaining life expectancy, wounds can also be present in patients in a palliative situation where there is a realistic chance of wound healing or of a reduction in the size of the wound (see below). Patients with an incurable underlying condition and with a wound that can heal are not covered in this guideline.

The wounds listed below are not covered in this guideline, but reference is made to the existing guidelines:

- Chronic wounds: Ulcus cruris venosum/arteriosum/mixtum/other and diabetic foot ulcer (National Expert Standard on care of people with chronic wounds of the German Network for Quality Development in Nursing ["Pflege von Menschen mit chronischen Wunden" 2015, Deutsches Netzwerk für Qualitätsentwicklung in der Pflege, 1. Aktualisierung] [381] and the AWMF S3 Guideline on local therapy of chronic wounds in patients with the risks of peripheral arterial occlusive disease, diabetes mellitus, chronic venous insufficiency [„Lokaltherapie chronischer Wunden bei Patienten mit den Risiken periphere arterielle Verschlusskrankheit, Diabetes mellitus, chronisch venöse Insuffizienz" 2012] [382])
- Tumour therapy-induced wounds and skin changes (e.g. S3 Guideline on supportive care for oncological patients ["Supportive Therapie bei onkologischen PatientInnen" - Langversion 1.1, 2017] [2]):
    - Tumour therapy-induced exanthema (see chapter 8.1)
    - Extravasation (see chapter 11)
    - Radiodermatitis (see section 12.5)
- Acute wounds, e.g. fractures, injuries from a fall, burns
- Care of stomata
- Therapy-related wounds, e.g. after operations, punctures, possibly with secondary wound healing

- Acute or chronic graft-versus-host disease (guidelines of the German Society for Haemato-oncology [383, 384])
- Pressure ulcer prevention and treatment (see below)

For patients in palliative care, the guideline "Prevention and treatment of Pressure Ulcers" of the National Pressure Ulcer Advisory Panel (NPUAP), European Pressure Ulcer Advisory Panel (EPUAP) and Pan Pacific Pressure Injury Alliance (PPPIA) [385] as well as the expert standard on pressure ulcer prevention ("Dekubitusprophylaxe in der Pflege" 2017, 2nd update) of the German Network for Quality Development in Nursing apply [386]. Both standards explicitly address the palliative situation. In patients with incurable cancer, the prevention of pressure ulcer is to be performed in accordance with the guidelines. In patients with pressure ulcer, the objectives (healing/size reduction/symptom relief) are weighed [387].

15.2. Assessment and Evaluation

No.	Recommendations	GoR	LoE	Sources
15.1.	In patients with malignant wounds, a comprehensive wound-specific medical history *shall* be performed at the beginning of the treatment to assess the following: • factors that affect the wound, • subjective wound perception of the patients and their family carers, • impairment of the quality of life due to the wound, • knowledge and self-management skills of the patient and family carers with respect to the wound.		EC	
15.2.	A written assessment of the malignant wound with a complete analysis of the wound *shall* be carried out with structured wound documentation sheets at the beginning of the treatment and for further monitoring regularly during the subsequent course of the disease.		EC	

The focus of the wound-specific medical history is on the course of the local care up to that time, the subjective perception of the patient and the effects of the wound on all areas of life (by means of a self-assessment or third-party assessment). In Table 27 and Table 29 possible focal points of the wound medical history and wound assessment are listed. Social and psychological influential factors or systemic effects on the family and the social environment should be recorded. Individual prioritisation is to be carried out in the assessment according to the specific situation. In Table 28 anamnestic questions are compiled for assessing the change in body image. These should be selected on a situation-specific basis in order to pro-actively address this taboo subject.

Table 27: Focal points for the medical history (compiled from various expert standards [375, 381, 388-392])

Focal points of the wound-specific medical history
Medical history of the wound (underlying disease, co-morbidities)
Previous treatment of the underlying disease, previous wound diagnostics, medication (e.g. cortisone, analgesics) and allergies
Information status/understanding of the disease by the patient/their family carers' understanding of the cause of the wound, wound condition, implementation of specific measures (e.g. pressure relief, compression therapy)
Wound has existed since... (wound duration)
Wound care concept (wound care products used, frequency of dressing changes, who has carried them out so far, restrictions due to the dressing)
Effects of the wound on the quality of life
Motor/functional limitations due to the wound (speaking, swallowing, hearing, seeing, relieving posture, contractures)
Effects on everyday life (e.g. sleep disturbance, life activities, choice of clothes, financial burdens)
Psychological and social significance of the wound for the patient and their family carers (e.g. isolation, embarrassment, feelings of disgust, loss of control)
Social background and wound care support
Effects of the wound on the self/body image
Effects of the wound on the partnership, intimacy, sexuality, family relationships
Previous coping strategies; self-management skills; external resources/support

Table 28: Anamnestic questions about the change in body image and effects on family carers and social environment (according to [393-396])

Impact area	Possible anamnestic questions
Effects of the wound on the body image	• Have you noticed changes in people around you since you have had the wound? • How do you feel about the changes to your body? • What do you find to be the worst? • Has there been changes with respect to the things that you can do on your own? Do you find this to be a problem? • Has your attitude towards yourself or your body changed since the onset of the disease? • How do you experience not being able to move as well as you could before or having to deal with other limitations of your bodily functions? • What is it like for you to live with the wound and its consequences?
Effects of the wound on the partnership, intimacy, sexuality, family	• How do you think your partner perceives you with your wound? • How and in what way does the wound change the relationship with your partner? How does that affect you? • Have you been experiencing a change in those around you since you have had the wound?

Impact area	Possible anamnestic questions
	• Have contacts and relationships with people close to you, friends and acquaintances changed? • Is the wound affecting your relationship with your family and/or friends?

Table 29: Criteria list for a wound-specific assessment (according to [375, 381, 388-392, 397, 398])

Criteria for wound assessment	
Wound type: e.g. skin metastasis, fistula, cutaneous infiltration by the primary tumour	
Wound location: Drawing on the diagram of the body	
Wound size (in cm): measuring with a measuring tape (depth, height, width, length), tracing (tracing of the wound edges on film), pockets, fistulas, undermining	
Wound bed (wound surface): e.g. coverings (fibrin, wet/dry necrosis), bones, tendons, fascia, epithelial tissue, granulation tissue	
Wound margin (epithelialized area between wound surface and layered skin with original layers): e.g. maceration, redness, livid discolouration, oedema	
Wound environment: area bordering on and surrounding the wound margin; e.g. swelling, maceration, tension blisters, scratch marks, oedema	
Local signs of inflammation: odour ↑, exudation ↑, redness, swelling	
Wound-related symptoms:	Pain in and close to the wound: continuous pain, pain upon movement, tenderness, NRS/VAS
	Itching: due to an inflammatory reaction, dressing materials, continuous, intermittent
	Wound odour: • **No odour** noticeable within proximity of the patient, dressing loosened (Cave: odour may still be perceived by the patient) • **Slight:** odour noticeable within proximity of the patient, dressing has become loose • **Moderate**: odour noticeable when entering the room (at a distance of 2-3 m from the patient), dressing has become loose • **Strong:** odour noticeable when entering the room (at a distance of 2-3 m from the patient) with intact dressing (cave: time of last change of dressing) • **Very strong:** odour noticeable on the ward/in the house with an intact dressing (cave: time of last change of dressing)
	Bleeding tendency: Spontaneous bleeding or contact bleeding, localisation of the bleeding (area of the wound margin, tumour), risk of bleeding to death/obstruction, amount (none, mild, moderate, severe)
	Exudate quantity: • **None** Dressing is dry • **Minimal** Dressing is moist • **Medium** Dressing is moist, clothing dry • **Strong** Dressing is wet and clothing moist • **Very strong** Dressing and clothing are saturated Exudate quality (examples of possible causes) • Clear, serous (physiological or e.g. lymphatic/urinary fistula)

Criteria for wound assessment	
	• Serous/turbid (fibrinogen= inflammation) • Slimy/tough (purulent = infected) • Yellow (e.g. urinary fistula, residues of hydrocolloid dressings) • Brown (e.g. enterofistula, residues of alginates, hydrocolloids) • Green (e.g. pseudomonas aeruginosa or chlorophyl-containing layers)

A frequent trigger of wound-specific pain is the manipulation of the wound as a result of the necessary dressing changes. For this reason, a distinction should be made in the assessment of this pain situation by means of targeted anamnestic questions (see Table 30).

Table 30: Anamnestic questions to record wound pain caused by the dressing change (according to [382, 399, 400])

Criteria	Specific anamnestic questions
Type of pain (nociceptive and neuropathic)	Describe the pain upon the last removal of the bandage
Location of the pain	Where was the pain? Was it restricted to the immediate area of the wound or did you feel it in the surrounding area?
Triggers of the pain	Which part of the procedure was the most painful, e.g. removal, cleaning, application of the dressing, exposing the wound?
Pain-reducing factors	What helped to reduce the pain, e.g. breaks, slow removal of the dressing, being able to remove the dressing yourself?
Painful period	How long did it take for the pain to subside after the procedure?

15.3. The Principles of Treatment

No.	Recommendations	GoR	LoE	Sources
15.3.	For patients with malignant wounds, an expert on wounds *should* be consulted in the following cases: • uncertainty in the wound assessment, • uncertainty in wound-specific symptom management, • uncertainty in the counselling of patients and family carers, • strong psychosocial burdens caused by wounds, • unforeseen changes to the wound situation, • specific circumstances and diagnostic tasks: e.g. extensive wounds, questions of fixation in certain wound locations.		EC	

15.4.	For the indication of specific therapies in the case of malignant wounds, experts in the respective discipline *should* be consulted.	EC
15.5.	If the patient with malignant wounds changes to another care setting, a wound transfer report *shall* be prepared to ensure the continuity of care. This report should contain the current status of the wound history and assessment, the targets and measures that are initiated for wound care.	EC

15.4. Relief of Wound-associated Symptoms

15.4.1. Relief of Psychosocial Burdens

No.	Recommendations	GoR	LoE	Sources
15.6.	The patient with a malignant wound *shall not* be simply reduced to their wound.		EC	
15.7.	In the treatment of patients with a malignant wound, self-management and the feeling of control *should* be strengthened.		EC	
15.8.	In empathic, respectful conversations, patients with malignant wounds and their family carers *should* be actively addressed about changes in their body image, sexuality and self-image and their effects on their partnership, relationships and social participation.		EC	

15.4.2. Relief of Pain

No.	Recommendations	GoR	LoE	Sources
15.9.	In order to avoid triggering pain by changing the dressing, special care *shall* be taken with atraumatic wound management for malignant wounds: • Use of non-adherent wound dressings, e.g. skin-friendly silicone dressing • Careful removal of the dressing, e.g. by moistening a dry dressing before removing it • Avoid mechanical irritation (e.g. by rinsing instead of wiping, wet-dry phase) • Use of warmed wound irrigation solution • Tension-free application of wound dressings and fixing bandage.		EC	

15.10.	If pain is to be expected when changing the dressing of the malignant wound, a fast-acting analgesic *shall* be administered preventively before changing the dressing.	EC		
15.11.	For the systemic pain therapy of permanent nociceptive or neuropathic pain in the case of malignant wounds, reference is made to the recommendations in the chapter on cancer pain (WHO pain-relief ladder and co-analgesics).	EC		
15.12.	In the case of wound pain, local therapy with a local anaesthetic or analgesic (morphine gel) *can* be considered.	0	4 2-	Local anaesthetic: [385] Local morphine: [404, 405]
15.13.	In the case of movement-induced pain caused by malignant wounds, patient-oriented positioning, adapted care with the use of aids and adapted movement therapy *should* be carried out.	EC		
15.14.	In patients with a malignant wound and associated lymphoedema, manual lymph drainage *can* be performed.	EC		

Despite a lack of evidence, sterile or aseptically produced 0.1% morphine gels have proven effective for local pain reduction in practice when applied once a day to the wound. If a polihexanide-containing morphine gel formulation is prepared, a longer use is possible; contamination must nevertheless be avoided. It therefore makes sense to fill in small quantities (see Table 31).

Table 31: Production of morphine gel 0.1% (after Herbig 2011) [406])

Morphine gel 0.1% preserved with polyhexanide, modified according to NRF formulation reference		
Formulation:	Morphine hydrochloride trihydrate	0.1 g
	Ethylene-diamine-tetra-acetic acid, sodium salt	0.1 g
	Hydroxyethyl cellulose 400	4.5 g
	Polihexanide concentrate 20% (m/V)	0.2 ml
	Purified water (Ph.Eur.)	Ad 100.0g
Shelf life:	4 weeks	
Indication:	Painful, infected, superficial wounds	
NRF= neues Rezeptur-Formularium (new recipe form)		

15.4.3. Itching of the Malignant Wound

No.	Recommendations	GoR	LoE	Sources
15.15.	If itching occurs in and around malignant wounds, possible causes (e.g. inflammatory reactions, allergy to or incompatibility of dressing materials) *should* be investigated and, if possible, corrected.		EC	

Medical history, physical examination and further diagnostics by the physician, as well as systemic and topical drug therapy, are described in detail in the S2k guideline on diagnostics and therapy of chronic pruritus ("Diagnostik und Therapie des chronischen Pruritus") [401]. The topical products recommended in the guideline are not all intended for use on the edge of the wound and wound environment. For example, preparations containing menthol or camphor and capsaicin products can trigger severe stinging/pain, especially in previously damaged skin.

15.4.4. Malodour Control

No.	Recommendations	GoR	LoE	Sources
15.16.	Malodourous malignant wounds *shall* be cleaned carefully and gently upon every dressing change in order to reduce odour.		EC	
15.17.	In the case of malodourous malignant wounds, the wound *can* be treated with local wound antiseptics to reduce odour.	0	3	[407-410]
15.18.	Metronidazole* *can* be used locally in the wound area to minimise germs and reduce malodours.	0	1-	[411-414]
15.19.	Metronidazole* *can* be administered systemically (orally/i.v.) in malodourous malignant wounds.	0	3	[415]
15.20.	In malodourous malignant wounds, the wound *should* be treated with exudate-absorbing and germ-absorbing dressing materials.	B	4	-
15.21.	In malodourous malignant wounds, wound dressings with activated carbon *can* be used for local odour absorption.	0	3	[412]
15.22.	In malodourous malignant wounds as a result of wound infection, the wound *can* be treated with antiseptic dressing materials.	0	2-	[411, 416]
15.23.	In order to reduce malodour and pain, the benefits and risks/burdens of the surgical removal of necrotic tissue *should* be carefully weighed with the patient.		EC	

The step-wise approach illustrates how the measures can build on one another (see Figure 10). If one step on the ladder is not sufficient to alleviate the odour, it should be supplemented by the measures in the next step.

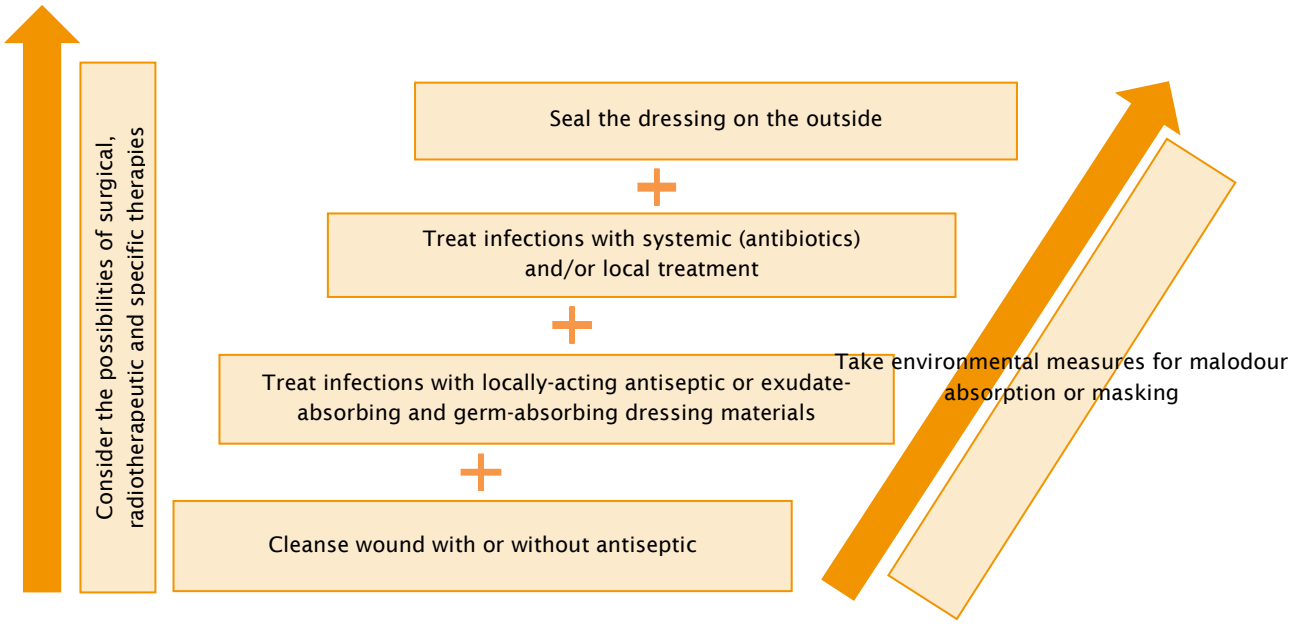


Figure 10: Step-wise measures to reduce malodour (prepared by the working group)

15.4.5. Exudate Management

No.	Recommendations	GoR	LoE	Sources
15.24.	Malignant wounds with heavy exudate *should* be covered with a sufficiently absorbent secondary dressing. In the case of malignant wounds with high exudate and a wound cavity, this *should* be filled with suitable wound dressings.	B	4	[385]
15.25.	In the case of malignant wounds with heavy exudation or increased exudate production due to fistula, drainage bags and stoma care materials *can* be used to collect the exudate.	EC		
15.26.	In the case of malignant wounds with increased exudate production, wound edge/periwound protection *shall* be provided to prevent maceration and the resulting pain thereof.	EC		
15.27.	In the case of malignant wounds with massive exudation and strong malodour, negative pressure therapy *can* be considered.	EC		

In the following overview (see Table 32), examples of possible relevant product groups for local wound management in the case of heavy exudate are listed.

Table 32: Possible wound dressings for exudate management (working group compilation)

Product group	Properties	Application
Silicone-based wound contact layer	Atraumatic removal Adhesion of the secondary dressing to the wound bed is avoided. Exudate is led away by a mesh in the secondary dressing. Cave: viscous exudate!	Select a suitable size Apply approx. 2 cm beyond the edge of the wound Apply in a single layer; double-layer application results in exudate accumulation and infection Cover with a suitable secondary dressing, e.g. absorbent compresses (with superabsorbent particles) or superabsorbent
Alginate	Wicking action Wound cleaning/autolysis Gel formation Haemostasis	Wound filler in compress or tamponade form Adapt to wound size Apply loosely in wound Cover with a suitable secondary dressing Ensure residue-free removal when changing dressings Releases moisture under pressure
Hydrofibre	Exudate binding Wound cleansing Gel formation Vertical fluid absorption; resulting in conditional maceration protection of the wound edge and wound environment Good retention of wound exudate	Wound filler in compress or tamponade form Apply approx. 2 cm beyond the edge of the wound Cover with a suitable secondary dressing Ensure residue-free removal when changing dressings
Cavity foam dressing	Rapid exudate binding Expansion in the case of exudate absorption	Wound filler in heterogeneous forms Follow the manufacturer's instructions for size adjustment; pad out max. 2/3 of the wound with it. Cover with suitable secondary dressing.
Superabsorbents	Rapid exudate binding Depending on product: High retention capacity Protection of wound edge and wound environment Available in different sizes and application forms	Select a suitable size Product should generally not be torn or cut to size

Product group	Properties	Application
Transparent skin protection film	Fast-drying, solvent-free, transparent, sterile liquid Long-lasting skin protection: between 72 and 96 hours, depending on the product Available on a silicone base Supports adhesion of wound dressings	Application according to manufacturer's specifications No simultaneous use of skin care products
Silicone-based fixation plasters	Atraumatic removal Skin-friendly fixation of the wound dressing, especially in the case of parchment-like/cortisone skin Cave: adheres, but does not stick; i.e. no secure fixation under shear forces, e.g. sacral region	Select suitable size and adapt if necessary
Foils/thin hydrocollides	Wound edge and environment protection Prevent wound dressings from rolling up with adhesive edge (border)	

15.4.6. Prophylaxis and Management of Bleeding

No.	Recommendations	GoR	LoE	Sources
15.28.	An atraumatic dressing change *shall* be performed to prevent contact bleeding of malignant wounds.	EC		
15.29.	To prevent bleeding from malignant wounds, the administration of anti-coagulant medications *shall* be critically evaluated and, if necessary, discontinued after careful consideration of the benefits and risks.	EC		
15.30.	In the case of expected acute, heavy bleeding from a malignant wound, arrangements *shall* be made with the patient for the case of bleeding and discussed with their family carers. A written emergency plan *shall* be drawn up for this purpose. The family carers, volunteers and other health care providers *shall* be prepared for the potential bleeding and trained in all emergency strategies.	EC		
15.31.	Vasoconstriction measures (e.g. cooling) *should* be used for mild bleeding from malignant wounds.	EC		
15.32.	In the case of heavy bleeding from malignant wounds, anti-fibrinolytics *should* be used systemically (orally/i.v.) or locally.	B	2+	[417]

15.33.	In the case of heavy bleeding from malignant wounds, haemostyptics *should* be applied locally on or in the wound to stop bleeding.	EC

In the case of bleeding from malignant wounds, a distinction is made between contact or spontaneous bleeding and bleeding from the wound bed, from the wound margin or caused by vascular involvement. The interventions depend on the intensity of the bleeding: no bleeding, light superficial bleeding, heavier or moderate bleeding, acute heavy bleeding (potentially stoppable or unstoppable); see Figure 11.

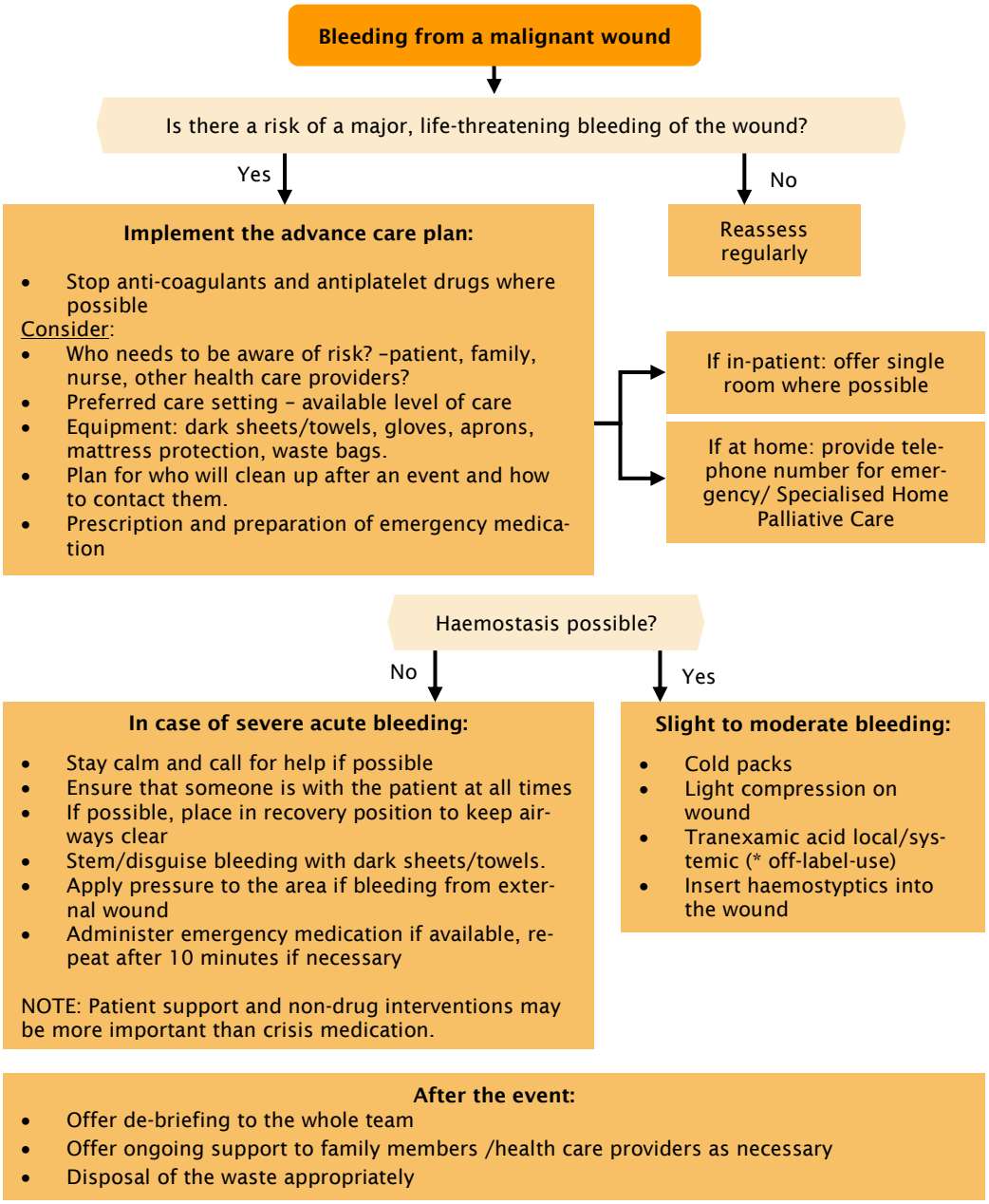


Figure 11: Management of wound bleeding (adapted from Hulme et al. 2008 [418])

15.5. Burden on the Team Members

No.	Recommendations	GoR	LoE	Sources
15.34.	Those involved in the treatment of patients with malignant wounds *shall* be offered opportunities to recognise and express their own consternation and burdens; solutions *shall* be developed in the team to provide them with relief and support.		EC	

16. Anxiety

Working Group Leaders: Vjera Holthoff-Detto, Urs Münch

16.1. Introduction

Along with depression, anxiety is one of the most common psychological burdens of patients with incurable cancer. Fears can differ in appearance depending on their contents, form and expression. Like the DSM, the ICD recognises various anxiety disorders such as agoraphobia, panic disorder, specific phobias, generalised anxiety disorder, mixed anxiety and depression. Post-traumatic stress disorder and an acute stress reaction are types of disorders described in a separate chapter, but they are closely related to anxiety in terms of the cause of the disorder and also subsumed in the Canadian Guideline for cancer patients under the heading Anxiety [419].

Anxiety disorders which meet the criteria of ICD-10 occur with a probability of 11.5% in patients with cancer during the course of the disease [420]. However, fears which are referred to in the literature as subsyndromal anxiety disorders and specific fears [421, 422] and which are perceived by the person affected as stressful, occur significantly more often. Subsyndromal anxiety includes anxiety syndromes that do not fully meet the ICD or DSM criteria for anxiety disorders and are therefore not classified as an anxiety disorder (panic disorder/agoraphobia, generalised anxiety disorder, social or specific phobia) [423]. Specific fears are fears that are triggered by the disease with all its accompanying symptoms. They are usually understandable and appropriate fears in view of the illness. The prevalence rate of these two fear groups is reported to be up to 48% [4]. It is assumed that these disorders and burdens occur even more frequently in patients with incurable cancer, although there are currently no reliable data available [422]. In the case of anxiety disorders, subsyndromal anxiety and specific fears, the treatment indication and planning are based on the suffering caused by the burden of symptoms experienced by the patient.

In relation to patients with incurable cancer, anxiety and anxiety disorders (subsyndromal or ICD-10-relevant) require (if possible and/or desired) an in-depth exploration by means of a psychological and psychopathological diagnostic assessment (see sections Introduction and Assessment). Risk factors for the occurrence of (subsyndromal) anxiety disorders and specific anxieties in patients with incurable cancers include affective and anxiety disorders in the medical history, poor communication with the treatment team, a lack of social support, inadequate symptom control (e.g. pain, breathlessness), prolonged treatment phases, surgical interventions, treatment side effects and adverse effects of the progressive disease [419, 424].

The causes of the specific fears are many and varied [419]. They can be caused by actual or feared symptoms and functional limitations, such as breathlessness, pain or loss of mobility. They may be related to planned or performed therapies, but also to possible suffering as a result of undersupply and inadequate support, accompanying symptoms of the disease (e.g. in the case of CNS tumours) or therapies (e.g. whole brain radiation) or a concomitant phenomenon of symptoms associated with the disease (e.g. breathlessness). The awareness or realization of the imminent end of life can trigger fear and insecurity. The fear can be directed towards various aspects (fear of the dying process, fear of being dead, fear of losing control, fear of the disease progressing, fear triggered by uncertainty about the care of family members, fear as an expression of an existential crisis of meaning). Furthermore, fear can also be the result of unfavourable communica-

tion or an information deficit on the part of the person affected. The latter can be exacerbated by inadequate clarification and information about the disease, the possible course of the disease and limited therapy and support options [425]. Within a family context, fear can also be a fear of the future regarding the loved ones, leaving them behind or causing them a great burden as a result of the own illness. In their anxiety, patients with incurable cancer usually experience an appropriate and healthy reaction to an existential challenge. A systematic description of the anxieties of patients with incurable, advanced cancer is provided in the section on Differential Diagnosis.

For the treatment of anxiety disorders according to ICD or DSM criteria, reference is made here to the S3 Guideline on the treatment of anxiety disorders [426]. Taking into account the individual situation, anxiety disorders should be diagnostically confirmed and psychiatric-psychotherapeutic treatment initiated in accordance with the guideline [426, 427]. If these anxiety disorders occur in patients with incurable cancer, it is important to agree on a therapy strategy together with the patient and the experts consulted (specialist in psychiatry and psychotherapy, specialist in psychosomatic medicine, psychotherapist), taking into account the expected remaining life time and the patient's state of health [419, 422] (see also sections Differential Diagnosis and Attitudes and General Non-pharmacological Measures).

As a distinction from the anxiety disorders classified according to ICD-10, the subsyndromal anxieties and the specific anxieties of palliative patients which are described as 'healthy' but associated with great suffering are referred to below as anxiety or **fear in palliative situations**. There is currently no guideline for these forms of anxiety in patients with incurable cancer.

16.2. Assessment

No.	Recommendations	GoR	LoE	Sources
16.1.	In patients with incurable cancer, the presence of anxiety *shall* be actively and regularly checked, as a treatment indication is based on the burden of symptoms and the suffering experienced by the patient. A medical history of possible pre-existing psychiatric disorders *shall* be carried out upon admission.		EC	
16.2.	A validated and standardised screening instrument *can* be used to detect anxiety in patients with incurable cancer.	0	3	[428-431]
16.3.	If anxiety symptoms are present in patients with incurable cancer, an in-depth exploration *shall* be carried out with regard to the content and intensity of the anxiety and the need for treatment.		EC	
16.4.	In patients with incurable cancer, possible anxiety-related and anxiety-inducing burdens of the family carers *should* also be assessed.		EC	

16.5.	In patients with incurable cancer who are unable to verbally express themselves, the anxiety level *shall* be determined by non-verbal body signals and a multi-professional team. The perceptions and assessment of the family carers *shall* also be taken into account.	EC

For treatment teams, the following may indicate the presence of distressing anxiety in patients and their family carers:

Possible manifestations of distressing anxiety, adapted from Howell et al. [432]
Feeling restless or on edge, irritable
Sense of dread
Physical symptoms such as dry mouth, palpitations, excessive sweating, abdominal pain, headaches, diarrhoea
Sleep difficulties
Fatigue
Difficulty concentrating
Tension in muscle
Breathlessness

In clinical practice in Germany, Generalised Anxiety Disorder-2 (GAD-2) and the Minimal Documentation System for Palliative Patients (MIDOS), the German version of ESAS, can be used as screening instruments. GAD-2 as an extraction of PHQ-4 assesses worries, fears and associated stress with two questions (see Figure 12) [429]. In the case of a positive short screening test, fears can be explored by further targeted questions. GAD-2 is also suitable as an instrument for follow-up screening. MIDOS comprises seven questions, one of which is aimed at anxiety (see Figure 13). MIDOS can be used to make a valid statement as to whether distressing anxiety is present at the time of the assessment.

Over the last 2 weeks, how often have you been bothered by the following problems?	**Not at all**	**Several days**	**Over half the days**	**Nearly every day**
Feeling nervous, anxious, or on edge	0	1	2	3
Not being able to stop or control worrying	0	1	2	3

Figure 12: Screening questionnaire GAD-2 (Generalised Anxiety Disorder) [429]

Please mark how severe your symptoms are today.				
Anxiety	☐ None	☐ Slight	☐ Moderate	☐ Strong

Figure 13: MIDOS (minimal documentation system) questionnaire for the symptom anxiety [433]

16.3. Differential Diagnosis

No.	Recommendations	GoR	LoE	Sources
16.6.	In patients with incurable cancer, anxiety in palliative situations *shall* be distinguished from panic disorders, phobias, generalised anxiety disorders, adaptation disorders and post-traumatic stress disorders.		EC	

Table 33 provides indications for the differential diagnosis of anxiety in palliative situations and ICD-10-relevant anxiety disorders.

Table 33: Differential diagnosis of anxiety disorders and non-ICD-10-relevant anxieties in palliative care (according to ICD 10 and DSM V, as well as Schulz 2012 [434])

Type of anxiety	Specific phobias	Panic disorder (with agoraphobia)	Post-traumatic stress disorder	Generalised anxiety disorder	Adjustment disorder	Fears in palliative situation (in the context of this guideline)
Severity of the anxiety state	Mild, moderate and severe	Moderate and severe	Moderate and severe	Moderate and severe	Mild, moderate and severe	Mild, moderate and severe
Contents of the anxiety	Fear of **a particular** situation or object (e.g. animal phobias, natural environment phobia, blood or syringe phobia), situational phobia (fear of heights, fear of flying, fear of tunnels, darkness or lifts/elevators) Avoidance behaviour	Fear that (in a situation) something bad will happen (recurring) Fear that help cannot come quickly enough or that the frightening situation can not be left quickly enough, including, for example, fear of suffocating, heart attack, an accident, etc.	Lasting memories of a traumatic experience or repeated reliving of a trauma in intrusive memories (reverberation memories, flashbacks, dreams or nightmares) or an inner feeling of distress in situations similar to or related to the stress	Generalised and persistent anxiety Expresses itself in constant worries (circles of worries) These cannot be resolved by rational explanation. Content: family/social relationships, work/performance, money, health issues, everyday life	Anxiety and concern about a critical life event with subjective distress and emotional impairment that interferes with social functioning and performance	Situational anxiety, organic anxiety, existential anxiety
Psychological symptoms	Avoidance behaviour, safety behaviour, possibly panic attacks	Panic attacks, safety behaviour Avoidance behaviour, fear of dying	Avoidance behaviour, high subjective stress and possibly dissociation, Jumpiness/being easily star-	Uncertainty, derealisation, depersonalisation, fear of loss of control, fear of dying without any indication of an actual life-	Subjective distress, emotional impairment, social behaviour disorder	The number of symptoms or the severity of the symptoms is not sufficient to diagnose a disorder according to

Type of anxiety	Specific phobias	Panic disorder (with agoraphobia)	Post-traumatic stress disorder	Generalised anxiety disorder	Adjustment disorder	Fears in palliative situation (in the context of this guideline)
			tled, difficulties concentrating, irritability and outbursts of anger common: social withdrawal, a feeling of numbness and emotional dullness, indifference towards other people, impairment of mood Intrusions (e.g. flashbacks)	threatening disease		ICD-10, or other criteria (cause, appropriateness) argue against a diagnosis according to ICD-10
Somatic symptoms	In the anxiety-causing situation or also in the case of mental confrontation: motor symptoms, e.g. physical restlessness, tension headache, trembling, inability to relax Vegetative symptoms: e.g. lightheadedness, sweating, freezing, tachycardia, breathlessness, upper abdominal pain, dizziness, dry mouth, urge to urinate, urge to defecate, etc., possibly also fainting	In the anxiety situation or partly also in the case of mental confrontation: motor symptoms, e.g. physical restlessness, tension headache, trembling, inability to relax Vegetative symptoms: e.g. lightheadedness, sweating, freezing, tachycardia, breathlessness, upper abdominal pain, dizziness, dry mouth, urge to urinate, urge to defecate, etc.	Nightmares, hypervigilance, jitteriness, high level of sensitivity to key stimuli	Motor symptoms: e.g. physical restlessness, tension headache, tremors, inability to relax Vegetative symptoms: e.g. light-headedness, sweating, freezing, tachycardia, breathlessness, upper abdominal pain, dizziness, dry mouth, etc.	Motor symptoms: e.g. physical restlessness, tension headache, inability to relax Vegetative symptoms: e.g. light-headedness, dizziness, etc	Anxiety symptoms (see left) cannot always be clearly distinguished from symptoms of the somatic illness in question or from interactions and side effects of medication. More frequent causes due to disease-related symptoms are possible (e.g. breathlessness, weakness)
Reference to critical life event	Possible	Yes	Yes (one, several or stress period)	Possible	Yes	As a rule

Type of anxiety	Specific phobias	Panic disorder (with agoraphobia)	Post-traumatic stress disorder	Generalised anxiety disorder	Adjustment disorder	Fears in palliative situation (in the context of this guideline)
Duration of symptoms	Only one situation that causes fear and triggers avoidance behaviour, no time criterion	At least 2 different situations that are linked to anticipatory anxiety, no time criterion	Traumatic experience (not more than 6 months before the onset of the symptoms (ICD-10), duration of the symptoms more than 1 month (DSM-V))	On the majority of days within at least 6 months relating to several events or activities until diagnosis is possible	No time criterion	No time criterion

In the case of ICD-10-relevant anxiety disorders, the following should be evaluated with regard to the corresponding guidelines [426, 435]:

- Treatment motivation of the patient
- Treatment options with respect to the disease situation
- Treatment options depending on the availability of the qualified specialists (licensed psychotherapist/medical specialist in psychiatry and psychotherapy or psychosomatic medicine)

16.4. Attitudes and General Non-pharmacological Measures

No.	Recommendations	GoR	LoE	Sources
16.7.	All professional groups involved in the treatment and care of patients with incurable cancer *shall* accompany the patients with empathy, take them seriously and be made sensitive to signs of anxiety.		EC	
16.8.	All those involved in the treatment and care of patients *shall* be supportive and strengthen confidence in their relationship through their choice of words and attitude towards patients with an incurable disease. Unnecessary verbal and non-verbal communication that triggers or reinforces anxiety *shall* be avoided.		EC	
16.9.	In the presence of uncontrolled symptoms, such as pain, breathlessness, nausea or acute states of confusion, such as delirium, which cause distressing anxiety, these symptoms *shall* be treated first or at the same time.		EC	

16.10.	The persons who are involved in the treatment of a patient with incurable cancer and anxiety *should* consult a licensed psychiatrist/psychotherapist • if, after using all of the team's own personnel resources, there are still uncertainties in the diagnosis and treatment planning of anxiety; • if the patient has a complex psychiatric history or a complex syndrome; • in cases of an acute danger of self-harm or harm to others.	EC
16.11.	In patients with incurable cancer and an anxiety disorder that meets the criteria of ICD-10, it *should* be determined to what extent the applicable psychiatric-psychotherapeutic guidelines (S3 Guideline on anxiety disorder treatment) can be followed.	EC

Dignity-preserving communication reflects a fundamental attitude. This attitude makes it possible to therapeutically identify resources and strengths, which can then be used and reinforced for anxiety reduction and stabilisation. This is summarised in the ABCD of Dignity (modified according to [436]):

- **A = Attitude**: The first step is consideration of one's own attitudes and assumptions towards a patient. One's own attitudes depend on how they are structured and conditioned and how they influence individual thinking and reactions in certain situations.
- **B = Behaviour**: Friendliness and respect are the basis for dignity-preserving behaviour. Once one is conscious of one's attitudes, it is possible to control one's own behaviour towards others more effectively. Many simple gestures can make the patient feel more like a person who deserves attention and respect and less like a body that is being pricked all over with needles or an obstacle that has to be worked around. Small acts of kindness and respect can improve trust and the relationship, such as: asking the patient for permission before actions ("Is it all right for you if I now..." or "May I..."), actively but sensitively showing interest in the individual, their history, skills and environment, as well as establishing and maintaining a conversation on equal terms, respecting and preserving privacy and intimacy, addressing things that express pride (e.g. photo of grandchildren on the bedside table).
- **C = Compassion**: Compassion is a deep awareness of another's suffering, tied to the desire to alleviate it. This basic human need is an essential quality in patient care. Compassion can be conveyed quickly and naturally through an endearing look or a soothing touch.
- **D = Dialogue:** Good medical care requires a good exchange of information. In order to be able to offer the best possible care, health care providers must obtain accurate information about the person as a whole, not only about the illness. Conversations with patients must acknowledge the person behind the disease and the emotional significance of the disease. There is a central question here: what should I know about you as a person in order to provide you with the best possible care?

16.5. Specific Non-pharmacological Measures

No.	Recommendations	GoR	LoE	Sources
16.12.	In patients with incurable cancer and anxiety, non-pharmacological therapy *should* be used in the case of stress and/or impairment resulting from anxiety.		EC	
16.13.	Psychological/psychotherapeutic interventions *can* be used for the specific, non-pharmacological therapy of patients with incurable cancer and anxiety.	0	1+	[437-439]
16.14.	Social work, spiritual and non-verbal interventions *can* be used for the specific, non-pharmacological therapy of patients with incurable cancer and anxiety.		EC	

Based on the systematic review by Fulton et al. [437], the following evidence-based psychological and psychotherapeutic interventions can be recommended (see recommendation 16.13.):

- Cognitive behavioural therapy interventions with a focus on strengthening the experience of self-efficacy, mindfulness and coming to terms with the disease can be used for situational, organic and existential anxiety.
- Existential behavioural therapy (group therapy for family carers which combines cognitive behavioural therapy with existential psychotherapy, with the aim of reducing stress through mindfulness and the strengthening of resources [440]).
- Mindfulness, MSBR (Mindfulness-Based Stress Reduction according to Kabat-Zinn): self-regulation of attention paid to the immediate experience and the present moment and the appropriation of openness and acceptance with respect to the empirical experience in the present.
- Acceptance and Commitment Therapy ACT: based on behavioural analysis, the acceptance of unpleasant feelings and training to create (new) freedom of thought and action through the mindful experience of perception through one's external senses, feeling one's own body, thinking and feeling, without distortion resulting from social desirability, avoidance or persuasion goals.

In practice, further interventions are offered for which there has not yet been sufficient evidence. These interventions are therefore recommended on the basis of expert consensus:

- Psychological/psychotherapeutic interventions (selection): psycho-education, information, education, anticipation; meaning-based interventions (such as Managing Cancer And Living Meaningfully: CALM [441, 442]; SMILE [443]; interventions of logotherapy/existence analysis (according to Frankl, [444, 445]); dignity therapy [446-448]; family-focused grief therapy as a systemic family psychotherapy [449, 450]; hypnotherapeutic interventions; interventions of depth psychology-founded psychotherapy; supportive-existential therapy.
- Breathing therapy

- Social work interventions
- Spiritual interventions (denominational or denominationally independent/ interdenominational)
- Artistic therapies
- Relaxation therapies
- Physiotherapeutic interventions (e.g. massage, mobilisation, lymphatic drainage)
- Basal stimulation
- Aromatherapy
- Speech therapy interventions
- Nutrition therapy interventions

16.6. Pharmacological Treatment

No.	Recommendations	GoR	LoE	Sources
16.15.	For the treatment of anxiety, patients with incurable cancer *shall* be offered pharmacological treatment with anxiolytic drugs: • if non-pharmacological measures are not possible; • in order to enable non-pharmacological therapy; • if, according to the patient, the treatment up to now has not led to a sufficient reduction in the symptoms.		EC	
16.16.	Short-acting benzodiazepines with a rapid onset of action *should* be used to treat acute anxiety symptoms in patients with incurable cancer. The dose and length of treatment *should* be based on the severity of the symptoms reported by the patient and result in symptom relief, which is satisfactory for the patient.	B	4	[426]
16.17.	If benzodiazepines are insufficiently effective or are not tolerated by patients with incurable cancer, the indication for antidepressants, anti-psychotics or other anxiolytic drugs *should* be evaluated.	B	1-	[451, 452]
16.18.	Acute panic attacks in patients with incurable cancer *shall* be treated with short-acting benzodiazepines. A step-wise approach *shall* be adopted: The first step is acute symptom relief with short-acting benzodiazepines. In the case of recurrence, the indication for longer-term treatment with antidepressants, anti-psychotics or other drugs with an anxiolytic effect *should* be evaluated.	A	4	[426]
16.19.	Patients with incurable cancer and currently recurring anxiety or panic states and a history of ICD-10-relevant anxiety disorder *should* be prescribed the pharmacological treatment that was previously clinically effective.	A	4	[426]

In anxiolysis, a step-by-step therapy indicated (see Table 34). The acute treatment of anxiety is carried out with short-acting benzodiazepines with the fastest onset of action (e.g. lorazepam, oxazepam, alprazolam) [426]. If longer-term treatment is foreseeable, a switch to an antidepressant with an anxiolytic effect (e.g. SSRI, SNRI or paroxetine) should occur if this is clinically feasible [453-455]. In everyday clinical practice, it has been shown that a combination may also be necessary in order to not to have to increase the dose of the benzodiazepines and still achieve a sufficient anxiolytic effect for the patient. In addition to the administration of antidepressants, a comparable approach with anti-psychotics is possible, for which an anxiolytic effect has also been shown [4, 454-456]. The duration of benzodiazepine administration depends on whether the patient has experienced satisfactory symptom relief and can undergo non-drug therapy for anxiety. A treatment-free interval begins with a slow reduction in the benzodiazepine every 4 days with close monitoring of potential withdrawal symptoms (e.g. restlessness, insomnia, nausea, racing heart, drop in blood pressure or sweating) which, if they occur, require an even slower reduction of the benzodiazepine dose, for example at 8-day intervals.

Table 34: Dose recommendations for anxiolytic acute and long-term medication in patients with incurable cancers

Acute therapy				
Indication	**Class of drug**	**Substance**	**Single dose**	
Acute anxiety state, panic attack	Benzodiazepines	Lorazepam Alprazolam Oxazepam Midazolam*	1.0-2.5 mg 0.5-1.0 mg 10-40 mg 2.5-(5) 10 mg	
Therapy in the case of prolonged disease progression				
Indication	**Class of drug**	**Substance**	**Single dose/ starting dose**	**Max. daily dose**
Recurrent anxiety or panic attacks	Antidepressants: SSRI SNRI	 Citalopram Escitalopram Sertraline Venlafaxine	 10-20 mg 5-10 mg 50 mg 37.5 mg	 40 mg 20 mg 200 mg 150 mg
Medical history of anxiety or panic disorder, generalised anxiety disorder and currently recurrent anxiety states	Antidepressants: SSRI SNRI	 Escitalopram Venlafaxine	 5-10 mg 37.5 mg	 20 mg 150 mg
	Anxiolytics	Opipramol	50 mg	300 mg
	Anti-psychotics (augmentation, if necessary)	Quetiapine* Olanzapine* Risperidone*	25 mg 5.0 mg 0.25 mg	200 mg 15 mg 2 mg
	Others	Pregabalin	25 mg	600 mg

Acute therapy
* Off-label use. Please refer to the S3 Guideline on anxiety disorders for the approvals for each specific type of disorder [426].

16.7. Social Environment

No.	Recommendations	GoR	LoE	Sources
16.20.	Since family carers can also develop distressing anxiety, they *shall* be offered helpful measures to prevent or reduce anxiety within the framework of the palliative care treatment.		EC	
16.21.	In the case of children as family of patients with incurable cancer who experience anxiety, special attention *shall* be paid to providing support, which is appropriate to the age and developmental level of the child, and an offer adapted to their age *shall* be provided.		EC	
16.22.	If professionals involved in the treatment and care of patients with incurable cancer experience anxiety, they shall also be given the opportunity for reflection.		EC	

17. Depression

Working Group Leaders: Martin Fegg, Klaus Maria Perrar

17.1. 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 [208].

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" [209], published in 2010, with direct relevance to palliative care and secondly the "S3-Guideline/National Disease Management Guideline (NDMG) Unipolar Depression", published in 2009 [210]. For the psycho-oncological support and treatment of patients with incurable cancer and depression we also refer to the S3-guideline "Psycho-oncology" [4].

17.2. Differential Diagnosis of Depression

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

Table 35 offers an overview of differential diagnostic criteria of depressive disorders according to ICD 10.

Table 35: Occurrence of depressive conditions in accordance with ICD 10 [208]

	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	Depressed mood The criteria for a mild or mod-	Depressed mood Capacity for interest and enjoyment is reduced, reduction of energy, in-	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)
	never or very rarely fulfilled.	erate depressive episode are never or very rarely fulfilled.	creased tiredness, psychomotor retardation/agitation, reduced concentration, reduced self-esteem, feelings of guilt, suicidal thoughts or acts, disturbed sleep, diminished appetite Day-to-day variations possible, however little change in the low mood day-to-day	
Psychotic symptoms	No	No	Possible, in that case, 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 lifelong	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

With patients with advanced cancer and especially with their loved ones it can be particularly difficult to differentiate depression from a normal reaction of grief. Table 36 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, information, referral to a palliative care physician or psychological interventions.

Table 36: Characteristics of depression in comparison to a reaction of grief [211]

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	Maintains a feeling of self-worth

Depression	Reaction of grief
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

17.3. Screening, Diagnosis and Assessment of Severity of Depression

17.3.1. Screening

No.	Recommendations	GoR	LoE	Sources
17.2.	In patients with incurable cancer, the existence of depression *shall* be actively and regularly assessed.	A	4	-
17.3.	In patients with incurable cancer, screening *should* be used to recognise depression.	B	1+	[212-214]
17.4.	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	-

17.3.2. Diagnosing Depression

No.	Recommendation	GoR	LoE	Sources
17.5.	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 37.

Table 37: Example questions for diagnosing depression [210]

Main symptoms	
Depressed mood	"Have you felt down 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) lately?" "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?"
Additional symptoms	
Reduced concentration and attention span	"Do you find it difficult to concentrate?" "Do you find it strenuous 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 that 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 lately?" "Have you lost weight without intending to?"

17.3.3. Assessment of the Severity

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

Figure 14 gives an overview of the assessment of severity according to ICD 10.

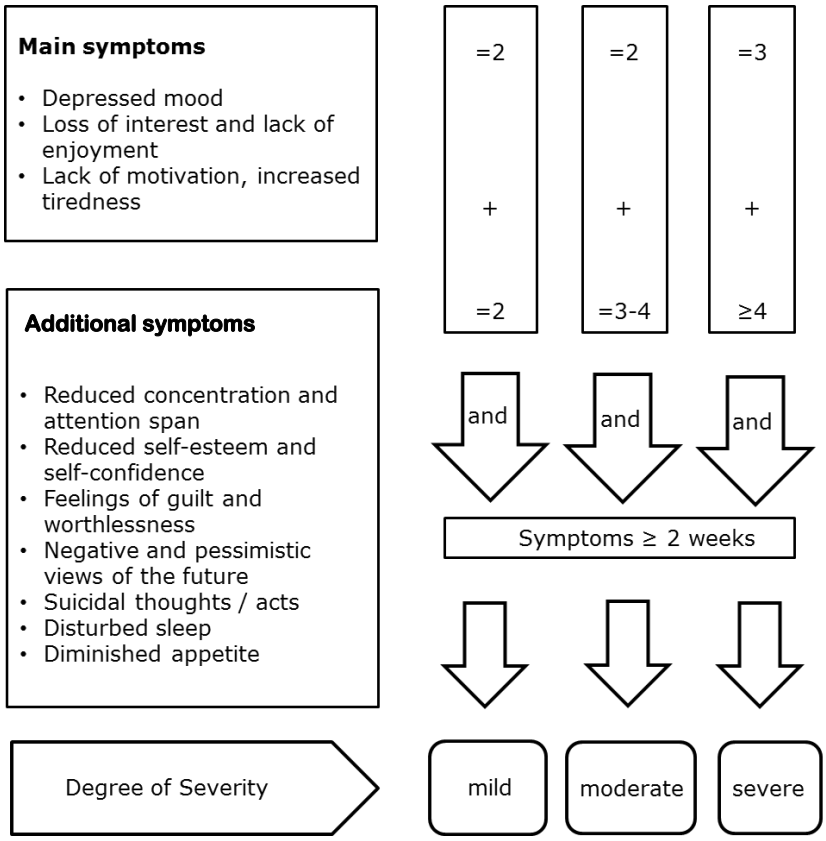


Figure 14: Diagnosis of depression according to ICD 10 (adapted figure from S3-Guideline/NDMG "Unipolar Depression" [210])

Depression is combined with an increased **risk of suicide** [210]. Depression is often found in connection with a wish for euthanasia or hastened death [215-218]. The following approach is recommended for the assessment and reduction of suicide risk:

1. Make time and space available (offer personal attention and support) [219];
2. Directly speak to patients with psychological problems about suicidal thoughts or plans [215].

Helpful questions for this approach are [219]:

- "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?"

17.4. Treating Depression

17.4.1. The Principles of Treatment

No.	Recommendations	GoR	LoE	Sources
17.7.	Patients with incurable cancer and depression *shall* receive both effective palliative care symptom control and professional psychosocial support.		EC	
17.8.	Patients *shall* be an integral part of the decision-making process with regard to treatment.		EC	
17.9.	The therapy of patients with incurable cancer and depression *shall* be adapted to the severity of the depressive symptoms. [Modified 2019]		EC	
17.10.	A psychiatrist/psychotherapist *shall* 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	

17.4.2. Treatment of Mild, Moderate or Severe Depression

No.	Recommendations	GoR	LoE	Sources
17.11.	Antidepressants *should not* be used generally in the initial treatment of mild depressive episodes, but only after carefully weighing the benefit-risk ratio		EC	[220]

No.	Recommendations	GoR	LoE	Sources
17.12.	For the treatment of acute mild to moderate depressive episodes in patients with incurable cancer, psychotherapy or a psychotherapeutic intervention *should* be offered, depending on the prognosis. [Modified 2019]		EC	[220]
17.13.	For the treatment of acute moderate depressive episodes, patients *shall* be offered antidepressant treatment.		EC	[220]
17.14.	In acute severe depressive episodes, combination treatment with drug therapy and, depending on the prognosis, psychotherapy or psychotherapeutic interventions *should* be offered. [Modified 2019]		EC	[220]

17.4.3. Treatment of Patients with Short Prognosis

No.	Recommendations	GoR	LoE	Sources
17.15.	Depression in patients with incurable cancer *shall* also be treated in cases of a short life prognosis of a few weeks.		EC	
17.16.	In the dying phase[1], treatment with antidepressants *shall* be stopped.		EC	

17.5. Non-pharmacological Measures

No.	Recommendations	GoR	LoE	Sources
17.17.	Patients with incurable cancer and depression *shall* receive basic psycho-social support.		EC	
17.18.	In cases of non-pharmacological treatment of depression, behavioural-therapy interventions (e.g. cognitive behavioural therapy interventions or problem-solving approaches), interpersonal psychotherapy interventions, mindfulness-based stress reduction or acceptance and commitment therapy *should* be delivered. [Modified 2019]	B	1-	[221]
17.19.	In cases of non-pharmacological treatment of depression, depth psychology-oriented methods or expressive therapy *can* be used.		EC	

[1] The “dying phase” refers to the final days of life (see chapter 19).

17.6. Pharmacological Treatment

17.6.1. Antidepressants

Nr.	Recommendations	GoR	LoE	Sources
17.20.	The psychopharmacotherapy of patients with incurable cancer and depression *shall* be in accordance with the available S3-Guideline/NDMG Unipolar Depression.	EC		
17.21.	In the pharmacological treatment of patients with incurable cancer and depression, there is no clear superior efficacy of one antidepressant over another.	ST	1-	[222-224]
17.22.	The choice of antidepressive substance *shall* 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		
17.23.	For prevention of recurrence, antidepressants *should* be taken for at least 4-9 months after remission following a depressive episode.	EC		[220]
17.24.	Antidepressants *should* be withdrawn gradually.	EC		

For the pharmacological treatment of depression there are various substances available (see Table 38).

Table 38: Medication for the treatment of depression modelled on Benkert/Hippius (2013) [225]; S3-Guideline/NDMG "Unipolar Depression" [210]

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)

Drug	Half-life	Dosage form	Initial dose	Standard daily dose
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 39 offers criteria for the selection of antidepressants.

Table 39: Selection criteria for antidepressants (table modelled on S3-Guideline/NDMG "Unipolar Depression" [210])

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, there are 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 episode	Effectiveness and compatibility of an earlier administration of antidepressants should 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. The SSRI group displays significant differences with regard to interac-

tions in the cytochrome P450 system. Potent CYP2D6 inhibitors prevent the transformation of tamoxifen into the biologically active endoxifen and thereby reduce the antitumour efficacy [4]. For this reason, breast cancer patients being treated with tamoxifen should not receive SSRIs or other drugs with strong or moderate inhibitory CYP2D6 activity [464, 475, 476].

17.6.2. Other Drugs

No.	Recommendation	GoR	LoE	Sources
17.25.	In patients with incurable cancer and depression, psychostimulants* *should not* be administered for the treatment of depression.	B	1-	[228, 229]

* Off-label use

18. The Desire to Die

Working Group Leaders: Reinhard Lindner, Raymond Voltz

18.1. Introduction

The phenomenon of the desire to die is understood and described differently in practice than in the literature. Desires to die have a complex relationship to suicidal tendencies, which is to be defined in this guideline. The aim is to take into account the full spectrum of this phenomenon.

Definition of "Desire to Die" in this guideline

The term "desire to die" in the context of this guideline describes a phenomenon in people with a life-limiting progressive disease. This wish manifests itself in the desire to die soon or the desire to be dead. The desire to die ranges from the acceptance of death in the sense of satiety of life, the hope of an early start of the dying process – with or without the wish to accelerate this process – to acute (consciously planned) suicidality with increasing pressure to act, the more urgent and acute the desire for self-induced dying is.

An international group of palliative care experts has defined the so called “wish to hasten death (WTHD)” in the consensus as “a reaction to suffering, in the context of a life-threatening condition, from which the patient can see no way out other than to accelerate his or her death. This wish may be expressed spontaneously or after being asked about it, but it must be distinguished from the acceptance of impending death or from a wish to die naturally, although preferably soon. The WTHD may arise in response to one or more factors, including physical symptoms (either present or foreseen), psychological distress (e.g. depression, hopelessness, fears, etc.), existential suffering (e.g. loss of meaning in life), or social aspects (e.g. feeling that one is a burden).” [479].

In this guideline, however, the dimension of the acceptance of death in the sense of satiety of life, is listed under desires to die in addition to the wish to hasten dying. This shows how multi-faceted the phenomenon of the desire to die is and that there are subtle differences between the different forms of desires to die.

The prevalence of the desire to die is stated as being widespread among patients with incurable cancer. This ranges from 8 to 22% [480-482]. According to a recent study of 377 participating cancer patients, 69.5% state that they have no desire to die, 18.3% express occasional thoughts about it and 12.2% say they had a serious desire to die [483].

18.2. The Phenomenon of the Desire to Die

18.2.1. Differentiation: Forms of Desires to Die

No.	Recommendations	GoR	LoE	Sources
18.1.	The desire to die of patients with incurable cancer *should* be considered a complex phenomenon with individually different causes, manifestations and consequences.	ST	3	[484]

Patients express a desire to die in different ways. Examples: "I want to die", "Please give me something to end my life", "I want to go to Switzerland to die"[1]. Although such statements express a similar wish, they harbour a complex phenomenon whose causes, significance and consequences have to be considered very differently.

Figure 15 presents research results that are described in the form of examples, which are intended to contribute to a better explanation of the range of the various forms of the desire to die and to formulating a conceptual understanding of a desire to die in connection with suicidal pressure to act/suicidality.

Authors	FORMS OF DESIRES TO DIE				
1) Ohnsorge et al. [485, 486]	Acceptance of dying		Wish to die as:		
			1) Looking forward to dying	2) Hypothetically considering hastening death	3) Current wish or action
2) Nissim et al. [487]	Letting go	Despair		Hypothetical exit plan	
3) Balaguer et al. [479]				Wish to hasten death (WTHD)	
4) Mod. according to Wolfersdorf [488-490] and Lindner [491]	Satiety of life	Tiredness of life	Non-specific wishes for peace and quiet	Suicidality (distanced -> latent -> acute)	

Suicidal pressure to act

Figure 15: Forms of desires to die according to different authors

(4) The breakdown into distanced, latent and acute suicidal tendencies characterises the continuum of increasing pressure to act with increasingly specific suicide plans – up to the mental fixation on killing oneself [492]. The terms listed for this purpose are defined as follows [491]:

[1] Refers to the Swiss organisations for assisted suicide, i.e. Dignitas.

- **Satiety of life** – Satisfied with what you have experienced and achieved – also dying without resentment: “C'est ici que j'attends la mort sans la desirer ni la craindre” - It is here where I await death, without desire and without fear (François Maynard, 1582-1646) [493].
- **Tiredness of life** – wish to die without one’s own actions: “Falling asleep in the evening and not waking up again.”
- **Distanced suicidal tendencies** – ideas, fantasies and plans to end one's own life through one's own actions or inactions – even without treatment of the suicidal tendencies, no life-ending pressure to act is to be expected.
- **Latent suicidal tendencies** – ideas, fantasies and plans to end one's life through one's own actions or inactions; without treatment, clear pressure to act can be expected in the event of (renewed) stress.
- **Acute suicidal tendencies** – ideas, fantasies and plans to end one's life through one's own actions or inactions – there is currently considerable pressure to act.
- **Suicide** – taking one’s own life.

18.2.2. Relationship between Desire to Die and Suicidal Tendencies

From a psychiatric perspective, a **suicidal tendency** has been defined with different nuances by various authors. According to Lindner, suicidality encompasses “all thoughts, feelings and actions, whether conscious or unconscious (and therefore not primarily accessible to the subject in terms of their significance), which are aimed at self-destruction through the self-induced termination of life” [491].

However, the special aspect of the phenomenon of the **desire to die** is that it can also occur without the desire to end one’s life more quickly or bring about the end of life [486]. In this respect it cannot be equated with suicidal tendencies - at least not with their acute forms, which are guided by an increasing pressure to act, even if the desire to die without any pressure to act and follow through can be an initial indication of suicidal tendencies. If, when, why and in which patients with incurable cancer a "transition" occurs from a desire to die to suicidal thoughts, intentions or actions requires further research [494]. To complicate this definition, it must be added that neither a desire to die as the main category, nor suicidal tendencies as a sub-category of the desire to die are stable phenomena. Their presence can vary greatly and take on different forms. For example, the desire to die can be associated with a (sub-)acute intention to let one’s life come to an end, or may instead be of a hypothetical nature in the sense of “taking precautions” for an anticipated future situation [486, 495].

18.2.3. Desire to Die and to Live, Dynamics and Progression

No.	Recommendations	GoR	LoE	Sources
18.2.	Patients with incurable cancer and a desire to die may at the same time have a desire for life within them. Over time and in terms of intensity, the desire to die and the will to live can change.	ST	3	[484]

18.2.4. Causes, Significance and Functions of Desires to Die

The following factors have been described as causes or risk factors for the development of desires to die in patients with incurable cancer [484, 486, 496-499]:

- physical symptoms
- mental symptoms (depressiveness, anxiety, hopelessness)
- social problems (isolation/being alone)
- personality (desire for autonomy and control, loss of identity)
- quality of the patient's relationships with people who are important to them
- existential, spiritual or ideological issues.

Meanings and Functions

The term “meanings of desires to die” refers to the subjective meanings that the patient ascribes to their own desire to die [486]. Functions of a desire to die are defined by Ohnsorge et al. as effects of the expressed desire to die on the social environment [486].

Even though the meanings and functions are not strictly separable from one another, they are not identical. For example, meanings can include the following aspects:

- Accepting death as a natural occurrence
- Ending suffering, that can no longer be endured, by bringing about death
- Drawing conclusions, with the result of ending unnecessary suffering – with death as the end point
- Not wanting to wait until death comes
- Preferring to maintain control than to give it up by dying.

Functions would be understood as follows:

- Manifestation of the desire to live
- Accelerated death is preferred in the dying process.
- The intolerability of the situation demands action without fail.
- Ways to escape from an intolerable situation
- Manifest final control
- Drawing attention to one's own individuality
- Gesture of altruism
- Attempt to manipulate the family, or
- Exclamation of despair, which is intended to illustrate the current distress.

18.3. Screening and Assessment

No.	Recommendations	GoR	LoE	Sources
18.3.	Patients with incurable cancer *should* be actively asked about the presence of desires to die during the course of the disease.	B	4	[427, 500]
18.4.	There is no evidence that addressing the subject of suicidal thoughts results in their development or increase.	ST	1-	[501-505]

No.	Recommendations	GoR	LoE	Sources
18.5.	When a desire to die is expressed by patients with incurable cancer, questions *shall* be asked about the course, severity and subjective causes, as well as possible suicidal thoughts, intentions and plans.	EC		
18.6.	Validated instruments *can* be used to record the desires to die of patients with incurable cancer alongside the discussion.	0	3	[506]

If patients with incurable cancer express thoughts or indications that they want to end their lives or that their lives should be ended, it is the duty of the health care providers to detect these indications, reflect on them in a joint conversation and concretise them.

Possible opening questions:

- How do you see the coming weeks?
- Have you ever thought about simply giving up?
- How burdened are you by the situation surrounding your illness?
- Are you afraid of the dying process?
- Do you have thoughts of wanting to hurt yourself?
- Do you have thoughts of wanting to end your life prematurely?
- Are you worried about talking to me about the thought of ending your life prematurely?

18.4. Caring for Patients with a Desire to Die

18.4.1. Terms

Professional **attitudes** comprise all the affects, feelings, thoughts and behaviours of the health care provider with regard to the patient that become apparent in the treatment situation and have an influence on the treatment process [507].

Professional **strategies** are based on the fundamental theoretical assumptions about communication in helping relationships.

Professional **techniques** are theory-based (verbal or non-verbal) activities in various, mostly critical situations of treatment.

18.4.2. Aims

As mentioned above, the desire to die is a differentiated phenomenon, so that the question initially arises about which goals should be pursued in dealing with patients who express a desire to die. A four-level objective is recommended:

- **Detection and Recognition:** The expression of a desire to die of patients with incurable cancer is to be detected and recognised by the professional companion.
- **Understanding:** This is associated with an understanding of the desire to die against the background of the medical and psychological situation, the

personality and life experience of the patient. This involves an empathetic process on the part of the professional companions to find meaning in conversation with the patient, also involving the family carers if necessary.

- **Competent Support:** It is then the task of the professional companion to accompany the patient with incurable cancer and a desire to die, which does not necessarily mean taking direct action, but possibly "only" the active enduring of the suffering, without being able to give an answer or even judge the desire to die. In all situations where this is possible and desirable, the suffering contained in the desire to die should be alleviated through concrete strategies and techniques.
- **Suicide prevention:** The prevention of suicidality and suicide/attempted suicide is a fourth goal in dealing with incurable cancer and a desire to die.

18.4.3. Attitudes

No.	Recommendations	GoR	LoE	Sources
18.7.	The discussion about desires to die *shall* be conducted with a basic attitude of openness, interest and respect for the patient's thoughts, experiences and actions. The attitude of respect does not necessarily imply agreement with the active termination of life.	EC		

18.4.4. Strategies and Techniques

No.	Recommendations	GoR	LoE	Sources
18.8.	When patients with incurable cancer express a desire to die, the presence of helplessness, hopelessness, pointlessness, futility, demoralisation and loss of faith, as well as depression and suicidality, *shall* be recorded and treated or support *shall* be offered.	A	3	[484]
Depression 17.4.	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	-
18.9.	If a patient with incurable cancer has a desire to die, coping strategies *should* be developed with him/her on how to handle the situation.	B	3	[447, 508-511]
18.10.	In the event of a desire to die combined with the experience of (impending) loss of control, possibilities *should* be worked out with a patient with incurable cancer as to how they can (again) experience or regain control over their situation.	EC		

No.	Recommendations	GoR	LoE	Sources
18.11.	In the case of a patient with incurable cancer and a persistent desire to die, the health care providers *should* bear this desire and give the patient advice and support in an empathetic manner.	EC		
18.12.	In the discussions with the patient about their desire to die, the goal of care and the resulting decisions about the beginning, continuation and termination of life-sustaining medical measures *shall* be addressed.	EC		
18.13.	Particularly in patients with incurable cancer and a desire to die, inadequately controlled symptoms such as pain, breathlessness, nausea, vomiting, anxiety, depression, etc. *shall* be controlled as good as possible.	A	3	[484]
18.14.	A licensed psychiatrist/psychotherapist *shall* be consulted in the following cases: • uncertainty in the diagnosis of a psychiatric disorder and the planning of its treatment • in the case of a (per)acute suicidal tendency • if there is a wish for advice on the part of the professional companion, e.g. in difficult conversations about handling the desire to die.	EC		

The following strategies and corresponding techniques are applied in dealing with patients with incurable cancer and a (potential) desire to die: see Table 40 and Table 41).

Table 40: Strategies and techniques for dealing with (potential) desires to die

Strategy	Technique
1. Exploring the patient's psychological and spiritual condition	Helplessness, hopelessness, pointlessness, futility, demoralisation and loss of faith, but also the permanence of and a lack of alternatives to the desire to die are to be recorded and clarified [484]. In this way, possible solutions can be considered and decided upon - taking the patient as the starting point if necessary. It may initially be necessary to give space to the patient's experience, not to become immediately active, but to adopt a wait-and-see approach (see recommendation 18.8. and point 7 below).
2. Assessing and clarifying any indications of depression or another severe psychiatric disorder that sustainably restricts the patient's judgement.	The current depression or another severe psychiatric disorder should be assessed and its severity clarified. 2-question screening is available for the assessment of the depressiveness (see the recommendation on depression 17.4.). In cases of uncertainty as to whether the patient's decision-making ability is severely impaired due to a mental disorder, a psychiatric examination is recommended.
3. Recognising one's own feelings in conversations with the patient.	One's own fear, distress, anger, sudden unforeseeable feelings, thoughts or physical states (e.g. tiredness, confusion, absence or even the sudden wish that the patient were dead) have to be recognised, defined and initially beared (see

Strategy	Technique
	above) in order to be able to think about their indicative character for the patient's situation (see the concept of transmission in the long version of the Guideline, section 18.4.3., Attitudes, and chapter on Anxiety).
4. If there are indications of a desire to die (by the patient or witnessed by health care providers), these shall be addressed pro-actively, even if the patient does not initiate this of their own accord.	In this context, it can be meaningful to conduct a probing conversation ("Are you thinking about giving up completely?" "... throwing everything away?" "Do you wish you were dead?" "Are you thinking about putting an end to your life yourself?" (addressing possible suicidal tendencies). If the patient withdraws in this situation or the health care provider feels inhibited, the following questions can be asked to investigate the situation in greater depth: "Did I understand you correctly...?", "Would you like to tell me in greater detail what you think about your situation?" (see section Screening and Assessment).
5. Involving family members	With the patient's agreement (caution: there may be intra-family conflicts) it makes sense to discuss the existence of a desire to die with the family members, to record their views and those of the patient and to take their position seriously (see section Family Carers).
6. Developing coping strategies to help patients to handle their situation	Coping positively with one's own (incurable) cancer can be a predictor of fewer depressive symptoms and a higher quality of life [512, 513]. Examples of techniques for coping with disease can be existential interventions such as meaning- or dignity-oriented therapies, the efficacy of which has been tested in studies with regard to a desire to die. Their aim is to promote the spiritual well-being of the patient at the end of life by addressing the subjective meaning of life and/or his/her own dignity (see recommendation 18.9.).
7. Exploring, promoting and regaining the desire for personal influence and control	Reflection on (the patient's) own opportunities for controlling the situation (jointly). If necessary, concrete steps are to be initiated to improve the evaluations and, in some circumstances, endure their inability to be fulfilled in the discussion with the patient (see recommendation 18.10.; see also the chapter on Anxiety).
8. Enduring or bearing the suffering that cannot be avoided	Repeated discussions with the patient can lead to situations in which it is not possible to remedy/relieve symptoms or conditions of suffering to a sufficient extent. In this situation, it is important to make oneself available to the patient (and one's own feelings) time and again, to endure them, discuss them and look for solutions (see recommendation 18.11.). If the desire to die persists, it is necessary to provide the opportunity to reflect in the context of the helping relationship. In such situations it is staying the course and – if desired and possible – talking that specifically constitute the offer. This enduring is not to be equated with passive acceptance or ignoring.
9. Changing the goal of care and deciding on the beginning, continuation and termination of life-sustaining medical measures	A possible change to the goal of care and the resulting decision on the beginning, continuation and termination of medical measures, as well as their conditions, technical implementation and consequences are to be discussed carefully with the patient and decided jointly with them. For the patient, such a conversation can in itself represent a form of addressing his/her desire to die and the reasons for it (see recommendation 18.12.).
10. Symptom control	Inadequately controlled symptoms, such as pain, breathlessness, nausea, vomiting, anxiety and depression play an important role in the development of a desire to die by interacting at the physical, psychosocial and existential levels of the individual [484]. Here, the best possible symptom relief is part of the care provided to patients with a desire to die (see recommendation 18.13.).

Strategy	Technique
11. Performing supervision and holding case discussions	In pressure, conflict and dilemma situations, supervision or case discussions, e.g. an ethics consultation, are an effective means of finding new ideas and options by consulting third parties (see the section on Health Care Team).
12. Consulting other experts	For specific issues (more detailed psychiatric diagnostics, religious conflicts, etc.), additional specialists (licensed psychiatrist/psychotherapist, social workers, pastors, music therapists and other non-verbal therapists: dance, movement, art and design therapists) should be consulted (see recommendation 18.14.).

18.4.5. Special Measures

No.	Recommendations	GoR	LoE	Sources
18.15.	In the case of peracute suicidal tendencies, i.e. when the suicidal action is imminent and cannot be avoided by other measures, the indication for committal to a psychiatric and psychotherapeutic clinic *shall* be evaluated, with critical consideration of the benefits and harm.		EC	
18.16.	Palliative sedation *can* be offered for symptom control in patients with incurable cancer and insufficiently manageable symptoms resulting in the desire to die.		EC	
Dying phase 19.37.	Palliative sedation *shall* be carried out by competent physicians and nurses experienced in palliative care.		EC	
18.17.	Those involved in the treatment of a patient with incurable cancer *shall* be further trained in the (professional) legal framework and the relevant concepts with regard to desires to die.		EC	

Table 41: Legal framework at the end of life in Germany

Form of euthanasia and terminal care	Legal situation
Voluntary euthanasia	Voluntary euthanasia (killing by request, "Tötung auf Verlangen") is a special form of killing. It is illegal in Germany. The precondition is that the perpetrator is motivated to commit this act of killing through the explicit and serious request of the patient (who assumes full responsibility). The shortening of life is intended and the primary goal of this intervention is terminating life. In this case, the so-called authority of action ("Tatherrschaft") does not lie with the patient: the perpetrator controls the events and carries out the action leading to death. A typical example is the administration of a lethal injection to the patient. Killing by request is prohibited by law in Germany according to Section 216 of the Penal Code (StGB) and can be punished by imprisonment from 6 months up to 5 years.
Assisted suicide [514]	According to the Federal Constitutional Court, the general right of personality includes a right to die in a self-determined manner - i.e. also a right to take one's own life and to seek help to do so (judgement of 26.02.2020). This judgement declared

Form of euthanasia and terminal care	Legal situation
	Section 217 of the German Criminal Code (StGB), which has been in force since 2015, to be unconstitutional. According to Section 217 StGB, assistance of suicide with intent of repeated conduct was prohibited. A new regulation on suicide assistance is still pending (as of 16.03.2020). Depending on the individual circumstances, whoever supports an act of suicide that is not an exercise of the patient's own free will may be liable to prosecution for failure to provide assistance (Section 323c of the Criminal Code (StGB)), killing by omission (Sections 212, 13 StGB), and under certain circumstances also for negligent or intentional killing (Section 222 or Section 212 StGB). Physicians are also subject to the requirements of professional law: Talking to the patient about the desire to die and the intention to commit suicide is the responsibility of the physician, assisting suicide is not. Furthermore, some State Chambers of Physicians have adopted a separate ban on medical suicide assistance in accordance with the German Model Professional Code for Physicians ("Musterberufsordnung").
Therapies at the end of life (formerly: indirect euthanasia)	Therapies at the end of life – also palliative care measures – are carried out in the last phase of life with the aim of alleviating suffering. Like all medical measures, these are permitted if they are indicated, the patient consents after being carefully informed and they are carried out properly. This also includes measures where there is a possibility that the natural process of dying is shortened, be it through a high-dose pain medication or strong sedation, without which the burdensome symptoms cannot be controlled. If these measures serve to alleviate the symptoms, if they are indicated with a view to this aim and if the patient who has been informed in detail has consented to them, the side effect of the "shortening of life" may be accepted as an unavoidable consequence. Under these conditions, such therapies at the end of life are not prohibited, but may even be ethically and legally required.
Allowing the patient to die (formerly: passive euthanasia)	Allowing the patient to die by not starting or by terminating life-prolonging or life-sustaining measures is permitted and even ethically and legally required if these measures are not or no longer indicated or if the patient does not or no longer consents to them. These include, for example, artificial respiration or artificial nutrition, which are either not started or discontinued. The obligation to provide (palliative) medical care to the dying person naturally continues [515].
Palliative sedation	Defined as the use of medication with the aim of achieving diminished or suspended consciousness (unconsciousness) in order to reduce the burden of therapy-refractory symptoms in an ethically acceptable manner for patients, family carers and health care providers [516]. The sedation can be used intermittently or permanently. The target sedation depth can range from shallow sedation to the permanent loss of consciousness.

18.5. Family Carers

No.	Recommendations	GoR	LoE	Sources
18.18.	In the event of a desire to die, the family carers *should* be included in the discussion with the patient.		EC	

18.6. Health Care Team

No.	Recommendations	GoR	LoE	Sources
18.19.	Suitable opportunities for reflection, such as case discussions, pastoral care and supervision (e.g. for interactional problems with the patient), as well as ethics consultation (e.g. on ethical issues) and further training *shall* be offered for teams caring for patients with a desire to die.		EC	

19. The Dying Phase

19.1. Introduction

925,200 people died in Germany in 2015 and 226,337 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 [230]. Almost 40% of people who are diagnosed with having cancer will die from the illness (the relative 5-year survival rates are currently estimated to be 62% for men and 67% for women) [518].

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 [11, 12].

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 [232].

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.

19.2. Diagnosing Dying

No.	Recommendations	GoR	LoE	Sources
19.1.	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 (e.g. Cheyne-Stokes breathing, death rattle) • Changes in emotions and consciousness • Reduction of urine excretion under 100 ml/24 h • Pulselessness of the radial artery • Increased weakness and a worsening of the patient's general condition • Skin changes; confusion; loss of interest in food and fluid intake • Intuition of those involved in the treatment	0	4	[11, 12, 233]

No.	Recommendations	GoR	LoE	Sources
19.2.	The assessment of whether the dying phase has begun in a patient with terminal cancer *should* occur as part of an inter-professional discussion.	B	4	[11, 12, 233]

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 reliable 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 (e.g. marbled limbs), confusion, and the loss of interest in food or fluid intake can be indirect indications for the dying phase. This list of observable signs does not claim to be complete or lack 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, general deterioration, consciousness, skin, intake of food and fluids, emotional state and opinions expressed by health care providers [11]. According to expert opinion, the intuition of those involved in the care of the patient ("gut feeling") was classified as clinically relevant [11].

19.3. Principles and Practical Issues of Care in the Dying Phase

No.	Recommendations	GoR	LoE	Sources
19.3.	When a patient with terminal cancer is dying this *shall* be recognised as a natural part of life by health care providers. The dying process *shall* be neither hastened nor delayed.		EC	
19.4.	The dying patient and their family carers *shall* be the focus of care respecting the physical, psychological, social and spiritual dimensions of dying.		EC	
19.5.	Treatment decisions and measures in the dying phase *shall* be in accordance with the needs of the dying patient and their family carers, while preserving the patient's dignity.		EC	
19.6.	Treatment decisions and measures in the dying phase *shall* be documented and continually reassessed.		EC	

No.	Recommendations	GoR	LoE	Sources
19.7.	The dying patient and his/her family carers *shall* be adequately informed about the approaching death and the changes to be expected in the dying phase.		EC	
19.8.	Family carers of the dying patient *shall* 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 *shall* receive offers of support.		EC	
19.9.	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 *shall* be carefully observed by the health care providers and their meaning assessed.		EC	
19.10.	The wish of a patient with terminal cancer concerning the place of death *should* be honoured.		EC	
19.11.	Involving competent volunteers in multi-professional care during the dying phase of a patient with terminal cancer *should* be part of palliative care.		EC	

19.4. Treatment of the most Common Symptoms

For the symptom Cancer pain, see the corresponding chapter of this guideline.

19.4.1. Breathlessness in the Dying Phase

See additionally the chapter Breathlessness.

No.	Recommendations	GoR	LoE	Sources
19.12.	In the dying phase of an incurable cancer patient who is no longer able to self-assess his or her breathlessness, the assessment as to the existence and intensity of breathlessness *shall* 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	
19.13.	Patients with breathlessness who are in the dying phase and who require pharmacological treatment for the relief of breathlessness *shall* be given opioids as the method of choice. In cases of symptoms of anxiety, benzodiazepines *can* be given in addition to opioids.		EC	

19.4.2. Delirium in the Dying Phase

No.	Recommendations	GoR	LoE	Sources
19.14.	The symptoms of delirium *shall* be detected as early as possible: i.e. sudden onset and fluctuating course, impaired consciousness, disturbance in attention, thinking and sleep-wake cycle.		EC	
19.15.	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	
19.16.	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	-
19.17.	In dying patients with delirium and the need for pharmacological treatment, haloperidol* *can* be administered for the treatment of delirium. [Modified 2019]	B	1-	[234-240]

* Off-label use

19.4.3. Death Rattle

No.	Recommendations	GoR	LoE	Sources
19.18.	Artificial hydration *should* not be administered in the dying phase when death rattle is present.		EC	
19.19.	Family carers of dying patients *shall* be informed early of the cause, the course and the consequence of death rattle. The use of informational brochures *can* provide additional help for family carers.		EC	
19.20.	In dying patients with distressing death rattle, suitable positioning for the mobilisation and drainage of secretion *can* be used.	0	4	-
19.21.	In dying patients with distressing death rattle, anticholinergic drugs* *can* be administered to reduce the death rattle.	0	1-	[241-243]
19.22.	In dying patients with distressing death rattle (without tracheostomy or endotracheal tube), tracheal secretion *should not* be sucked.	B	4	-

* Off-label use

19.4.4. Dry Mouth (Xerostomia)

No.	Recommendations	GoR	LoE	Sources
19.23.	Dry mouth *shall* be regularly assessed, including the causes (e.g. medication), the level of distress and whether the xerostomia requires treatment.		EC	
19.24.	In cases of distressing xerostomia, the oral mucosa and the lips *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. [Modified 2019]	B	4	-

19.4.5. Anxiety and Agitation in the Dying Phase

(see also the chapter Anxiety)

No.	Recommendations	GoR	LoE	Sources
19.25.	The emergence of anxiety *shall* be regularly assessed in the dying phase. In addition to verbal statements, clinical signs such as agitation, sweating, facial expressions or defence reactions *shall* be observed.		EC	
19.26.	In cases of agitation during the dying phase, the main triggering causes *shall* be determined, e.g. pain, constipation, urinary retention, breathlessness, anxiety and/or delirium.		EC	
19.27.	Dying patients with anxiety – with or without accompanying symptoms of agitation – *shall* be supported with the use of general measures: e.g. calm setting, trust-building communication and continuity in care.		EC	
19.28.	Benzodiazepines can be administered in the dying phase to relieve anxiety, whether accompanying symptoms of agitation are present or not.		EC	
19.29.	In cases of agitation as part of delirium in the dying phase, the delirium *shall* primarily be treated.		EC	

19.5. Medication and Measures in the Dying Phase/Withdrawal of Medication and Measures in the Dying Phase

No.	Recommendations	GoR	LoE	Sources
Principles 4.7.	The patient's wishes are to be considered in every phase of the treatment, including in the dying phase. If the patient is not able to express himself/herself, 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.		ST (EC)	
19.30.	All measures taken in the dying phase *shall* 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 *shall* be considered.		EC	
19.31.	Only drugs that aim to ensure the best possible quality of life in the dying phase *shall* be started or continued. This particularly includes the substances from the groups of opioids, antipsychotics, benzodiazepines and anticholinergics.		EC	
19.32.	Cancer-specific drugs and treatment measures *shall* be stopped in the dying phase.		EC	
19.33.	All medical, nursing and physiotherapeutic treatment measures, which do not support the goal of care of ensuring the best possible quality of life, *shall not* be introduced or, if they were introduced previously, *shall* be stopped: e.g. ventilation, cardiopulmonary resuscitation, dialysis/hemofiltration, therapy in the intensive care unit, positioning for decubitus or pneumonia prevention. [Modified 2019]		EC	
19.34.	Measuring and documenting blood pressure, pulse, respiration rate, blood glucose level, oxygen saturation and body temperature *shall* be stopped when there is no benefit concerning symptom relief.		EC	
19.35.	If drugs for symptom relief can no longer be administered enterally, an adjusted dose *shall* be given using a parenteral (subcutaneous, intravenous), transmucosal (nasal, buccal, sublingual) or rectal route of administration.		EC	

No.	Recommendations	GoR	LoE	Sources
	A sufficiently effective transdermal treatment *can* also be continued in the dying phase.			
19.36.	In dying patients who have an implanted cardioverter-defibrillator (ICD), the defibrillation function (shock function) *should* be deactivated in the dying phase. [Modified 2019]	EC		
19.37.	Palliative sedation *shall* 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 may 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 [244, 245]. However, there is no consensus across the board that palliative sedation is indicated for these non-physical symptoms [245, 246].

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 [244].

19.6. Artificial Nutrition and Hydration

No.	Recommendation	GoR	LoE	Sources
19.38.	Following a thorough investigation on an individual basis (e.g. satisfying hunger or thirst), artificial nutrition and hydration *should not* be continued or started for dying patients.	B	2	[247-249]

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 oedema, pulmonary oedema, increased death rattle), require an invasive

route of application (i.v, subcutaneous, PEG) and lead to an increased medical and nursing involvement, 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 [250]. Due to the fact that artificial hydration does not relieve xerostomia, mouth care is advisable independent from rehydration (see also the section Dry Mouth (Xerostomia)) [251].

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 [252, 253].

19.7. The Aftermath of Death: The Deceased and Grief

No.	Recommendations	GoR	LoE	Sources
19.39.	The family carers of the deceased *shall* be informed of the death in a sensitive and timely manner.		EC	
19.40.	Following the death, the family carers *shall* be allowed to say goodbye in accordance with their needs and resources, cultural practices and religious duties.		EC	
19.41.	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	

19.8. Dying and Death and the Health Care Team

No.	Recommendations	GoR	LoE	Sources
19.42.	For the dignified care of dying people and their family carers, supportive conditions *shall* 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	
19.43.	In order to stabilise teamwork and to reduce distress, reliable and transparent ways of decision-making *shall* be jointly agreed upon and defined. Decisions concerning treatment and care *shall* be adequately communicated within the team. Changes in goals of care and adjustments in treatment measures *shall* be transparently documented for the whole team.		EC	

No.	Recommendations	GoR	LoE	Sources
19.44.	Mutual support, both emotionally and in practice, as the predominant protective factor against stress in a team *shall* be maintained in an appropriate culture.		EC	
19.45.	Rituals for saying goodbye *can* be introduced for support and coping. Such rituals *should* be jointly developed and agreed upon.		EC	
19.46.	Suitable room for reflection such as case conferences, supervision, team days and further training *shall* be implemented for teams that care for dying patients.		EC	

20. Quality Indicators (QIs)

Quality indicators are parameters, which are ascertained to assess the quality of the underlying structures, processes and/or outcomes [541, 542]. Quality indicators are an important tool of quality management. The aim of their use is the continuous improvement of care by presenting the results of the care, critically reflecting on them and, if necessary, improving them. The present selection of quality indicators has been compiled according to the methodology of the Guideline Programme for Oncology [543].

The numerator is always a subset of the denominator. Quality indicator 6 can be documented with the basic oncological data set of the cancer registries (as of: March 2019).

The QIs 1, 2, 3, 4 and 10 must be assessed with the screening instruments IPOS or MIDOS/ESAS[1]). 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.

Quality indicator	Reference recommendation	Evidence basis
QI 1: Reduction of Breathlessness (since 2015)		
Numerator: Number of patients with reduction of breathlessness within 48h **Denominator:** All patients with the diagnosis “incurable cancer” (receiving generalist or specialist palliative care) and with moderate/severe breathlessness at inpatient admission	**8.3** A repeated assessment of breathlessness before, during and following a symptomatic therapy *shall* be part of the evaluation. **Objective of the guideline**: improvement of symptom control; to this end, the common symptoms and problems shall be treated according to current scientific evidence and clinical expertise (chapter Breathlessness, Cancer pain, Fatigue, Sleep related disorders/Nocturnal Restlessness, Nausea and Vomiting (not cancer therapy-induced), Constipation, Malignant Bowel Obstruction (MBO), Malignant Wounds, Anxiety and Depression)	**EC** **Quality objective:** As often as possible, reduction in breathlessness within 48 hours of hospital admission in the case of patients diagnosed with "incurable cancer" **Screening instruments** (open list of validated instruments): • Modified Borg Dyspnea Scale • Visual Analog Scale • Numeric Rating Scale • MIDOS/ESAS, IPOS • (HOPE/national palliative care registry)
QI 2: Reduction of Pain (since 2015)		

[1] MIDOS is the German version of ESAS.

Quality indicator	Reference recommendation	Evidence basis
Numerator: Number of patients with reduction of pain within 48h **Denominator:** All patients with the diagnosis “incurable cancer” (receiving generalist or specialist palliative care) and with moderate/severe pain at inpatient admission	**9.1** Pain history and a pain related clinical examination *shall* be part of every diagnosis of pain. **Objective of the guideline**: improvement of symptom control; to this end, the common symptoms and problems shall be treated according to current scientific evidence and clinical expertise (chapter Breathlessness, Cancer pain, Fatigue, Sleep related disorders/Nocturnal Restlessness, Nausea and Vomiting (not cancer therapy-induced), Constipation, Malignant Bowel Obstruction (MBO), Malignant Wounds, Anxiety and Depression)	**EC** **Quality objective:** As often as possible, reduction of pain within 48 hours of hospital admission in the case of patients diagnosed with "incurable cancer" **Screening instruments** (open list of validated instruments): • McGill Pain Questionnaire • Verbal Rating Scale • Numeric Rating Scale • MIDOS/ESAS, IPOS • (HOPE/ national palliative care registry) • in case of suspicion of neuropathic pain, also painDETECT or DN4

QI 3: Opioids and Laxatives (since 2015)

Numerator: Number of patients without therapy with osmotic and/or stimulant laxatives **Denominator:** All patients with the diagnosis “incurable cancer” (receiving generalist or specialist palliative care) on opioids outside of the dying phase (= 7 days before death)	**9.25** Laxatives *shall* be routinely prescribed for the management or prophylaxis of opioid-induced constipation. **13.6** Osmotic and/or stimulant laxatives *shall* be used for the pharmacological mono- or combination therapy of constipation for patients with incurable cancer.	**GoR A, LoE 1+** **Quality objective:** As often as possible, administration of laxatives for patients diagnosed with “incurable cancer” and opioid medication

QI 4: Symptom Assessment in the Dying Phase (since 2015)

Numerator: Number of patients with symptom assessment by means of a validated screening instrument in the last 72h before death	**19.25** The emergence of anxiety *shall* be regularly assessed in the dying phase. In addition to verbal statements, clinical signs such as	**EC** **Quality objective:** As often as possible, symptom assessment in the dying phase

Quality indicator	Reference recommendation	Evidence basis
Denominator: All deceased patients (receiving generalist or specialist palliative care)	agitation, sweating, facial expressions or defence reactions *shall* be observed.	**Screening instruments** (open list of validated instruments): • MIDOS/ESAS • IPOS • HOPE/ national palliative care registry

QI 5: Assessment of Agitation in the Dying Phase (since 2015)

Numerator: Number of patients with agitation assessment in the last 72h before death **Denominator:** All deceased patients (receiving generalist or specialist palliative care)	**19.26** In cases of agitation during the dying phase, the main triggering causes *shall* be determined, e.g. pain, constipation, urinary retention, breathlessness, anxiety and/or delirium.	**EC** **Quality objective:** As often as possible, assessment of restlessness in the dying phase **Screening instruments:** Agitation will be assessable with IPOS and MIDOS/ESAS in the future.

QI 6: Stopping Cancer-specific Measures in the Dying Phase (since 2015)

Numerator: Number of patients receiving cancer-specific measures (systematic therapies, radiotherapy) within 14 days before death **Denominator:** All deceased patients (receiving generalist or specialist palliative care)	**19.32** Cancer-specific drugs and treatment measures *shall* be stopped in the dying phase.	**GoR A, LoE 1+** **Quality objective:** As often as possible, termination of tumour-specific measures in the dying phase

QI 7: Oral Care (new)

Numerator: Number of patients with oral hygiene **Denominator:** All patients diagnosed with "incurable cancer" (receiving	**14.12** In order to relieve a dry mouth in patients with incurable cancer and MBO, ice cubes to suck, crushed ice, frozen fruit pieces, sour sweets and/or chewing	**EC** **Quality objective:** As often as possible, oral hygiene for patients with incurable cancer

Quality indicator	Reference recommendation	Evidence basis
generalist or specialist palliative care) and dry mouth (ICD-10-GM R 68.2)	gum *should* be offered.	

QI 8: Assessment of Malignant Wounds (new)

Numerator: Number of patients assessed for an exulcerating tumour using a specific assessment instrument according to the guideline **Denominator:** All patients diagnosed with "incurable cancer" (receiving generalist or specialist palliative care) and exulcerating tumour	**15.2** A written assessment of the malignant wound with a complete analysis of the wound *shall* be carried out with structured wound documentation sheets at the beginning of the treatment and for further monitoring regularly during the subsequent course of the disease.	**EC** **Quality objective:** As often as possible, assessment of malignant wounds in patients with incurable cancer and an exulcerating tumour **Specific assessment tools**: • HOPE • FKB-20 • FLQA-wk • Wound-QoL • Pain assessment in patients with chronic wounds

QI 9: Documentation of Goals of Care (new)

Numerator: Number of patients with documented goals of care at the time of the diagnosis of "incurable cancer" **Denominator:** All patients diagnosed with "incurable cancer" (receiving generalist or specialist palliative care)	**7.7** Goals of care associated with the treatment of patients with incurable cancer *shall* be regularly reviewed and adapted to the current stage of the disease and treatment situation and/or to the changed wishes, values and goals of the patient.	**EC** **Quality objective:** Documentation as frequently as possible of the goals of care in the case of patients with incurable cancer

QI 10: Screening by Means of MIDOS/ESAS[1] and IPOS (since 2015)[2]

[1] MIDOS is the German version of ESAS.

[2] DEGAM voted that the quality indicator 10 does not apply to general practitioners, since there is no reliable evidence at this level of care of the benefits of such a procedure for patient-relevant outcomes.

Quality indicator	Reference recommendation	Evidence basis
Numerator: Number of patients with screening by means of MIDOS/ESAS or IPOS **Denominator:** All patients with the diagnosis "incurable cancer" (receiving generalist or specialist palliative care)	**5.5** 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 *shall* be assessed repeatedly and when there is a change in the clinical situation.	**EC** **Quality objective:** Symptom assessment as frequently as possible by means of MIDOS/IPOS for patients with incurable cancer

QI 11: Specialist Palliative Care (new)

Numerator: Number of patients who have received specialist palliative care (inpatient: palliative care unit, palliative care support team, palliative day-care, inpatient hospice; out-patient: "SAPV" [specialist palliative home care], specialist palliative out-patient clinic) **Denominator:** All patients who have died from a cancer	**International investigation according to quality indicators:** **QI: Specialised palliative care** **Numerator:** number of people who died with cancer who received specialised palliative care (hospital palliative unit OR palliative day-care centre OR multidisciplinary home care) in the last 2 years prior to death **Denominator**: number of people who died with cancer [254]	**EC** **Quality objective:** Evaluation of the care situation of cancer patients with regard to specialised palliative care

21. List of Figures

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23. Bibliography

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