IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. V12-02

Systematic guideline search and appraisal, as well as extraction of relevant recommendations, for the DMP "breast cancer"[1]

Executive Summary

[1] Translation of the executive summary of the final report *Systematische Leitlinienrecherche und -bewertung sowie Extraktion relevanter Empfehlungen für das DMP Brustkrebs* (Version 1.0; Status: 20 May 2014). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

Publishing details

Publisher:

Institute for Quality and Efficiency in Health Care

Topic:

Systematic guideline search and appraisal, as well as extraction of relevant recommendations, for the DMP “breast cancer”

Commissioning agency:

Federal Joint Committee

Commission awarded on:

15 March 2012

Internal Commission No.:

V12-02

Address of publisher:

Institute for Quality and Efficiency in Health Care
Im Mediapark 8 (KölnTurm)
50670 Cologne
Germany

Tel.: +49 (0)221 – 35685-0
Fax: +49 (0)221 – 35685-1
E-Mail: berichte@iqwig.de
Internet: www.iqwig.de

This report was prepared in collaboration with external experts.

The responsibility for the contents of the report lies solely with IQWiG.

According to §139b (3) No. 2 of Social Code Book (SGB) V, Statutory Health Insurance, external experts who are involved in the Institute's research commissions must disclose "all connections to interest groups and contract organizations, particularly in the pharmaceutical and medical devices industries, including details on the type and amount of any remuneration received". The Institute received the completed *Form for disclosure of potential conflicts of interest* from each external expert. The information provided was reviewed by a Committee of the Institute specifically established to assess conflicts of interests. The information on conflicts of interest provided by the external experts and external reviewers is presented in Appendix I of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

External experts:

- Monika Becker, Institute for Research in Operative Medicine (IFOM), Witten/Herdecke University, Germany
- Michaela Eikermann, Institute for Research in Operative Medicine (IFOM), Witten/Herdecke University, Germany
- Monika Neumann, Interdisciplinary Breast Centre, Clinic of Gynaecology, Düsseldorf University Hospital, Germany
- Esther Jacobs, Institute for Research in Operative Medicine (IFOM), Witten/Herdecke University, Germany
- Maren Walgenbach, Institute for Research in Operative Medicine (IFOM), Witten/Herdecke University, Germany

IQWiG employees:[2]

- Corinna Ernsting
- Carmen Bartel
- Catharina Brockhaus
- Susanne Ein Waldt
- Meike Hansen
- Wiebke Hoffmann-Eßer
- Ulrike Lampert

[2] Due to legal data protection regulations, employees have the right not to be named.

- Ulrich Siering

Executive summary

In its letter of 15 March 2012, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to undertake a systematic literature search for and appraisal of guidelines and extract relevant recommendations for the DMP “breast cancer”.

Research question

The aim of this study was to specify a potential need for updating and supplementation of the existing DMP “breast cancer” by means of a systematic search for new evidence-based guidelines relevant to the subject and by the synthesis of the guideline recommendations.

The study was organized as follows:

- literature search for and selection of current guidelines on the subject of breast cancer
- appraisal of the methodological quality of the selected guidelines
- extraction and synthesis of guideline recommendations relevant to the existing DMP “breast cancer”
- identification of recommendations that might justify the potential need to revise and supplement the DMP “breast cancer”

It was not the aim of the study to provide recommendations in terms of an IQWIG benefit assessment.

Methods

A systematic Internet search for topic-specific guidelines was conducted via the guideline databases of the Association of the Scientific Medical Societies (AWMF), the Guidelines International Network (G-I-N), and the National Guideline Clearinghouse (NGC), as well as by searching the websites of multidisciplinary and specialist guideline providers. The search covered the period from November 2007 to November 2013.

The methodology of the guidelines included was assessed using the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument. The AGREE II instrument is used to assess the methodological quality of a guideline and contains 23 appraisal criteria. Six domains are allocated to these criteria, each of which describes a separate dimension of methodological guideline quality. Each criterion within the individual domains was assessed on a 7-point scale. The scale indicates to what extent a criterion is fulfilled in the guideline to be assessed. The results of the AGREE II appraisal are not a criterion for the inclusion or exclusion of guidelines in the study. By means of the AGREE II instrument it was to be presented transparently whether and in which domains of the instrument the evidence-based guidelines included showed particular methodological strengths or weaknesses.

The recommendations relevant to the research question were extracted and allocated to the health care aspects of the G-BA's directive on the regulation for the design of structured treatment programmes according to §137f (2) Social Code Book (SGB) V of 16 February 2012 (DMP directive). Finally, a synthesis of the extracted recommendations according to the health care aspects of the DMP directive was carried out and compared with the requirements of the DMP "breast cancer".

In order to achieve comparability of the largely different systems of the grade of recommendation (GoR) and level of evidence (LoE), for this report the GoR and/or LoE used in the guidelines were in each case allocated to a reference standard. The GoR used in the guidelines were allocated to 1 of 3 recommendation categories according to the procedure of the National Care Guideline (Nationale VersorgungsLeitlinie [NVL]). The LoE used in the guidelines were transferred to the evidence classification used in the G-BA's Rules of Procedure.

A potential need for updating and supplementation of the DMP was determined for recommendations that were consistent in content and largely showed a high GoR (strength of recommendation "A" according to the NVL classification). With recommendations that were consistent in content across different guidelines and sometimes featured a high GoR/LoE category (inconsistent GoR/LoE category), a potential need for updating and supplementation of the DMP could be raised for discussion. This was also the case if new aspects for the DMP were only presented by a single guideline but were provided with a high GoR. If a guideline did not provide a GoR, alternatively to the highest GoR category, a high LoE (Ia/Ib according to the G-BA's evidence classification) was used to determine a need for updating and supplementation. For guidelines that provided inconsistent or contradictory statements with regard to content and largely featured a high GoR and/or LoE, no concrete statement could be made on the need for updating or supplementation. These recommendations are specifically mentioned in the discussion section. In these cases, a renewed examination under inclusion of relevant primary literature may be necessary. Recommendations that featured neither a GoR nor LoE were not used for identifying a potential need for updating and supplementation.

In the event of a potential need for updating and supplementation with regard to a health care aspect, it was consistently checked whether further IQWiG reports on this topic were available. When determining a potential need for updating and supplementation, the corresponding IQWiG reports were taken into account.

In addition, recommendations on drugs were examined with regard to their indication-specific reimbursability in Germany as well as their approval status. This was performed in those areas where a potential need for updating and supplementation exists or is put up for discussion. In the case of discrepancies between guideline recommendations on drugs and the German approval status as well as their indication-specific reimbursability, this was presented conclusively and considered in the synthesis.

Results

A total of 26 guidelines were included, appraised and their recommendations extracted. The guidelines were issued by institutions in Germany (n = 4), Europe (n = 9), Australia (n = 9), New Zealand (n = 1), Canada (n = 1) and the United States (n = 2).

Six of the guidelines included deal with the complete care of patients with breast cancer and address nearly all of the health care aspects included in the DMP directive. Seven guidelines focus on the care of patients with early breast cancer. Four guidelines focus on the care of patients with advanced breast cancer (stage IV). The remaining 9 guidelines deal with different health care aspects such as diagnostics, radiotherapy, breast reconstruction, treatment-induced bone loss and specifics of breast cancer during pregnancy.

In the methodological appraisal with the AGREE II instrument, which was performed by 2 independent reviewers, on average the highest standardized domain values were primarily awarded in Domain 4 (Clarity of Presentation). On average the lowest standardized domain values were primarily awarded in Domain 5 (Applicability).

Information on the handling of unpublished data was provided in 19 of the 26 guidelines included, either in the guideline itself or in a methods report or in accompanying documents.

Potential need for updating and supplementation

With one exception (local recurrences), recommendations on all health care aspects of the medical care of breast cancer patients named in the DMP directive [1] were found in the 26 guidelines included. With regard to content, the statements are largely consistent with the statements of the DMP directive; however, discrepancies were found with regard to various health care aspects. However, most extracted recommendations are more detailed compared with the text of the DMP directive. In addition, some guidelines address topics not considered in the current DMP directive.

The results of the comparison with the DMP directive are presented in the following text, sorted by health care aspects. The health care aspects "Diagnostics" (1.2 of the DMP directive) and "Measures in primary therapy" (1.3 of the DMP directive) were summarized. The same applies to the health care aspects "Principles of treatment" (1.4.1 of the DMP directive) and "Patient information" (4.2 of the DMP directive).

Health care aspect "Definition of breast cancer" (1.1 of the DMP directive)

Invasive breast cancer

Two guidelines contain definitions of invasive breast cancer. As the information on the definition of invasive breast cancer are not recommendations, no statements on GoR/LoE are available. The definitions are largely consistent with the DMP directive, but more detailed. Due to the missing information on GoR/LoE, no statement can be made on the potential need for updating or supplementation.

Early breast cancer

Several guidelines contain definitions on early breast cancer. As the information on the definition of early breast cancer are not recommendations, no statements on GoR/LoE are available. As the DMP directive does not differentiate between early breast cancer and advanced breast cancer, these are additional statements. Due to the missing information on GoR/LoE, no statement can be made on the potential need for updating or supplementation.

Advanced breast cancer

Several guidelines contain definitions on advanced breast cancer. As the information on the definition of advanced breast cancer are not recommendations, no statements on GoR/LoE are available. As the DMP directive does not differentiate between early breast cancer and advanced breast cancer, these are additional statements. Due to the missing information on GoR/LoE, no statement can be made on the potential need for updating or supplementation.

Ductal carcinoma in situ (DCIS)

Several guidelines contain definitions of DCIS. As the information on the definition of DCIS are not recommendations, no statements on GoR/LoE are available. The definitions are largely consistent with the DMP directive, but more detailed. Due to the missing information on GoR/LoE, no statement can be made on the potential need for updating or supplementation.

Special forms of breast cancer

One guideline contains definitions of lobular carcinoma and of triple negative breast cancer. As the information on the definition of lobular carcinoma and triple negative breast cancer are not recommendations, no statements on GoR/LoE are available. In comparison with the DMP directive, the definitions are additional statements. Due to the missing information on GoR/LoE, no statement can be made on the potential need for updating or supplementation.

Health care aspects "Diagnostics" (1.2 of the DMP directive) and "Measures in primary therapy" (1.3 of the DMP directive)

Basic diagnostics

Several guidelines provide recommendations, with a largely high GoR category, on the necessary basic examinations. The statements on mammography, ultrasound of the breast and biopsy are largely consistent with the DMP directive, but more differentiated. There is no need for updating or supplementation.

One guideline provides a recommendation, with a moderate GoR category, on the consideration of the effect of endogenous and exogenous hormones when carrying out and interpreting diagnostic tests. In comparison with the DMP directive this is an additional recommendation. Due to the moderate GoR category, there is no need for updating or supplementation.

One guideline provides a negative recommendation, with a high GoR category, on conducting scintigraphy of the breast or PET in primary diagnostics. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

A further guideline provides a recommendation, with a high GoR category, on the use of scintigraphy of the breast only in individual cases. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

One guideline provides a recommendation, without information on GoR and with non-allocatable LoE, on the classification of mammogram findings based on the BI-RADS system. In comparison with the DMP directive these are additional recommendations. Due to the lack of GoR and non-allocatable LoE, no statement can be made on the need for updating or supplementation.

Magnetic resonance imaging (MRI)

Several guidelines provide recommendations, with a largely high GoR category, on carrying out an MRI in primary or preoperative diagnostics. Two guidelines, with a high GoR category, explicitly advise against routine MRI scans. Several guidelines provide recommendations for specific therapeutic indications for an MRI scan. In comparison with the DMP directive the guidelines contain additional recommendations. There is a potential need for updating or supplementation.

Staging

Several guidelines provide recommendations, with an inconsistent GoR category, on the search for distant metastases. The recommendations are largely consistent with the DMP directive, but more differentiated. There is no need for updating or supplementation.

Two guidelines provide recommendations, without information on GoR and with non-transferable LoE, on the use of PET/CT as an alternative to conventional imaging staging and as additional examination if locoregional recurrence or distant metastases are suspected. In comparison with the DMP directive these are additional recommendations. Due to the lack of information on GoR and non-allocatable or non-transferable LoE, no statement can be made on the need for updating or supplementation.

Two guidelines provide negative recommendations, with a low GoR category, on the measurement of tumour markers in the blood. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

Several guidelines provide recommendations, with an inconsistent GoR/LoE category, on the use of imaging techniques for the staging of the axilla. One guideline, with moderate LoE

category, generally advises against the sole use of imaging techniques; and one guideline, with a high GoR category, specifically advises against routine PET scans. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Minimal-invasive diagnostics and image-guided and open biopsy

One guideline provides recommendations, with a largely high GoR category, on minimal-invasive diagnostics and image-guided biopsy. Punch biopsy, vacuum biopsy or open excision biopsy are recommended for the histological diagnosis of suspicious findings. Moreover, intraoperative rapid-section diagnosis of dignity or primary open excision biopsy is only recommended in exceptional cases. Recommendations are also provided on preoperative marking of nonpalpable findings. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Preoperative cytologic examination

One guideline provides a negative recommendation, with a high GoR category, on fine needle aspiration as standard method for the confirmation of diagnosis. This is an additional recommendation. A potential need for updating or supplementation can be discussed.

One further guideline provides recommendations, without information on GoR and with non-allocatable LoE, on preliminary preoperative cytologic examination. In comparison with the DMP directive these are additional recommendations. Due to the lack of information on GoR and non-allocatable LoE, no statement can be made on the need for updating or supplementation.

Histopathologic examination of the tumour and the surgical margins

Two guidelines provide recommendations, with a largely high GoR category, on histopathologic examination of the tumour including the surgical margins. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Examination of (sentinel) lymph nodes

Several guidelines provide recommendations, with an inconsistent GoR category, on the assessment of the lymph node status. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Assessment of prognostic and predictive factors

Several guidelines provide recommendations, with a largely high GoR category, on the assessment of the hormone receptor status. In contrast, one further guideline, without information on GoR and with non-allocatable LoE, advises against routine assessment of the progesterone status. The recommendations are largely consistent with the DMP directive, but more differentiated. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a high GoR category, on the assessment of the HER2 status. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

One guideline provides recommendations, with a largely high GoR category, on the assessment of predictive factors. The menopausal status should be generally assessed. Regarding the proliferation marker Ki-67, routine use is not advised. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

One guideline provides a negative recommendation, with a low GoR category, on the use of gene expression analyses in the routine assessment of predictive values. One further guideline provides a recommendation, without information on GoR and with non-allocatable LoE, on the use in individual cases. In comparison with the DMP directive this is an additional recommendation. Due to the low GoR category, there is no need for updating or supplementation.

One guideline provides recommendations, with a high GoR category, on the assessment of prognostic factors, i.e. pTNM status, margin of resection and safety margins as well as histologic type and grading. These recommendations are consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides recommendations, with a largely moderate/low GoR/LoE category, on the assessment of further prognostic factors such as lymph and blood vessel invasion, age, urokinase plasminogen activator (uPA) and plasminogen activator inhibitor (PAI) concentration in the tumour tissue in node-negative breast cancer. In comparison with the DMP directive these are additional recommendations with regard to these factors. Due to the largely moderate/low GoR/LoE categories, there is no need for updating or supplementation.

Diagnostics during pregnancy

One guideline provides recommendations, with a low GoR category, and one guideline provides recommendations, without information on GoR and with non-allocatable LoE, on diagnostics during pregnancy. In comparison with the DMP directive these are additional recommendations. Due to the low GoR categories, there is no need for updating or supplementation.

Diagnostic tests in complementary and alternative treatment concepts

One guideline provides a recommendation, with a moderate GoR category, on diagnostic tests in the framework of complementary and alternative treatment concepts. In comparison with the DMP directive this is an additional recommendation. Due to the moderate GoR category, there is no need for updating or supplementation.

Health care aspect "Treatment" (1.4 of the DMP directive)

Health care aspect "Principles of treatment" (1.4.1 of the DMP directive)

General principles of patient information and consent

Several guidelines provide recommendations, with a largely low GoR category, on general principles of patient information and consent. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Specific aspects of patient information and consent

Several guidelines provide recommendations, with a largely high GoR category, on informing the patient about the options of surgical procedures. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR category, on informing the patient about the risks of lymphoedema and the options for preventing and treating it. In comparison with the DMP directive these are additional recommendations. There is a potential need for updating or supplementation.

One guideline provides recommendations, with a high GoR category, on information about rehabilitation and palliative care. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Planning of treatment

Several guidelines provide recommendations, largely without information on GoR/LoE or with non-allocatable LoE or non-transferable GoR, on the planning of treatment for invasive breast cancer. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Several guidelines provide recommendations, with an inconsistent GoR category, on treatment concepts for DCIS. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Supportive therapy

One guideline provides recommendations, with a high GoR category, on supportive therapy. The recommendation for physical activity of the patient during chemotherapy and radiotherapy is an additional recommendation in comparison with the DMP directive. A potential need for updating or supplementation can be discussed.

Interdisciplinary cooperation and communication

Several guidelines provide recommendations, with a largely low GoR category, on interdisciplinary cooperation and communication in breast cancer patient care. The

recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Psychosocial care

Several guidelines provide recommendations, with a largely high GoR/LoE category, on psychosocial care. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

Complementary therapy and alternative methods

One guideline provides recommendations, with a largely moderate GoR category, on complementary therapy and alternative methods. In comparison with the DMP directive these are additional recommendations. Due to the largely moderate GoR category, there is no need for updating or supplementation.

Specifics of breast cancer during pregnancy and in women of childbearing age

Two guidelines provide recommendations, with a largely low GoR category, and one further guideline provides recommendations, without information on GoR and with non-allocatable LoE, on the specifics of breast cancer during pregnancy. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

Two guidelines provide recommendations, with an inconsistent GoR category, and one further guideline provides recommendations, without information on GoR and with non-allocatable LoE, on the information of patients of childbearing age on possible effects of breast cancer treatment on fertility. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Health care aspect “Surgical treatment of breast cancer without special forms” (1.4.2 of the DMP directive)

Several guidelines provide recommendations, with a largely high GoR category, on shared decision-making with the informed patient about the suitable surgical procedure. In comparison with the DMP directive these are additional recommendations. There is a potential need for updating or supplementation.

One guideline provides a recommendation, with a high GoR category, on the width of surgical margins. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

One guideline provides recommendations, with a high GoR category, on the primary systemic treatment of patients with primarily unresectable or inflammatory breast cancer. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Health care aspect "Approach for nonpalpable findings" (1.4.2.1 of the DMP directive)

One guideline provides recommendations, with a high GoR category, on preoperative marking of nonpalpable findings. The recommendations are largely consistent with the DMP directive, but some of them are more differentiated. There is no need for updating or supplementation.

Health care aspect "Breast-conserving treatment" (1.4.2.2 of the DMP directive)

General

Several guidelines provide recommendations, with a largely high GoR/LoE category, on breast-conserving treatment. The recommendations are largely consistent with the DMP directive, but are more differentiated with regard to the patient target group and the type of breast-conserving treatment. There is no need for updating or supplementation.

Primary systemic treatments

Several guidelines provide a recommendation, with a high GoR/LoE category, on a primary systemic treatment with the goal of breast-conserving surgery. The recommendation is largely consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides a recommendation, without information on GoR and with non-allocatable LoE, on contraindications to breast-conserving surgery after primary systemic treatment. The recommendation is largely consistent with the DMP directive, but is more differentiated. There is no need for updating or supplementation.

Assessment of surgical margins

One guideline provides recommendations, with a low GoR category, and 2 further guidelines provide recommendations, without information on GoR and with non-allocatable LoE, on the assessment of the surgical margins after breast-conserving surgery. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

One guideline provides recommendations, with a low GoR category, on the safety margin between the tumour and the margin of resection of at least 2 mm. One further guideline, without information on GoR and with non-allocatable LoE, recommends a tumour-free margin of $\geq$ 1 mm. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Health care aspect "Modified radical mastectomy" (1.4.2.3 of the DMP directive)

Several guidelines provide recommendations, with a high GoR category, on (modified radical) mastectomy if a breast-conserving approach is not possible. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides recommendations, without information on GoR/LoE, on the types and performance of mastectomy. In comparison with the DMP directive these are additional recommendations. Due to the missing information on GoR/LoE, no statement can be made on the potential need for updating or supplementation.

Health care aspect "Surgical treatment of the axilla" (1.4.2.4 of the DMP directive)

Indications and contraindications for sentinel lymph node biopsy or axillary dissection

Several guidelines provide recommendations, with a largely high GoR/LoE category, on indications and contraindications for sentinel lymph node biopsy. The recommendations are largely consistent with the DMP directive, but more detailed. In contrast to the guidelines that explicitly advise against sentinel lymph node biopsy in case of multifocality, according to one further guideline, without information on GoR and with non-allocatable LoE, this procedure can also be performed in this case. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR/LoE category, on indications for axillary dissection. Two guidelines mention the option, with an inconsistent GoR category, and 2 further guidelines mention the option, without information on GoR and with non-allocatable LoE, particularly for patients with breast-conserving treatment and 1 or 2 positive sentinel lymph nodes, to dispense with axillary dissection after positive sentinel lymph node biopsy. In comparison with the DMP directive these are contradictory recommendations. A need for updating or supplementation can be discussed.

Performance of the sentinel lymph node biopsy

Several guidelines provide recommendations, with a largely moderate/low GoR/LoE category, on training and experience as well as multidisciplinarity of the responsible surgical team as precondition for the use of sentinel lymph node biopsy. In comparison with the DMP directive these are additional recommendations. Due to the moderate/low GoR/LoE, there is no need for updating or supplementation.

Several guidelines provide recommendations, with an inconsistent GoR/LoE category, on the marking of the sentinel lymph nodes and preoperative lymphoscintigraphy. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides a recommendation, with a high LoE category, on the intraoperative assessment of the sentinel lymph nodes. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Two guidelines provide recommendations, with an inconsistent GoR/LoE category, on the definitive histopathologic confirmation after the intraoperative rapid-section diagnosis. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Patient information and consent and concomitant supportive treatment

Several guidelines provide recommendations, with a largely high GoR/LoE category, on informing the patient about the benefits and risks of surgery and radiotherapy of the axilla and/or of sentinel lymph node biopsy. In comparison with the DMP directive these are additional recommendations. There is a potential need for updating or supplementation.

One guideline provides a recommendation, with a high GoR category, on informing the patient about the options of detection, prophylaxis and treatment of postoperative lymphoedema. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

One guideline provides recommendations, with a high GoR category, on physiotherapy after axillary dissection. Two guidelines provide a recommendation on this aspect, without information on GoR and with non-allocatable LoE. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Health care aspect "Plastic reconstruction surgery" (1.4.2.5 of the DMP directive)

Planning of treatment and time point for plastic reconstruction surgery

One guideline notes, with a high GoR category, that immediate breast reconstruction after mastectomy has no disadvantage with regard to survival in comparison with later breast reconstruction. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

One guideline provides a recommendation, with a moderate GoR category, on the influence of breast reconstruction on the result of the oncological treatment. In comparison with the DMP directive this is an additional recommendation. Due to the moderate GoR category, there is no need for updating or supplementation.

Two guidelines provide recommendations, with a low GoR category, on the time point for plastic surgery. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

One guideline provides recommendations, with a largely moderate/low LoE category, on factors that may influence the result of breast reconstruction. These should be considered when deciding about the time point and the type of plastic reconstruction surgery. In comparison with the DMP directive these are additional recommendations. Due to the largely moderate/low LoE categories, there is no need for updating or supplementation.

One guideline provides recommendations, with a largely moderate/low GoR category, on risk factors for postoperative complications. In comparison with the DMP directive these are additional recommendations. Due to the largely moderate/low GoR category, there is no need for updating or supplementation.

One guideline provides a recommendation, without information on GoR/LoE, on complications of plastic surgery. In comparison with the DMP directive this is an additional recommendation. Due to the missing information on GoR/LoE, no statement can be made on the need for updating or supplementation.

One guideline provides a recommendation, with a moderate GoR category, on the optimum time point for radiotherapy after mastectomy. The same guideline provides a recommendation, with a low GoR category, on the time point of radiotherapy for patients with mastectomy and plastic reconstruction surgery. In comparison with the DMP directive these are additional recommendations. Due to the moderate/low GoR category, there is no need for updating or supplementation.

Patient information and consent regarding breast reconstruction

Several guidelines provide recommendations, with a largely low GoR category, on information and consent of the patient regarding plastic reconstruction surgery. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Options and performance of plastic reconstruction surgery

One guideline provides a recommendation, with a low GoR category, on the preoperative administration of an antibiotic when breast reconstruction is performed. In comparison with the DMP directive this is an additional recommendation. Due to the low GoR category, there is no need for updating or supplementation.

One guideline provides recommendations, with a low GoR category, and one further guideline provides recommendations, without information on GoR and LoE, on the use of an acellular dermal matrix. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

Health care aspect "Radiotherapy of breast cancer" (1.4.3 of the DMP directive)

General aspects

Several guidelines provide recommendations, with an inconsistent GoR category, on different intervals between radiotherapy and surgery. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

One guideline provides a negative recommendation, with a moderate LoE category, on partial breast radiotherapy as the sole intraoperative or postoperative radiotherapy. In comparison with the DMP directive this is an additional recommendation. Due to the moderate LoE category, there is no need for updating or supplementation.

Combination of radiotherapy with systemic treatments

Several guidelines provide different recommendations, with largely moderate/low GoR/LoE categories, on the treatment sequence of systemic treatments and radiotherapy. In comparison with the DMP directive these are additional recommendations. Due to the largely moderate/low GoR/LoE, there is no need for updating or supplementation.

One guideline, without information on GoR and with non-allocatable LoE, names detailed indications for radiotherapy following primary systemic treatment. In comparison with the DMP directive these are additional recommendations. Due to the lack of information on GoR and non-allocatable LoE, no statement can be made on the potential need for updating or supplementation.

Hypofractionated radiotherapy (general)

Several guidelines provide recommendations, with a largely high GoR/LoE category, on the use of hypofractionated radiotherapy. In comparison with the DMP directive these are additional recommendations. There is a potential need for updating or supplementation.

Health care aspect "Radiotherapy after breast-conserving surgery" (1.4.3.1 of the DMP directive)

General statements on indication

Several guidelines provide recommendations, with a largely high GoR category, on the indication of radiotherapy after breast-conserving surgery. The recommendations of the guidelines are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

Performance of the radiotherapy

Several guidelines provide recommendations, with a largely high GoR category, on the target volume in percutaneous radiotherapy and on additional boost radiation after breast-conserving surgery. The recommendations of the guidelines are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Two guidelines provide negative recommendations, with an inconsistent GoR category, on partial breast radiotherapy as exclusive radiotherapy. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Three guidelines provide recommendations, with an inconsistent GoR/LoE category, on the use of hypofractionated radiotherapy. In comparison with the DMP directive, these are additional recommendations on the criteria for performing hypofractionated radiotherapy. A potential need for updating or supplementation can be discussed.

Health care aspect "Radiotherapy after mastectomy" (1.4.3.2 of the DMP directive)

Several guidelines provide recommendations, with a largely high GoR category, on the indication of radiotherapy after mastectomy. In comparison with the DMP directive this is an additional recommendation with regard to the consideration of the just tumour-free surgical margins. A potential need for updating or supplementation can be discussed.

Three guidelines provide recommendations, with a largely moderate GoR category, on the indication of radiotherapy after mastectomy and low/moderate risk of recurrence. One guideline advises against regular postoperative radiotherapy in patients with a low risk of recurrence. In comparison with the DMP directive these are additional recommendations. Due to the moderate GoR category, there is no need for updating or supplementation.

One guideline provides a recommendation, with a largely moderate GoR category, on the optimum time point for radiotherapy after mastectomy. The same guideline provides a recommendation, with a low GoR category, on the time point of radiotherapy for patients with mastectomy and plastic reconstruction surgery. In comparison with the DMP directive these are additional recommendations. Due to the moderate/low GoR category, there is no need for updating or supplementation.

One guideline provides a negative recommendation, with a low GoR category, on the use of additional boost radiation after mastectomy in patients with positive surgical margins. In comparison with the DMP directive this is an additional recommendation. Due to the low GoR category, there is no need for updating or supplementation.

Health care aspect "Radiotherapy of the lymphatic pathways" (1.4.3.3 of the DMP directive)

Several guidelines provide recommendations, with a largely moderate GoR category, on radiotherapy of the supra-/infraclavicular lymph nodes. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely low GoR/LoE category, on decision-making regarding radiotherapy of the lymphatic pathways. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides a negative recommendation, with a high GoR category, and one further guideline provides a negative recommendation, without information on GoR/LoE, on radiotherapy of the regional lymphatic pathways when lymph nodes are not affected. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR/LoE category, on radiotherapy of the axilla in selected situations. The recommendations are largely consistent

with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

One guideline provides negative recommendations, with a high GoR category, and 2 further guidelines provide negative recommendations, without information on GoR and/or with non-allocatable LoE, on radiotherapy of the axilla when lymph nodes are not affected and/or sentinel lymph node biopsy is negative. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

One guideline provides a negative recommendation, with a high GoR category, on radiotherapy of the regional lymphatic pathways when there is proof of isolated tumour cells or micrometastases. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Several guidelines provide recommendations, with an inconsistent GoR category, on radiotherapy of the internal mammary chain. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Health care aspect "Systemic adjuvant treatment (endocrine therapy, chemotherapy and antibody therapy)" (1.4.4 of the DMP directive)

Planning of treatment

Several guidelines provide recommendations, with inconsistent GoR/LoE category, on the planning of an adjuvant systemic treatment. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

Adjuvant endocrine therapy

Several guidelines provide recommendations, with a largely high GoR/LoE category, on adjuvant endocrine therapy. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Several guidelines provide recommendations, largely without information on GoR and with non-allocatable LoE, on bone density measurement before initiating treatment with aromatase inhibitors. These are additional recommendations. Due to the lack of information on GoR and non-allocatable LoE, no statement can be made on the potential need for updating or supplementation.

Adjuvant chemotherapy

Several guidelines provide recommendations, with a largely high GoR category, on the indication of adjuvant chemotherapy. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR/LoE category, on chemotherapy. The guidelines explicitly name taxane-containing and/or anthracycline-based regimens. In comparison with the DMP directive these are additional recommendations. There is a potential need for updating or supplementation.

Adjuvant antibody therapy

Several guidelines provide recommendations, with a largely high GoR category, on adjuvant treatment with trastuzumab for HER2-positive tumours. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

One guideline with a moderate GoR category and one further guideline without information on GoR and with non-allocatable LoE provide a recommendation on the expansion of the therapeutic indication for treatment with trastuzumab. In comparison with the DMP directive this is an additional recommendation. Due to the moderate GoR category, there is no need for updating or supplementation.

Several guidelines provide recommendations, with an inconsistent GoR category, on regular monitoring of the cardiac function during treatment with trastuzumab. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Adjuvant treatment with bisphosphonates

Two guidelines provide recommendations, with an inconsistent GoR/LoE category, and 4 further guidelines provide recommendations, without information on GoR and with non-allocatable LoE, on the adjuvant use of bisphosphonates[3] in selected patients. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Two guidelines, on the one hand with a high GoR category, on the other hand with an inconsistent LoE category, advise against the routine use of bisphosphonates[3]. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Systemic adjuvant treatment during pregnancy/breastfeeding

Two guidelines provide largely negative recommendations, with a low GoR category, and one further guideline provides largely negative recommendations, without information on GoR and with non-allocatable LoE, on systematic adjuvant treatment during pregnancy and

[3] The guidelines do not present with consistent transparency whether the recommendations refer to oral or intravenous administration of bisphosphonates. Hence the 2 forms of administration are not differentiated in this report.

breastfeeding. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

Health care aspect "Primary systemic/neoadjuvant treatment" (1.4.5 of the DMP directive)

Several guidelines provide recommendations, with an inconsistent GoR category, on the administration of a primary systemic treatment for inflammatory breast cancer or locally advanced primary unresectable breast cancer. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Two guidelines provide recommendations, with a high GoR category, 3 further guidelines provide recommendations, without information on GoR and with non-allocatable LoE, on the administration of a primary systemic treatment with the goal to achieve breast-conserving surgery. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides a recommendation, with a low GoR category, on primary endocrine therapy in case of contraindications to surgery. The recommendation is largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

One further guideline specifies, with a high LoE category, the endocrine therapy to be used (aromatase inhibitors). In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

One guideline provides recommendations, with a high GoR category, and 2 further guidelines provide recommendations, without information on GoR and with non-allocatable LoE, on treatment with trastuzumab for HER2-positive tumours. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

One guideline provides recommendations, with an inconsistent GoR category, and one further guideline provides recommendations, without information on GoR and with non-allocatable LoE, on the recording of clinical and pathomorphological findings before initiating neoadjuvant systemic treatment. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

Health care aspect "Approach for special forms of breast cancer" (1.4.6 of the DMP directive)

Health care aspect "Ductal carcinoma in situ (DCIS)" (1.4.6.1 of the DMP directive)

General treatment concept

One guideline provides a recommendation, with a high GoR category, on the interdisciplinary preparation of the treatment concept when preinvasive neoplasia is present. In comparison

with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Surgical treatment

One guideline provides a recommendation, with a low GoR category, on decision-making regarding the type of surgery. Two further guidelines provide recommendations, with a high GoR and/or moderate LoE category, on informing the patient about the surgical options. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR category, on the safety margin between the tumour and the margin of resection of at least 2 mm as well as indications for further excision. One further guideline, without information on GoR and with non-allocatable LoE, recommends a tumour-free margin of ≥ 1 mm. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR category, on the performance of sentinel lymph node biopsy and axillary dissection. One guideline, with a high GoR category, and 2 further guidelines, without information on GoR and with non-allocatable LoE, do not recommend routine sentinel lymph node biopsy in patients with preoperative diagnosis of DCIS. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Several guidelines, with a largely high GoR category, generally advise against axillary dissection. In comparison with the DMP directive these are additional recommendations. There is a potential need for updating or supplementation.

Radiotherapy

Several guidelines provide recommendations, with a largely high GoR/LoE category, on the use of radiotherapy after breast-conserving surgery. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Endocrine therapy

Several guidelines provide recommendations, with a largely low GoR category, on balancing adjuvant endocrine therapy in hormone receptor positive DCIS. One further guideline with a high GoR explicitly recommends endocrine therapy in these patients. Two further guidelines, without information on GoR and with non-allocatable LoE, generally advise against endocrine therapy after breast-conserving surgery in patients with DCIS. These are contradictory statements. Due to the inconsistency with regard to content, no statement can be made on the need for updating or supplementation.

Health care aspect "Locally advanced breast cancer" (1.4.6.2 of the DMP directive)

Several guidelines provide recommendations, with a largely high GoR category, on the treatment of locally advanced breast cancer. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Health care aspect "Breast cancer and multimorbidity" (1.4.6.3 of the DMP directive)

Several guidelines provide recommendations, with inconsistent GoR/LoE category, on systemic adjuvant treatment of patients with breast cancer and comorbidities. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

Health care aspect "After-care" (1.5 of the DMP directive)

General aspects

Several guidelines provide recommendations, largely without information on GoR/LoE on general principles of after-care. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Follow-up examinations and intervals

Several guidelines provide partly deviating recommendations, with an inconsistent GoR/LoE category, on the intervals between the follow-up examinations. One guideline recommends, with a high GoR category, follow-up examinations every 3 months during the first 3 years. This is in contrast to the DMP directive, according to which follow-up examinations are usually to be performed every 6 months. A potential need for updating or supplementation can be discussed.

Several guidelines provide recommendations, with inconsistent GoR/LoE category, on the annual performance of mammography. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides recommendations, with a low GoR category, and one further guideline provides recommendations, without information on GoR and with non-allocatable LoE, on follow-up examinations for patients with breast reconstruction. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR/LoE category, on indications for more extensive device-based and laboratory diagnostics or MRI for specific patients. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

Two guidelines provide recommendations, with an inconsistent GoR/LoE category, on the after-care of the axilla in negative sentinel lymph node biopsy. In comparison with the DMP

directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Diagnostics and treatment of side effects and consequences of primary and long-term treatments

Several guidelines provide recommendations, with a largely high GoR category, on informing the patient about risks, prevention and treatment of lymphoedema. In comparison with the DMP directive these are additional recommendations. There is a potential need for updating or supplementation.

One guideline provides recommendations, with a high GoR category, and one further guideline provides recommendations, without information on GoR and/or LoE, on contraindications to hormone replacement therapy. In comparison with the DMP directive these are additional recommendations. A potential need for updating or supplementation can be discussed.

Two guidelines provide recommendations, without information on GoR and with non-allocatable LoE, on physiotherapy after axillary surgery or in case of persisting immobility of the shoulder-arm region. In comparison with the DMP directive this is an additional recommendation. Due to the lack of information on GoR and with non-allocatable LoE, no statement can be made on the potential need for updating or supplementation.

Specific aspects in the planning and the avoidance of pregnancy after breast cancer treatment

One guideline provides recommendations, with a low GoR category, on specific aspects in the planning or the avoidance of pregnancy after breast cancer treatment. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

Health care aspect "Psychosocial care" (1.5.1 of the DMP directive)

Several guidelines provide recommendations, with a largely high GoR/LoE category, on psychosocial care. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

Health care aspect "Physical activity and diet" (1.5.2 of the DMP directive)

Several guidelines provide recommendations, with a largely high GoR/LoE category, on physical activity during after-care and rehabilitation. The recommendations are largely consistent with the DMP directive. There is no need for updating or supplementation.

One guideline provides a recommendation, with a low GoR category, on positive factors influencing bone density, such as a healthy diet and normal body weight. The recommendation is largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Health care aspect “Diagnostics and treatment of advanced disease” (1.6 of the DMP directive)

Health care aspect “Local recurrence” (1.6 of the DMP directive)

The guidelines included do not contain any general recommendations on this health care aspect.

Health care aspect “Treatment of local recurrence” (1.6.1.1 of the DMP directive)

Several guidelines provide recommendations, with a largely high GoR category, on the treatment of local recurrence. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

Health care aspect “Distant metastases” (1.6.2 of the DMP directive)

Several guidelines provide recommendations, with a largely high GoR/LoE category, on diagnostic tests for the detection of metastases. The recommendations are largely consistent with the DMP directive, but more differentiated. There is no need for updating or supplementation.

Several guidelines provide recommendations, with a largely high GoR category, on measures before initiating treatment of the metastatic disease. In comparison with the DMP directive these are additional recommendations. There is a potential need for updating or supplementation.

Health care aspect “Treatment of metastatic disease” (1.6.2.1 of the DMP directive)

Planning of treatment

One guideline provides recommendations, with a moderate and otherwise non-transferable GoR, and one further guideline provides recommendations with a non-transferable GoR on the information and involvement of the patient in the planning of treatment. In comparison with the DMP directive these are additional recommendations. Due to the moderate GoR category, there is no need for updating or supplementation.

Endocrine therapy

Several guidelines provide recommendations, with a largely high GoR/LoE category, on endocrine therapy for metastatic disease. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Chemotherapy

One guideline provides a recommendation, with a high GoR category, on the regular assessment of toxicity. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Several guidelines provide recommendations, with a largely high GoR/LoE category, on the administration of chemotherapy for metastatic disease. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Antibody therapy/targeted therapies

Several guidelines provide recommendations, with a largely high GoR/LoE category, on the use of anti-HER2 targeted therapy in metastatic disease. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Several guidelines provide recommendations, with inconsistent GoR/LoE category, on treatment with bevacizumab[4]. These are contradictory statements. Due to the inconsistency with regard to content, no statement can be made on the need for updating or supplementation.

Treatment of side effects and complications

One guideline provides recommendations, without information on GoR/LoE, on the treatment of side effects and complications in patients with metastatic breast cancer. In comparison with the DMP directive these are additional recommendations. Due to the missing information on GoR/LoE, no statement can be made on the potential need for updating or supplementation.

Specific treatment of bone metastases and metastatic spinal compression syndrome

Several guidelines provide recommendations, partly with high GoR/LoE category, partly without information on GoR/LoE or with non-transferable GoR/LoE, on radiotherapy and surgery for the specific treatment of bone metastases/metastatic spinal compression syndrome. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Several guidelines provide recommendations, with inconsistent GoR/LoE category, on the indications for treatment with bisphosphonates[3] for bone metastases. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Specific treatment of brain metastases

Several guidelines provide recommendations, with an inconsistent GoR category and partly without information on GoR/LoE on the specific treatment of brain metastases. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

[4] A "red hand letter" on bevacizumab was published in May 2013 (see Discussion).

Specific treatment of visceral metastases

One guideline provides recommendations, with a low GoR category, on the specific treatment of visceral metastases. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

Health care aspect "Palliative care" (1.7 of the DMP directive)

Several guidelines provide recommendations, partly with high GoR/LoE category, partly without information on GoR/LoE or with non-transferable GoR, on palliative care. The recommendations are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

One guideline provides a recommendation, with a high GoR category, on the information of patients and relatives about palliative care. In comparison with the DMP directive this is an additional recommendation. A potential need for updating or supplementation can be discussed.

Health care aspect "Rehabilitation" (1.8 of the DMP directive)

One guideline provides recommendations, with a high GoR/LoE category, and 2 further guidelines provide recommendations, without information on GoR and with non-allocatable LoE, on rehabilitation. The recommendations of the guidelines are largely consistent with the DMP directive, but some of them are more detailed. There is no need for updating or supplementation.

Health care aspect "Cooperation of health care sectors" (1.9 of the DMP directive)

General aspects

Several guidelines provide general recommendations, with an inconsistent GoR category, on multidisciplinary care and continuity of health care. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Cooperation of the health care sectors in diagnostics and treatment

Four guidelines provide recommendations, with a largely high GoR category, and 6 further guidelines provide recommendations without information on GoR/LoE and/or with non-transferable GoR/LoE or with non-allocatable LoE on the multidisciplinary cooperation in diagnostics and treatment regarding specific health care aspects. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Two guidelines provide recommendations, with a largely high GoR category, and 4 further guidelines provide recommendations, without information on GoR/LoE and/or with non-allocatable LoE, on requirements for referrals and ensuring the timely access to specific

therapeutic institutions. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Cooperation of the health care sectors in after-care

One guideline provides recommendations, with a moderate/low GoR category, and 4 further guidelines provide recommendations, without information on GoR/LoE or with non-allocatable LoE or with non-transferable GoR, on the cooperation of the health care sectors in after-care. The recommendations are largely consistent with the DMP directive, but more detailed. There is no need for updating or supplementation.

Cooperation of the health care sectors in breast cancer during pregnancy

One guideline provides recommendations, with a low GoR category, on the cooperation of the health-care sectors in breast cancer during pregnancy. One guideline provides recommendations, without information on GoR and with non-allocatable LoE. In comparison with the DMP directive these are additional recommendations. Due to the low GoR category, there is no need for updating or supplementation.

Conclusions

By comparing the recommendations extracted from current evidence-based guidelines with the requirements of the DMP directive forming the basis of the DMP "breast cancer", health care aspects could be identified for which a potential need for updating or supplementation exists or can be discussed.

There is a potential need for updating or supplementation for the following health care aspects:

- "Diagnostics and measures in primary therapy" with regard to the performance of an MRI scan in specific indications. Routine MRI scan is not advised.
- "Principles of treatment" on the information of patients about the risks of lymphoedema and the options for preventing and treating it.
- "Surgical treatment of breast cancer without special forms" with regard to shared decision-making with the informed patient about the suitable surgical option.
- "Surgical treatment of the axilla" with regard to the information of the patient about the benefits and risks of surgery and radiotherapy of the axilla and/or of sentinel lymph node biopsy.
- "Radiotherapy of breast cancer" on the use of hypofractionated radiotherapy.
- '"Systemic adjuvant treatment (endocrine therapy, chemotherapy and antibody therapy)" on the indication of a taxane-containing and/or anthracycline-based chemotherapy.
- "Ductal carcinoma in situ (DCIS)"; axillary dissection is generally not advised.
- "After-care" on the information of patients about risks, prevention and treatment of lymphoedema.

- "Distant metastases" with regard to measures before initiating treatment of the metastatic disease.

A potential need for updating or supplementation can be discussed for the following health care aspects:

- "Diagnostics and measures in primary therapy":
  - Negative recommendations with regard to conducting scintigraphy of the breast or PET in primary diagnostics. One further guideline recommends scintigraphy of the breast in individual cases, however.
  - With regard to the use of imaging techniques for the staging of the axilla. Particularly the sole use of imaging techniques and routine PET scans are advised against.
  - On minimal-invasive diagnostics and image-guided and open biopsy. Punch, vacuum and open excision biopsy are recommended. Intraoperative rapid-section diagnosis of dignity or primary open excision biopsy should only be conducted in exceptional cases. Recommendations are additionally provided on preoperative marking of nonpalpable findings.
  - On preoperative cytologic examination. Fine needle aspiration as standard method for the confirmation of diagnosis is advised against.
  - On the assessment of prognostic and predictive factors regarding the regular assessment of menopausal status. In contrast, routine assessment of the proliferation marker Ki-67 is advised against.
- "Principles of treatment":
  - With regard to the information about rehabilitation and palliative care.
  - With regard to supportive treatment regarding physical activity during chemotherapy and radiotherapy.
  - On the information of patients of childbearing age about the effects of breast cancer treatment on fertility.
- "Surgical treatment of breast cancer without special forms" with regard to the width of surgical margins
- "Surgical treatment of the axilla":
  - With regard to the indications for axillary dissection; no axillary dissection in patients with breast-conserving treatment and 1 or 2 positive sentinel lymph nodes.
  - For the intraoperative assessment of the sentinel lymph nodes and for the histopathologic confirmation after intraoperative rapid-section diagnosis.
  - On the information of the patient about the options of detection, prophylaxis and treatment of postoperative lymphoedema.

- For physiotherapy after surgical treatment of the axilla.

- "Plastic reconstruction surgery" with regard to the survival rates in immediate breast reconstruction compared with mastectomy without breast reconstruction.
- "Radiotherapy of breast cancer" with regard to the suitable interval between radiotherapy and surgery.
- "Radiotherapy after breast-conserving surgery":
  - With regard to negative recommendations for partial breast radiotherapy as exclusive radiotherapy.
  - On the use of hypofractionated radiotherapy.
- "Radiotherapy after mastectomy":
  - On the indication of radiotherapy after mastectomy with regard to the consideration of the just tumour-free surgical margins.
- "Radiotherapy of the lymphatic pathways":
  - Negative recommendations regarding radiotherapy of the regional lymphatic pathways when there is proof of isolated tumour cells or micrometastases.
  - On the indication of radiotherapy of the internal mammary chain.
- "Systemic adjuvant treatment (endocrine therapy, chemotherapy and antibody therapy)":
  - With regard to regular monitoring of the cardiac function during treatment with trastuzumab.
  - With regard to the adjuvant use of bisphosphonates in selected patients.
  - Routine use of bisphosphonates is not advised.
- "Primary systemic/neoadjuvant treatment":
  - Specification of the endocrine therapy to be used.
  - On treatment with trastuzumab in HER2-positive tumours.
- "Ductal carcinoma in situ (DCIS)"
  - With regard to the preparation of a treatment concept when preinvasive neoplasia is present.
  - With regard to the performance of a sentinel lymph node biopsy, which is not recommended for patients with preoperative diagnosis of DCIS.
- "After-care":
  - With regard to the intervals between the follow-up examinations.
  - With regard to the after-care of the axilla in negative sentinel lymph node biopsy.
  - On contraindications to hormone replacement therapy.

- "Treatment of metastatic disease" regarding regular assessment of toxicity under chemotherapy.
- "Palliative care" regarding the information of patients and their relatives about palliative care.

Due to inconsistent and/or contradictory statements, no statement can be made on the potential need for updating or supplementation for the following health-care aspects:

- "Ductal carcinoma in situ (DCIS)" regarding adjuvant endocrine therapy in hormone-positive DCIS.
- "Treatment of metastatic disease" regarding treatment with bevacizumab.

It is unclear whether the lack of consideration of unpublished data in the guidelines included results in bias in the external evidence underlying the recommendations. If this does lead to bias, the direction and extent of bias is not assessable on the basis of the information available.

Keywords: breast neoplasms, disease management programme, methodological guideline appraisal

References

1. Gemeinsamer Bundesausschuss. Richtlinie des Gemeinsamen Bundesausschusses zur Regelung von Anforderungen an die Ausgestaltung von strukturierten Behandlungsprogrammen nach §137f Abs. 2 SGB V (DMP-Richtlinie/DMP-RL) [online]. 16 February 2012 [accessed: 14 June 2012]. URL: http://www.g-ba.de/downloads/17-98-3242/DMP-RL_2012-02-16.pdf.

The full report (German version) is published under https://www.iqwig.de/de/projekte_ergebnisse/projekte/versorgungsqualitat/v12_02_systematische_leitlinienrecherche_und_bewertung_sowie_extraktion_neuer_und_relevanter_empfehlungen_fur_das_dmp_brustkrebs.2160.html.