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Evidence-based recommendations on care for breast cancer survivors for primary care providers: a review of evidence-based breast cancer guidelines

Inge Spronk,[1] Joke C Korevaar,[1] Francois G Schellevis,[1,2] Tit Albreht,[3] Jako S Burgers[4,5]

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[1]General Practice, NIVEL Netherlands Institute for Health Services Research, Utrecht, The Netherlands
[2]Department of General Practice & Elderly Care Medicine, Amsterdam Public Health Research Institute, VU University Medical Center, Amsterdam, The Netherlands
[3]Centre for Health System Analyses, National Institute of Public Health, Ljubljana, Slovenia
[4]Dutch College of General Practitioners, Utrecht, The Netherlands
[5]Department Family Medicine, School CAPHRI, Maastricht University, Maastricht, The Netherlands

Correspondence to
Dr Joke C Korevaar;
j.korevaar@nivel.nl

ABSTRACT

Objective To review evidence-based (EB) recommendations on survivorship care for primary care providers (PCPs) in EB breast cancer guidelines.

Design and setting Guidelines were collected via experts and via literature database, guideline database and cancer agency websites searches.

Method EB guidelines in any language published between 2012 and 2017 were collected. EB recommendations on survivorship care relevant for PCPs were extracted and grouped into three categories (recurrence detection, long-term effects and recurrence prevention). The content of the recommendations was analysed and summarised in the number and type of clinical topics addressed. The Appraisal of Guidelines for Research and Evaluation II instrument was used to evaluate the methodological quality of the guidelines.

Results Six guidelines, of which two were of acceptable methodological quality, were included. One was specifically made for general practitioners. Fifteen clinical topics were identified. Guidelines differed in the clinical topics addressed and for some identical topics in the content of the recommendations. Many recommendations were based on low-quality evidence. Recurrence detection received most attention, physical examination and mammography were often highlighted. Potential complications largely varied in number and type. Intimacy concerns, vaginal dryness, dyspareunia, fatigue, menopausal symptoms, peripheral neuropathy and lymphedema were reported in more than one guideline. Recurrence prevention was mentioned in four guidelines; all recommended physical activity.

Conclusion The number of EB recommendations in guidelines is limited. Moreover, recommendations differ between guidelines and most are based on low-quality evidence. More high-quality research is needed to develop and adapt guidelines to support PCPs in providing optimal breast cancer survivorship care.

Strengths and limitations of this study

- This study is the first to evaluate evidence-based (EB) recommendations on care for breast cancer survivors relevant for primary care providers (PCPs) in EB breast cancer guidelines.
- Input from 36 countries was received; hereby, we were able to create a fairly complete overview of EB recommendations on care for breast cancer survivors for PCPs.
- The main limitation includes the validation of translations by non-native speakers; hereby, details of recommendations may be misinterpreted.
- Other limitations are that we have not assessed PCPs' views on the guidelines and that we have not examined the use of the guidelines by PCPs in practice.

INTRODUCTION

Due to the growth and ageing of the population, breast cancer prevalence rates are increasing.[1] Improvements in early detection and cancer treatment led to a growing number of women surviving breast cancer.[2]

After curative breast cancer treatment, patients usually receive follow-up care to detect cancer recurrence and to manage late and long-term consequences of treatment.[3] Primary care providers (PCPs) are increasingly involved in the follow-up care as a result of limited secondary care facilities, the growing number of breast cancer survivors and increasing costs.[4–6] Besides, a systematic review showed that there is evidence that follow-up for breast cancer survivors is effective in primary care.[7]

Another result of the rising number of survivors is that PCPs are seeing an increased number of survivors.[8 9] Many breast cancer survivors face short-term and long-term health consequences from cancer and cancer treatment, including physical and psychological consequences such as depression, pain and fatigue[10 11] and have more contacts with their PCP compared with control patients.[8 9]

Therefore, it is important that PCPs are able to provide optimal care for cancer survivors and meet the needs of these patients. Studies examining PCPs' views showed that PCPs prefer more guidance regarding recurrence risk management and consequences of cancer treatment.[12 13] To investigate which evidence-based (EB) recommendations on care for cancer survivors are currently available in clinical practice guidelines relevant to PCPs, we assessed existing breast cancer guidelines and created an overview of EB recommendations on PCP care for breast cancer survivors.

METHODS

Two strategies were used to collect guidelines. As part of the European Union Joint Action Cancer Control (CanCon; www.cancercontrol.eu), which aims to contribute to reducing the cancer burden in the European Union, an inventory of existing guidelines in European countries via national experts was undertaken. In addition, the scientific literature, guideline databases and cancer agency websites were searched to complete the inventory of guidelines.

European inventory of guidelines

In Autumn 2014, experts from all European Union Member States and four non-European Union (EU) countries (Norway, Switzerland, Iceland and Turkey) were asked to collect existing guidelines in their own country. Experts included representatives from national primary care associations, nursing associations, universities with a medical department and CanCon-associated partners. At least three experts per country were approached. In December 2014, delegates were approached from the Cancer and Primary Care Research International Network, the European Forum for Primary Care, the European Society of General Practice/Family Medicine (World Organisation of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA) Europe) and CanCon collaborating partners from non-responding countries. Inclusion criteria were that the guidelines needed to contain guidance on care for adult breast cancer survivors, subsequent to intentionally curative treatment, and that they were relevant to PCPs. Both national and regional guidelines were eligible.

Literature, guideline databases and cancer agency websites search

A bibliographical database search using the terms 'guideline' and 'breast cancer' was conducted in January 2015 to complete the inventory of guidelines (see online supplement 1 for the search strategy). Databases included Embase and Medline. Also, the National Guideline Clearinghouse website in the USA, the Guidelines International Network website and national cancer agency websites were searched for relevant breast cancer guidelines (see online supplement 2 for all cancer agency websites that were searched). Searches were conducted without any language restriction. The inclusion criteria were the same as for selection of the guidelines from the inventory. In June 2017, the literature, the guideline databases and cancer agency websites searches were repeated to reveal updates from the guidelines and guidelines published after January 2015.

Selection of guidelines

Guidelines obtained from the guideline databases and cancer agency websites searches were selected on the basis of title. Records from the scientific literature search were screened on the basis of title and abstract/summary. Screening of guidelines was performed by one researcher (IS). Records were considered if they included breast cancer guidelines. Guidelines meeting the following criteria were reviewed in full text: the guideline originated from Western countries (EU countries, Iceland, Norway, Switzerland, Turkey, USA, Canada, New Zealand and/or Australia) and focused on adult patients with breast cancer. Inclusion criteria were a publication date from 2012 to 2017, as older guidelines may be outdated,[14] and meeting the definition of an EB guideline[15] including recommendations intended to optimise patient care that are informed by the best available knowledge. If more versions of a guideline existed, the most recent version of a guideline was used. Guidelines were excluded if oncologists were the only target audience, if they duplicated another guideline, if the guideline only focused on one phase in the care process such as early detection, screening, treatment or palliative care, on advanced cancer or metastasis or on hereditary cancer survivors, and if guidelines did not link recommendations to graded evidence or to scientific citations. Information from guidelines in languages other than English or Dutch were translated. Data from the Croatian, Danish, Finnish, Norwegian and Polish guidelines were translated by the expert who provided the guidelines. Colleague researchers from the Netherlands Institute for Health Services Research (NIVEL) institute who master the specific language translated the data from the French, German and Italian guidelines.

Quality assessment

The methodological quality of the guidelines was assessed using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument.[16] AGREE II is a validated 23-item instrument used to evaluate six domains: scope and purpose (three items), stakeholder involvement (three items), rigour of development (eight items), clarity of presentation (three items), applicability (four items) and editorial independence (two items). These six domains are followed by two extra items ('Overall assessment'), which indicate the overall quality of the guideline and whether the reviewers recommend the guideline for use in practice. The English and Dutch guidelines were assessed by two researchers (IS and JCK); the German and Italian guidelines were each reviewed

by two colleagues with a high mastery of the specific language. All items were rated from 1 (strongly disagree) to 7 (strongly agree). Items for which scores differed more than one point were discussed by the reviewers. Rationales for scores were explained and scores were revised when this was considered necessary. Afterwards, a total score for each domain was calculated by summing up all item scores within a domain and by scaling the total score as a percentage of the maximum possible score of a domain.[17] Domain scores greater than 60% were considered acceptable.[18–21] The researchers recommended to use guidelines when three or more domains were scored as acceptable and the rigour of development was of good quality.[18] In addition, the researchers recommended modifications before using the guideline when at least two domains were considered acceptable and when the rigour of development was of moderate quality. Lower scores resulted in the recommendation to not using the guideline.

Content analysis

EB recommendations were categorised into 'recurrence detection', 'long-term effects' and 'recurrence prevention' by two researchers independently (IS and JCK). Subsequently, a clinical topic list per category was composed. EB recommendations were independently allocated to clinical topics by two researchers (IS and JCK). Disagreements arising from decisions on either categorisation or allocation into clinical topics were resolved by discussion with a third researcher (FGS). The categorisation and clinical topics were discussed and approved in a meeting of experts participating in work package 7 (community cancer care) of the European Union Joint Action Cancer Control.[22 23] Experts from five European countries participated in this meeting.

RESULTS

Guidelines

Response was received from 45 experts from all 32 approached countries and 16 provided a current breast cancer guideline. The literature search yielded 419 results, the guideline databases and cancer agency websites searches in 279 results. In total, 16 additional potentially relevant guidelines were considered (figure 1).

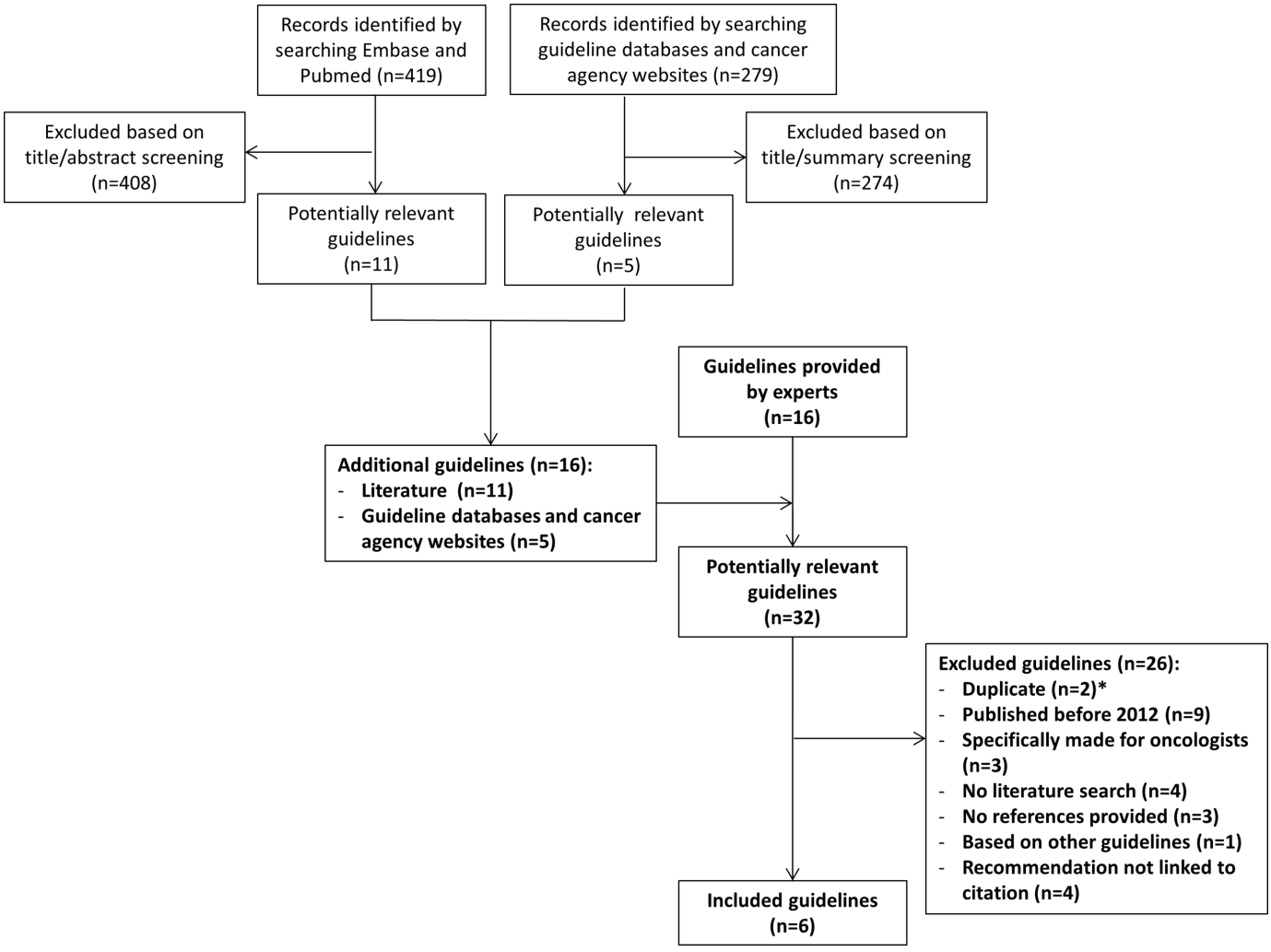

Figure 1 Flowchart outlining guideline selection.

Table 1 Included breast cancer guidelines

Country (ID code)	Year of publication	Title in English
Canada Alberta (CA)	2015	Follow-up care for early-stage breast cancer[27]
Europe (EU)	2015	Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[26]
Germany (GE)	2012	Interdisciplinary S3 guideline for the diagnosis, treatment and aftercare of breast cancer[29]
Italy (IT)	2016	Breast cancer guideline[30]
The Netherlands (NL)	2016	NHG Guideline Breast cancer[28]
United States (US)	2015	American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline[25]

ESMO, European Society for Medical Oncology; NHG, Dutch College of General Practitioners.

After removal of one duplicate and one guideline[24] of which recommendations on care for breast cancer survivors were included in another guideline that focused on breast cancer survivors[25] and elimination of guidelines based on other exclusion criteria (figure 1), six guidelines were included (table 1). These guidelines originated from Canada, Germany, Italy, the Netherlands and the USA. And also, the guideline from the European Society for Medical Oncology was included. This organisation publishes guidelines that may be adopted by European countries. However, most European countries develop their own guideline. Three guidelines were published in English,[25–27] one in Dutch,[28] one in German[29] and one in Italian.[30] One guideline was specifically made for general practitioners.[28]

Methodological quality

The guidelines were evaluated by the researchers using the AGREE II instrument. Mean scaled domain percentages, mean overall appraisal scores and appraiser recommendations for the use of guidelines are shown in online supplementary 3. Two guidelines (NL and US) were recommended by the reviewers for use in clinical practice without modifications. Both of these guidelines scored 'acceptable' on five out of the six domains; only the scores on the domain 'applicability' were moderate. For two other guidelines (CA and GE), modifications were recommended by the reviewers before using these guidelines in practice. These guidelines scored 'acceptable'

Table 2 Overview of clinical topics covered (Y) in included guidelines

	CA	EU	GE	IT	NL	US
Recurrence detection						
Awareness	_	_	_	Y	_	Y
Self-examination	Y	_	_	_	Y	_
Physical diagnostic tests	_	_	_	Y	Y	Y
Laboratory diagnostic tests	_	Y	Y	Y	_	Y
Diagnostic imaging	_	Y	Y	Y	Y	Y
Risk of recurrence	_	Y	_	Y	_	_
Organisation of care	_	_	_	_	_	Y
Long-term effects						
Potential complications	Y	Y	Y	Y	Y	Y
Treatment of complications	Y	_	Y	Y	Y	Y
Psychological support	_	_	Y	_	_	Y
Recurrence prevention						
Physical activity	Y	Y	Y	Y	_	Y
Nutrition	_	_	_	_	_	Y
Weight management	Y	Y	_	Y	_	Y
Alcohol consumption	Y	_	_	Y	_	Y
Smoking cessation	_	_	_	Y	_	Y

CA, Canada Alberta; EU, Europe; GE, Germany; IT, Italy; NL, The Netherlands; US, United States.

Table 3 Evidence-based recommendations on frequency of diagnostic tests after curative breast cancer treatment

Country of guideline	Recommendation	Level of evidence
History and physical examination		
IT	Every 3–6 months in the first 3 years after primary treatment, then every 6–12 months for the next 2 years, then annually	1
NL	After 5 years*: annually	1
US	Every 3–6 months in the first 3 years after primary treatment, then every 6–12 months for the next 2 years, then annually	3
Mammography		
EU	Annually ipsilateral (after breast conserving therapy) and/or a contralateral with ultrasound	3
IT	One year after the diagnostic mammography or at least 6 months after the end of radiotherapy, then annually	3
NL	After 5 years*: every 2 years	1
US	Annually on the intact breast for women who have received a unilateral mastectomy and annually of both breasts for women with lumpectomies	3

Level of evidence 1=meta-analysis or systematic review, level of evidence 3=non-randomised controlled trial study.
*Five years after primary treatment, the PCP is in charge of the care for cancer survivors.
EU, Europe; IT, Italy; NL, The Netherlands; US, United States.

on two domains and moderate on the rigour of development domain. In particular, the quality of the rigour of the development of these guidelines needed improvement. Two guidelines (EU and IT) were not recommended for use due to the low methodological quality.

Mean overall scores ranged between 2.5 and 6, with the highest score for the US guideline. Domain scores varied per domain. The only domain on which all guidelines scored 'acceptable' was the clarity of presentation domain (mean 71.3%, range: 63.9%–80.6%). Four guidelines scored 'acceptable' on the scope and purpose domain (mean 67.1%, range: 25.0%–91.7%). More variable scores were seen on the domains 'rigour of development' (mean 51.9%, range: 35.4%–66.7%), 'editorial independence' (mean 18.6%, range 12.5%–70.8%) and 'stakeholder involvement' (mean 50.0%, range: 13.9%–86.1%). The only domain that scored overall 'moderate' was the applicability domain (mean 40.3%, range: 18.8%–50.0%).

Level of evidence

Guidelines used different systems to grade the evidence. To enable comparisons of the level of evidence of selected recommendations, we created a uniform grading system of research studies: (1) Meta-analysis or systematic review, (2) randomised controlled trial (RCT) study, (3) non-RCT study. Online supplement 4 provides a table showing the reclassification of gradations used in the guidelines.

Clinical recommendations

Within the three categories (recurrence detection, long-term effects and recurrence prevention), 15 clinical topics were identified (table 2). None of the guidelines contained recommendations on all topics. Most recommendations were available on recurrence detection and most of these concerned diagnostic testing. Mammography was recommended in the follow-up of patients with breast cancer in five guidelines and physical examination in three. Other imaging or laboratory testing was not recommended in routine recurrence detection, except for ultrasound, which was recommended in one guideline in combination with mammography. Three guidelines recommended genetic counselling for risk evaluation and one advised to educate patients about signs of recurrence.

Five guidelines contained recommendations on long-term effects of breast cancer. Long-term effects are defined as 'problems that are caused by breast cancer or the treatment of breast cancer that may continue for months or years'.[31] Potential complications of breast cancer and/or breast cancer treatment were listed in the guidelines. For some of these complications, treatment options were given. Recommendations on psychological support were given in two guidelines; it was highlighted that psycho-oncological care is part of the overall concept of the care for breast cancer survivors and that psychosocial care should be offered if needed.

Five guidelines included recommendations on recurrence prevention and all recommended an active lifestyle for breast cancer survivors. Counselling to achieve or maintain a healthy body weight was recommended in four guidelines. The other recommendations on recurrence prevention included a healthy diet, limited alcohol consumption and smoking cessation.

Recommendations on frequency of diagnostic testing

Three guidelines provided recommendations on frequency of history taking and physical examination (table 3). All stated that history taking and physical examination are important to detect recurrence. The recommended frequency was the same in two

Table 4 Potential complications of breast cancer (treatment)

Potential complication	Associated treatment	Country of guideline	Level of evidence
Symptoms/complaints musculoskeletal system			
Osteoporosis	H	EU	1
Immobilised shoulder	NS	GE	1
Sexual problems			
Painful intercourse, loss of sensation, intimacy concerns, decreased libido	NS	CA	3
	NS	NL	3
Vaginal dryness	H	CA	3
	H	US	2
Dyspareunia, other symptoms of vulvovaginal atrophy	H	CA	3
	NS	NL	3
General/unspecified complaints			
Pain	G, H, R, S	US	1
Fatigue	NS	GE	1
	C, G	NL	1
	C, R	US	1
Shortness of breath	R	US	1
Menopausal problems			
(premature) symptoms of menopause	NS	CA	3
	NS	US	2
Neurological complaints			
Peripheral neuropathy	C	CA	3
	C, S	US	2
Psychological problems			
Cognitive impairment	C	US	2
Distress, depression and anxiety	G	US	1
Other problems			
Lymphedema	AL	GE	2
	AL, R	NL	1
Cardiac problems	H	IT	2

Level of evidence 1=meta-analysis or systematic review, level of evidence; 2=at least one randomised controlled trial (RCT) study, level of evidence; 3=non-RCT study.
AL, axillary lymphadenectomy; C, chemotherapy; CA, Canada Alberta; EU, Europe; G, general; GE, Germany; H, hormone therapy; IT, Italy; NL, The Netherlands; NS, not specified; R, radiotherapy, S, surgery; US, United States.

guidelines despite that the level of evidence differed. The third guideline, specifically targeting general practitioners, included recommendations on history taking and physical examination 5 years after primary treatment, when the PCP is in charge of follow-up.

Four guidelines included recommendations on the frequency of mammography. Three recommended annual mammography and one recommended a mammogram every 2 years after 5 years. Specifications for mammography differed among the guidelines. One guideline recommended to perform mammography with ultrasound, two indicated at which side the mammography should take place and one included a time frame after which the first mammography after initial treatment should take place.

Potential complications of breast cancer and breast cancer treatment

All guidelines listed potential complications of breast cancer and breast cancer treatment but differed in the number and nature of these complications (table 4). The EU guideline mentioned one potential complication, whereas the US guideline reported eight potential complications. The guidelines reported a total number of 14 different potential complications, of which seven (intimacy concerns, vaginal dryness, dyspareunia fatigue,

menopausal symptoms, peripheral neuropathy and lymphedema) were reported by two guidelines. All guidelines attributed (some of) the potential complications to cancer treatment. Five potential complications were associated with hormone therapy, four were linked to chemotherapy and three to radiotherapy.

DISCUSSION

Access to the best available evidence is crucial for providing optimal patient care. EB clinical guidelines summarise the available evidence and contain scientifically valid recommendations. This guideline inventory study is the first to evaluate whether recommendations on care for breast cancer survivors relevant for PCPs are available in EB breast cancer guidelines, representing the current status of EB recommendations on care for breast cancer survivors. We identified six EB guidelines, of which only two had acceptable methodological quality, including a limited number of EB recommendations. Two guidelines were specific on care for breast cancer survivors and only one guideline specifically targeted PCPs. Moreover, recommendations differed between guidelines and most were based on low-quality evidence.

Strengths and limitations

A strength of this study is the international input of 36 countries, including 32 European countries and Canada, USA, Australia and New Zealand. This enabled us to create a fairly complete overview of EB recommendations from EB guidelines for PCPs on care for breast cancer survivors. A limitation of our study is the absence of validation of translations by non-native speakers. Details may be misinterpreted, but we do not expect that the key recommendations of the guidelines differed. Another limitation is that only one researcher screened the literature, the guideline databases and cancer agency websites to identify additional guidelines. However, in case of any doubt, the inclusion was discussed with a second researcher. Finally, we have not examined the views of PCPs on the guidelines and their use of the guidelines in clinical practice nor the views of breast cancer patients on the care of PCPs.

Comparison with existing literature

Only one guideline specifically mentioned PCPs as target audience despite increasing demands for greater involvement of PCPs in care for breast cancer survivors.[4–6] The fact that recommendations are often not targeted at PCPs was also highlighted in a recent publication that stated that the role of the PCP in care for cancer survivors is currently not well defined. However, PCPs can have an important role in the care for cancer survivors as they know details of patient's history and social context, comorbidity and are alert on considering individual views and preferences.[32]

The guidelines included recommendations on different categories and clinical topics. The categories identified were consistent with the domains described by the Institute of Medicine report: 'From Cancer Patient to Cancer Survivor: Lost in Transition'.[3] In addition, we defined 15 topics. None of the guidelines discussed all these topics. A possible explanation for this is lack of evidence on specific topics[33] or the focus on follow-up care and recurrence detection rather than on the whole care process for breast cancer survivors.

The content analyses on the available topics revealed consensus on seven topics, such as the frequency of tests to detect breast cancer recurrence. On four topics, recommendations differed between the guidelines. In particular, listed potential complications differed considerably. Univocal guidance would help PCPs to raise awareness on the potential consequences of both cancer and its treatment.[34]

Guidelines were only included if they were published after 2011. This selection criterion was applied as it is has been demonstrated that guidelines may be outdated after a few years[14] and that the turnover rate of research evidence is high in the field of cancer.[32] Ten guidelines were excluded due to lack of transparency on the supporting evidence. A previous study[35] showed that the quality of oncology guidelines was higher than non-oncology guidelines. Our study revealed that there is still room for improvement concerning oncology guidelines.

Implications for practice and research

The 'American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline' yielded EB recommendations on most clinical topics (on 13 out of the 15 identified topics) and mentioned the PCPs specifically as target group of the guideline. Furthermore, this guideline scored highest on the AGREE II evaluation and was recommended for use in clinical practice by both researchers that appraised the guidelines. Currently, this guideline seems to be the most useful guideline for PCPs. However, this guideline does not include EB recommendations on all clinical topics and many recommendations are based on low-quality evidence.

Therefore, more high-quality evidence is needed to develop and adapt breast cancer guidelines to support PCPs in providing optimal breast cancer survivorship care. Guidelines should not be solely designed for PCPs as it is important to provide integrated care to breast cancer survivors. PCPs being part of integrated care indicated that they need more guidance in order to provide good quality care to cancer survivors. Therefore, it is important to involve PCPs in the development and adaptation of the guidelines and to specifically consider PCPs as target group of the guideline in order to provide optimal breast cancer survivorship care. If PCPs are supported by high-quality EB guidelines, transfer of care for breast cancer survivors from secondary to primary care could be better facilitated.

In addition to the availability of high-quality EB guidelines, it is important to consider the views of PCPs and patients with breast cancer on optimal care in developing

guidelines. Exploring views of PCPs and patients on the usefulness of guidelines and the preferred setting of care for breast cancer survivors is an area for future research .

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Contributors IS, JCK, FGS, TA and JSB conceptualised the study and defined the content analysis strategy. IS collected and reviewed the guidelines and extracted the data. IS and JCK categorised the recommendations and allocated recommendations into clinical topics. IS, JCK, FGS and JSB provided preliminary interpretation of findings. IS, JCK, FGS, TA and JSB contributed in drafting the manuscript, critically helped in the interpretation of the results and provided relevant intellectual input.

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