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Review Paper

Long-term quality of life among breast cancer survivors eligible for screening at diagnosis: a systematic review and meta-analysis

N. Moshina [a, *], R.S. Falk [b], S. Hofvind [a, c]

[a] Cancer Registry of Norway, Section of Cancer Screening, P.O. 5313, Majorstuen, Oslo, 0304, Norway
[b] Oslo University Hospital, Oslo Centre for Biostatistics and Epidemiology, P.O. 4950, Nydalen, Oslo, 0424, Norway
[c] Department of Health and Care Sciences, UiT The Artic University of Norway, P.O. 6050, Tromsø, 9037, Norway

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ABSTRACT

Objectives: This study aimed to explore the long-term quality of life (QoL) among breast cancer survivors eligible for mammographic screening at diagnosis and compare that to QoL among women with no history of breast cancer.
Study design: Systematic review and meta-analysis.
Methods: A systematic review of randomised controlled trials and observational studies published between January 2000 and July 2019 was performed. Eight studies were included in the review. Six studies with QoL measurement scales (0–100) were included in the meta-analysis. We used fixed and random effects models to obtain Cohen's d with 95% confidence interval (CI). Heterogeneity among studies was evaluated by the I^2 statistics.
Results: Information about 6145 breast cancer survivors diagnosed between 1995 and 2012 and followed for >1–10 years was analysed. Four studies used SF-36/RAND-36, three studies used EORTC QLQ-C30, one study used FACT-G and one study used FACT-B. The mean score of QoL for breast cancer survivors varied from 63.0 (RAND SF-36, 0–100) to 110.5 (FACT-B, 0–123). Two studies showed better, three studies showed similar and two studies showed poorer mean scores for breast cancer survivors compared with women with no history of breast cancer. The meta-analysis showed no significant differences in QoL for breast cancer survivors compared with women with no history of breast cancer (Cohen's d = −0.07, 95% confidence interval [CI] −0.14 to 0.00 and I^2 = 83.7% for the fixed effect model; Cohen's d = −0.00, 95% CI −0.18 to 0.17 and I^2 = 82.4% for the random effects model).
Conclusion: QoL did not differ between breast cancer survivors eligible for mammographic screening at diagnosis and followed for >1–10 years and women with no history of breast cancer.

Introduction

Breast cancer is the most common cancer and cause of cancer death among women worldwide.[1] Organised mammographic screening aims to reduce breast cancer mortality by detecting tumours at an early stage and decreasing the side-effects of treatment.[2] Screening and improved treatment have been considered the main reasons for the increase in survival from breast cancer during the last decades.[3,4] However, long-term side-effects of the treatment represent a major harm.[5–13] Moreover, the detection of dormant and small, low proliferation tumours by screening brings another challenge to this secondary prevention because of the potential for overtreatment and accompanying long-term side-effects.[14,15]

Long-term quality of life (QoL) among breast cancer survivors has been evaluated in numerous studies,[10,16–20] whereas the results from studies on women diagnosed with ductal carcinoma in situ or early-stage invasive breast cancer are limited.[18,21,22] However, as far as we are aware, no studies based on individual data investigated long-term QoL among women with screen-detected breast cancer and women with no history of breast cancer.[23,24] Therefore, the objectives of this review were to explore long-term QoL among breast cancer survivors eligible for mammographic screening at diagnosis between 1995 and 2018 and to compare the long-term QoL between these women and women with no history of breast

* Corresponding author. Cancer Registry of Norway, P.O. 5313, Majorstuen, Oslo, 0304, Norway. Tel.: +47 23 33 39 89.
E-mail addresses: Nataliia.Moshina@kreftregisteret.no (N. Moshina), rs@ous-hf.no (R.S. Falk), Solveig.Hofvind@kreftregisteret.no (S. Hofvind).

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cancer eligible for mammographic screening. Similar long-term QoL for women with screen-detected breast cancer and women with no history of breast cancer might imply that organised breast cancer screening and modern treatment positively affected the management and consequences of the disease.

Materials and methods

We carried out a systematic review of peer-reviewed papers published between January 2000 and July 2019. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline's checklist was used to ensure that relevant considerations were taken in all parts of the study.[25]

The long-term QoL was defined as perceived physical and mental health for >1–10 years since breast cancer diagnosis for breast cancer survivors or over a corresponding follow-up period for women with no history of breast cancer. A period of more than 1 year was chosen as a cutpoint for a long term, as we intended to include women with an early-stage breast cancer, which treatment, except the long-lasting hormonal therapy, might last less than 6 months and the effects of the treatment might be considered long-term effects for 14–18 months since diagnosis.[26,27,28] QoL represented scores for general or global health scores[29] obtained by various patient-reported outcome instruments (EORTC-QLQ-C30 [European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire], SF-36 [Short-Form Health Survey], FACT [Functional Assessment of Cancer Treatment Questionnaire], VAS [Visual Analogue Scale] and EQ-5D [EuroQual Questionnaire Five Dimensions]). Women residing in the countries where mammographic screening had been available since 1995 and the treatment of the disease had improved regardless of stage at diagnosis were considered eligible for screening.[30,31] Women's age was not restricted, but women aged 45–75 years were included in the analyses from the studies that performed stratification by age, as women of this age range are recommended mammographic screening.[32] Furthermore, we restricted the search to early-stage breast cancer and the length of follow-up from >1 to 10 years since diagnosis or corresponding time frame for women with no history of breast cancer. Early-stage breast cancer included ductal carcinoma in situ, small invasive tumours (<20 mm) and/or early-stage invasive breast cancer (stages I and II).

Literature search

We conducted a search in MEDLINE, Embase, Google Scholar and Cochrane from 1 to 25 July 2019. We used the 'PICOS' (Population, Intervention, Comparison, Outcome and Study design) framework to identify the main terms for the literature search.[33] The review aimed to explore the long-term QoL (O) among women with breast cancer (P) who were eligible for mammographic screening (I). Women eligible for screening with no history of breast cancer was an optional criterion for comparison (C). Each search included a combination of the following terms: quality of life, treatment, treated, breast cancer, breast neoplasm, breast carcinoma, screening, screen-detected, mass screening and early detection. The combination of terms used is shown in Appendix A.

The study design included randomised controlled trials and observational studies. Systematic reviews and meta-analyses were used for literature check. Abstracts or poster presentations were not included. All titles of the identified papers were reviewed independently by N.M. and S.H. and discussed when the opinions were discordant (Fig. 1). The same authors read the abstracts of the papers with relevant titles and agreed on the papers that fulfilled the 10 criteria for inclusion in the review (Fig. 1). An additional optional criterion was inclusion of women diagnosed at the recommended screening age (45–75 years) if the differentiation of the results by age groups was performed.[34] After reading the full text of the remaining papers, eight papers were included in the study.[21,35–41]

Literature analysis

For all included studies, data on aims, country and design, age and number of women studied and included in the review, data source, data collection method, month and year of breast cancer diagnosis, study period and coverage of organised breast cancer screening were extracted, tabulated and analysed (Table 1). Furthermore, data on breast cancer types/stages, long-term definition, comparison groups, methods to evaluate QoL and main findings were analysed (Table 2). Types and risk of biases in the studies were described in Appendix B, Table B1. The main results were defined as scores for QoL, including general or global health, and functioning scales. The scores were presented as means with standard deviation (SD), 95% confidence interval (CI), or standard error (SE), based on the available data. The higher scores for QoL and all functioning scales corresponded to better QoL, whereas the higher scores for bodily pain corresponded to worse QoL. The mean scores for QoL were used to compare breast cancer survivors and the reference groups. The reference groups were defined as healthy women with no history of breast cancer, eligible for mammographic screening.[21,35–40] The *P* values for comparison in the included studies were two sided and were obtained using *t*-tests and unadjusted or age-adjusted analysis of variance.[21,35–40] For the purpose of this review, all breast cancer survivors from the included studies were assumed to have screen-detected breast cancer, and women with no history of breast cancer were assumed either screening attendees or those who had attended screening and never been diagnosed with the disease.

We performed a meta-analysis for QoL assessed on scales 0–100 (EORTC-QLQ-C30 and SF-36) using fixed and random effects models. Two studies were excluded from meta-analysis; one study used FACT-G with a scale of 0–108, and the other one did not have any comparison group.[37–41] For each study included in the meta-analysis, Cohen's d effect size with 95% CI and weights (percentage) was calculated as the mean difference between QoL scores for breast cancer survivors compared with the reference groups divided by the pooled SD; negative effect sizes reflected deficits compared with the reference groups.[42] The results from the study by Klein et al. were used for the longest follow-up (10 years) performed with EORTC-QLQ-C30, as SF-36 was not considered breast cancer specific.[39] Solely crude scores for QoL were included in the meta-analysis from Klein et al. Information on SD for the mean score from the studies by van Gestel et al. and Koch et al. was imputed using predictive mean matching for a continuous variable.[36,40] Statistical heterogeneity among studies was assessed through the I^2 statistics, where a value of $\geq$75% was interpreted as high heterogeneity.[43] The funnel plot was used to estimate small-study effects. A *P* value of <0.05 was considered statistically significant. All statistical analyses were performed using STATA/MP 16.0 (College Station, TX). The quality of the included studies was assessed according to the Cochrane guidelines and the CONSORT-PRO criteria, and the main limitations were presented.[44,45]

Results

A total of 1558 papers were identified, whereas 1459 were excluded due to irrelevant titles (Fig. 1). Of the 25 papers eligible for full-text review, 17 were excluded, leaving eight papers representing eight studies for the review and six for the meta-analysis.

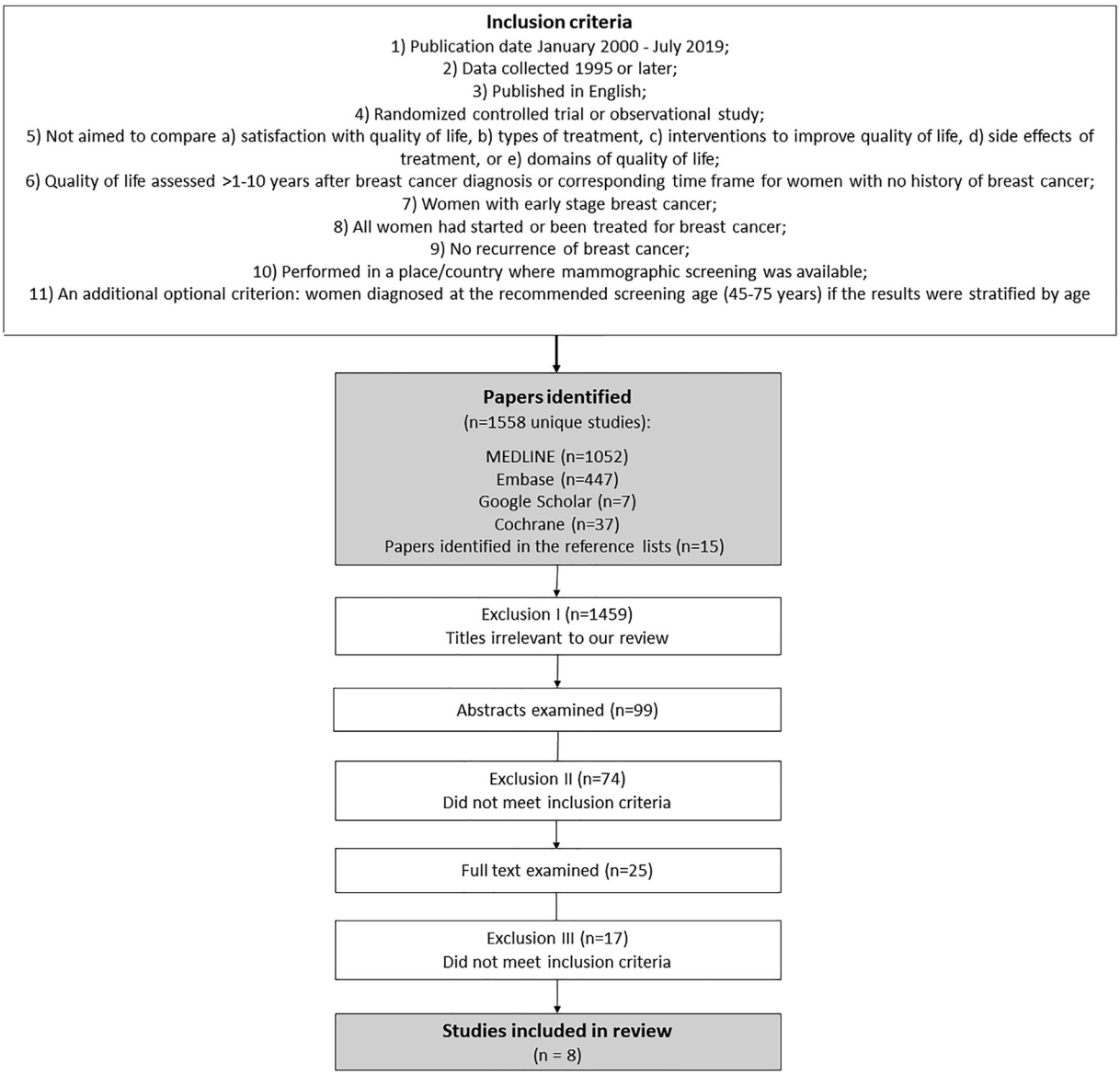

Fig. 1. Selection process with inclusion criteria.

The reasons for the exclusion of the papers read in full are described in Appendix C, Table C1.

Characteristics of the studies

The eight studies included information about 6145 breast cancer survivors aged 21–80 years, diagnosed 1995–2012, and data collected during the period from 1996 to 2014[21,35–41] (Tables 1 and 2). The screening coverage in the countries where the included studies were performed varied from 40.0% to 91.5%.[46,47] Two studies aimed to explore QoL among women with early-stage breast cancer,[21,36] and the other included data from women with various stages of breast cancer at diagnosis.[35,37–41] Five studies originated from Europe,[35,36,38–40] one from Australia,[37] and two from North America.[21,41] Four studies used SF-36/RAND (Research and Development Corporation)-36,[21,36,38,39] three EORTC studies used QLQ-C30,[35,39,40] one study used FACT-G[37] and one study used FACT-B.[41] The studies reported QoL >1–10 years after diagnosis or surgical treatment[21,35–41] (Table 2). The reference groups included predominantly women aged ≥18 years with no history of breast cancer.[21,35–41] One study did not use a reference group but compared the results on QoL scores for early-stage breast cancer, locally advanced and metastatic breast cancer patients using FACT-B[41] (Table 3).

QoL components

In six studies, women followed >1–10 years postdiagnosis or since surgical treatment had lower mean scores for physical, cognitive, social and emotional functioning or well-being and higher mean scores for bodily pain compared with the reference groups[21,35,36,38–40] (Table 2). However, in the study from Australia, women followed for 1.5 years postdiagnosis reported higher mean scores for social (23.4, 95% CI: 22.6–24.2 vs 19.8, 95% CI: 19.1–20.5) and functional well-being (22.5, 95% CI: 21.7–23.2 vs 20.2, 95% CI: 19.5–20.9; $P < 0.05$) compared with the reference group.[37] In the study from the United States, women followed for 1.5–3 years since surgical treatment

Table 1
Characteristics of the studies included in the review.

First author, publication year, ref #	Study aim	Study country and design	Women studied (age, n)	Women included in the review (age, n)	Data source	Data collection method	Diagnosis of breast cancer (month, year)	Study period (month, year)	Screening coverage (%)[b]
Schou et al., 2005[35]	To compare HRQL of women diagnosed with breast cancer with the general female population at diagnosis and 12 months since surgical treatment (≥14 months postdiagnosis)	Norway; longitudinal cohort study	Age 21–78 years (n = 161)	Age 21–78 years (n = 161)	Ullevål University Hospital	Self-reported questionnaire	2002–2003	2003–2004	91.5[47]
Van Gestel et al., 2007[36]	To compare the HRQL, perceived disease impact and risk perception of recurrence and dying of breast cancer in patients with DCIS and EIBC 2–3 years posttreatment	The Netherlands; cross-sectional study	Age 30–80 years (n = 135)	Age 50–69 years (n = 75)	Eindhoven Cancer Registry of the Comprehensive Cancer Centre South	Self-reported questionnaire	January 2002 to December 2003	May to June 2005	85.0[61]
DiSipio et al., 2008[37]	To describe the HRQL among breast cancer survivors at 6, 12 and 18 months postdiagnosis compared with the general female population in Queensland	Australia; cohort study	Age 20–74 years (n = 287)	Age 50–74 years (n = 193)	Brisbane, Queensland and Queensland Cancer Registry	Self-reported questionnaire	January to December 2002	2002–2004	58.0[46]
Klein et al., 2011[39]	To compare QoL of breast cancer survivors 5 and 10 years since diagnosis with QoL of healthy controls	France; cross-sectional study	Aged <54 and 75+ years (n = 652)	Age <54 and 75+ years diagnosed 10 years ago (n = 210)	Population-based cancer registries of Bas-Rhin (North-Eastern France), Calvados (North-Western France), and Doubs (Eastern France)	Self- reported questionnaire	1995	2005	40.0[62]
Jeffe et al., 2012[21]	To examine changes in QoL in a cohort of incident early-stage breast cancer and of women with no history of breast cancer (controls)	U.S.; longitudinal case–control study	Age 40+ years (n = 549)	Age 40+ years (n = 549)[a]	Siteman Cancer Center at Barnes-Jewish Hospital, Washington, and St Louis University School of Medicine	Computer-assisted telephone interviews	*Information not available*	October 2003 to June 2007	71.4[63]
Browall et al., 2013[38]	To compare HRQL in postmenopausal		Age 55–80 years (n = 102)	Age 55–80 years (n = 102)	Sahlgrenska University	Self- reported questionnaire	2003–2005	2003–2010	70.0[64 c]

	women with breast cancer receiving adjuvant treatment after surgery and five years posttreatment, with a general population	Sweden; longitudinal cohort study			Hospital: Department of Breast Surgery, Gothenburg; Karolinska University Hospital: Department of Oncology, Stockholm; Skövde Hospital, Dep of Surgery, Skövde				
Koch et al., 2013[40]	To explore in detail whether and to what extent restrictions in breast cancer survivors persist in the long run and whether changes or aggravations in QoL occur over time	Germany; longitudinal cohort study	Age 18–80 years or older (n = 387)	Age 50–64 years (n = 76)	Population-based study in Saarland	Self-reported questionnaire	October 1996 to February 1998	1996–2010	n/a[d]
Hamer et al., 2017[41]	To examine the symptom burden and QoL of different patient groups across the breast cancer continuum	Canada; cross-sectional study	Age <49 to ≥70 years (n = 1489)	Age 51–70 years (n = 857)	Louise Temerty Breast Centre	Self-reported questionnaire	2012 or earlier	January to August 2014	68.0[65]

HRQL, health related quality of life; QoL, quality of life.

[a] The study was included in the review as the age when women typically start screening in the United States is 40 years, and the mean age for breast cancer survivors and the reference group was 58.9 (standard deviation, SD: 10.7) years and 57.2 (SD: 10.6) years, respectively, indicating that the majority of the included women were aged >50 years at enrolment.

[b] Screening coverage is the percentage for screening attendance among eligible groups of women for the period when breast cancer was diagnosed.

[c] Data available solely for Stockholm county.

[d] Information is not available.

Table 2
Study population, methods and main findings on quality of life and its components among breast cancer survivors eligible for screening from the studies included in the review.

First author, publication year, ref #	Women included in the review (n, %)[b]	Breast cancer types/ stages included in the study	Long-term definition	Reference groups (n)	Methods to evaluate the QoL	Main findings on QoL and QoL components
Schou et al., 2005[35]	Age 21–78 years (n = 161, 100%)	Invasive BC stage I-II (n = 161)	1 year after surgical treatment	Normal population without diseases aged 18–93 years (data from 1998), using EORTC QLQ-C30 (n = 949)	EORTC QLQ-C30	BCS had a lower mean score for cognitive[a] (82.0, SD: 18.3 vs 86.6, SD: 19.2, $P = 0.008$[c]) and social functioning (80.0, SD: 23.4 vs 84.6, SD: 22.4, $P = 0.009$[c]) compared with the reference group.
Van Gestel et al., 2007[36]	Age 50–69 years (n = 75, 64%)	DCIS (n = 21) and invasive BC stage I, T1, N0 and M0[b] (n = 54)	1.5–3 years postdiagnosis	Normal population without diseases (data from SF-36, collected 1992–1996), from the National study, averages for SF-36 domains, age and gender adjusted	RAND SF-36	Women with DCIS had a higher mean score for bodily pain (85.4 vs 75.2, $P = 0.02$[f]) and general mental health (77.8 vs 70.5, $P = 0.05$[f]) compared with women with early-stage BC, and for bodily pain (85.4 vs 67.1, $P < 0.001$[f]) and the physical component scale (49.6 vs 44.9, $P < 0.05$[f]) compared with the reference group. Women with early-stage BC had a higher mean score for bodily pain (75.2 vs 67.1, $P < 0.05$[f]) compared with the reference group.
DiSipio et al., 2008[37]	Age 50–74 years (n = 193, 74%)	Unilateral invasive BC	1.5 years (18 months) postdiagnosis	Normal population without diseases, aged 30–74 years were interviewed using QoL data from 2004 (n = 675)	FACT-G	BCS had a higher mean score for social (23.4, 95% confidence interval, CI: 22.6–24.2 vs 19.8, 95% CI: 19.1–20.5)[g] and functional well-being (22.5, 95% CI: 21.7–23.2 vs 20.2, 95% CI: 19.5–20.9)[g] compared with the reference group. BCS had a clinically better mean score for QoL (91.0, 95% CI: 88.9–93.1 vs 86.0, 95% CI: 84.5–87.5)[g] compared with the reference group.
Klein et al., 2011[39]	Age <54–75+ years diagnosed 10 years ago (n = 210, 100%)	BC with no treatment during the last 5 years	10 years postdiagnosis	Normal population matched by age and place of residency to patients using QoL data from 2005 (n = 1188)	EORTC QLQ-C30	BCS had a lower mean score for physical (81.6 vs 84.6), role (80.3 vs 84.5) and social (85.8 vs 88.6) functioning compared with the reference group ($P < 0.0001$ for all)[d].
Jeffe et al., 2012[21]	Age ≥40 years (n = 549, 100%)[f]	DCIS (n = 148) and a first primary stage 0-IIA breast cancer without neoadjuvant chemotherapy (n = 365)	2 years following definitive surgical treatment	Normal population frequency-matched by age (40–49, 50–69, ≥70 years) to patients were interviewed 2 years and 2 weeks after normal/benign screening (n = 547)	RAND 36-Item Health Survey 1.0	Women with early-stage BC had a lower mean score for physical functioning (76.3, SD: 25.3 vs 83.8, SD: 20.2) and role limitations due to physical functioning (70.3, SD: 41.8 vs 78.2, SD: 36.0), and a higher mean score for emotional well-being (82.2, SD: 16.8 vs 79.0, SD: 16.9) compared

Table 2 (*continued*)

First author, publication year, ref #	Women included in the review (n, %)[b]	Breast cancer types/ stages included in the study	Long-term definition	Reference groups (n)	Methods to evaluate the QoL	Main findings on QoL and QoL components
						with the reference group ($P < 0.05$[h] for all).
Browall et al., 2013[38]	Age 55–80 years (n = 102, 100%)	Invasive breast cancer stage I-III (n = 102)	5 years postdiagnosis	Normal population matched by age (55–80 years) to patients using QoL data from 2003 to 2010 (n = 426)	SF-36	BCS had a higher mean score in physical functioning (78.7, SD:20.5 vs 67.8, SD:27.0), physical role functioning (77.9, SD: 33.9 vs 61.2, SD: 43.0), bodily pain (77.3, SD: 23.8 vs 64.8, SD:29.5), vitality (70.5, SD: 20.9 vs 62.8, SD: 25.0), social functioning (88.8, SD:20.9 vs 82.7, SD:24.8) and mental health (82.7, SD:18.7 vs 76.6, SD: 22.5) compared with the reference group ($P < 0.05$[h] for all)
Koch et al., 2013[40]	Age 50–64 years (n = 76, 42%)	Stage at diagnosis local, regional and distant BC	10 years postdiagnosis	Normal population aged 18 to 65+ years selected by random-route-technique, interviewed 1998, using EORTC QLQ-C30 (n = 968)	EORTC QLQ-C30	BCS had a lower mean score for physical (84.5, standard error, SE: 2.0 vs 89.4, SE: 0.9), role (74.0, SE: 3.8 vs 87.9, SE: 1.3), emotional (60.2, SE: 3.3 vs 77.4, SE: 1.3), cognitive (72.8, SE: 3.6 vs 91.1, SE: 1.2) and social functioning (79.9, SE: 3.3 vs 91.1, SE: 1.2) compared with the reference group ($P < 0.05$[i] for all).
Hamer et al., 2017[41]	Age 51–70 years (n = 857, 58%)	DCIS (n = 83), invasive BC T1-T2 (n = 464), T2N3 or T3[e] (n = 214) and metastatic BC (n = 98)	1–10 years postdiagnosis	Comparison between the BC groups (stages)	FACT-B	No significant differences in the overall mean QoL score were found for women with different breast cancer stages. The overall mean QoL score reduced by stage for those aged 51–70 years (120.0, SD: 18.6 for DCIS, 117.4, SD: 20.3 for early-stage invasive BC 112.6, SD: 20.8 for locally advanced and 101.4, SD: 23.7 for metastatic BC).

SF, short form; QoL, quality of life; BC, breast cancer; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer quality of life questionnaire-core 30-item; DCIS, ductal carcinoma in situ; EIBC, early-stage invasive breast cancer; FACT-G, functional Assessment of cancer therapy–general; FACT-B, functional assessment of cancer therapy–breast; BCS, breast cancer survivors.

[a] The higher scores for QoL and all functioning scales except bodily pain corresponded to better QoL, whereas the higher scores for bodily pain corresponded to worse QoL.

[b] Number and percentage of the entire sample of breast cancer survivors for each study.

[c] Based on *t*-tests.

[d] Adjusted for registry area, age, place of residence (urban/rural), marital status, education level, employment status, mean household monthly income, comorbidities and hospitalisation during the last 12 months (analysis of variance).

[e] Based on TNM Classification of Malignant Tumours (Union for International Cancer Control. J Brierley, M Gospodarowicz and C Wittekind. Wiley Blackwell, 2017).

[f] Based on *t*-tests; standard deviation values were not available.

[g] *P*-values were not available; data were presented with 95% confidence intervals.

[h] Based on unadjusted analysis of variance.

[i] Based on age-adjusted analysis of variance.

reported better emotional well-being (82.2, SD: 16.8 vs 79.0, SD: 16.9; $P < 0.05$) compared with the reference group.[21] In the study from Sweden, women followed for 5 years post-diagnosis had higher mean scores for physical functioning (78.7, SD: 20.5 vs 67.8, SD: 27.0), social functioning (88.8, SD: 20.9 vs 82.7, SD: 24.8) and mental health (82.7, SD: 18.7 vs 76.6, SD: 22.5) compared with the reference group ($P < 0.05$ for all).[38]

Table 3
Mean values of quality of life among breast cancer survivors eligible for screening, in a long term, assessed using visual analogue scale (0–100), FACT-B and FACT-G, compared with the reference groups of women.

First author, publication year, ref #	Years since diagnosis to assessment	Measurement instrument	Age of breast cancer survivors	Mean quality of life of breast cancer survivors	Age of reference group	Type of the reference group	Mean quality of life of reference group	*P*-value for comparison between breast cancer survivors and reference group
Schou et al., 2005[35]	>1 year[a]	EORTC QLQ-C30 (0–100)	21–78 years	75.7[b] (standard deviation, SD: 21.4) (n = 161)	18–93 years	Healthy women	72.0 (SD: 24.5) (n = 949)	0.28[m]
Van Gestel et al., 2007[36]	1.5–3 years	RAND SF-36 (0–100)	50–69 years	63.0[c] (n = 75)	50–69 years	Healthy women	63.0 (not available)	–
DiSipio et al., 2008[37]	1.5 years	FACT-G (0–108)	50–74 years	91.0 (95% confidence interval, CI: 88.9–93.1) [h] (n = 193)	30–74 years	Healthy women	86.0 (95% CI: 84.5–88.4)[h] (n = 675)	Significant clinical difference[i]
Klein et al., 2011[39]	10 years	EORTC QLQ-C30 (0–100)	<54–75+ years	66.3[g] (n = 210)	<54–75+ years	Healthy women	69.2 (n = 1188)	0.0035[k]
Jeffe et al., 2012[21]	2 years[i]	RAND 36-Item Health Survey 1.0 (0–100)	≥40 years	68.0[c] (SD: 22.6) (n = 549)	≥40 years	Healthy women	73.4 (SD: 21.1) (n = 547)	0.0017[k]
Browall et al., 2013[38]	5 years	SF-36 (0–100)	55–80 years	70.5[f] (SD:20.9) (n = 102)	55–80 years	Healthy women	62.7 (SD: 25.0) (n = 426–475)	<0.001[k]
Koch et al., 2013[40]	10 years	EORTC QLQ-C30 (0–100)	50–64 years	68.0[e] (standard error, SE: 2.6) (n = 76)	50–64 years	Healthy women	68.1 (SE: 2.1) (n = 968)	0.86[l]
Hamer et al., 2017[41]	1–10 years	FACT-B (0–123)	51–70 years	110.5[d] (SD: 21.6) (n = 857)	–	–	–	–

[a] Time since surgical treatment was at least 12 months.
[b] Women with early stage (I-II) breast cancer.
[c] Women with early-stage invasive breast cancer.
[d] Mean quality of life score for women with all types of breast cancer excluding ductal carcinoma in situ.
[e] Women with all types of breast cancer including ductal carcinoma in situ.
[f] Women with stage I-III breast cancer.
[g] Adjusted for registry area, age, place of residence (urban/rural), marital status, education level, employment status, mean household monthly income, comorbidities and hospitalisation during the last 12 months (analysis of variance).
[h] Mean health-related quality of life score for women with invasive breast cancer.
[i] Time since surgical treatment.
[j] Based on 95% confidence intervals.
[k] Based on unadjusted analysis of variance.
[l] Based on age-adjusted analysis of variance.
[m] Based on linear regression analysis.

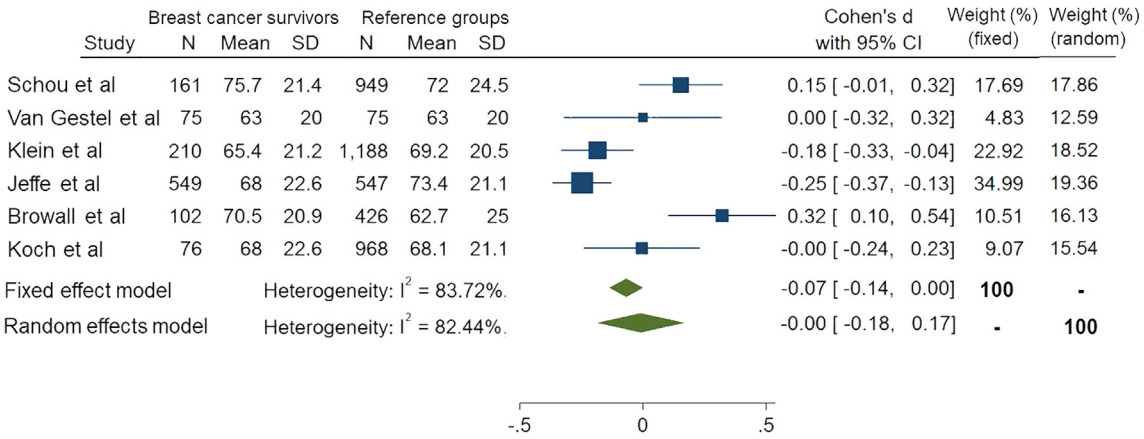

Fig. 2. Meta-analysis of six studies comparing self-reported quality of life among breast cancer survivors eligible for screening in a long term, assessed using a scale 0–100, compared with the reference groups of women. N, number; SD, standard deviation.

Quality of life

A mean score for QoL among breast cancer survivors followed for >1–10 years postdiagnosis or since surgical treatment varied from 63.0 (on a scale of 0–100) to 110.5 (on a scale of 0–123)[37,38] (Table 3). Seven studies compared QoL among breast cancer survivors and the reference groups.[21,35–40] In three studies, the mean score for QoL did not differ between breast cancer survivors followed for >1–10 years postdiagnosis and the reference groups.[35,36,40] In two studies, breast cancer survivors reported a higher mean score for QoL compared with the reference groups (91.0, 95% CI: 88.9–93.1 vs 86.0, 95% CI 84.5–87.5 on a scale of 0–108; and 70.5, SD: 20.9 vs 62.7, SD: 25.0 on a scale of 0–100, $P < 0.05$, respectively).[37,38] In two studies, breast cancer survivors reported a lower mean score for QoL compared with the reference groups (68.0, SD: 22.6 vs 73.4, SD: 21.1 on a scale of 0–100; $P < 0.05$; and 66.3 vs 69.2 on a scale of 0–100, $P < 0.05$, respectively).[21,40] In the study from Canada, the mean score for QoL for women aged 50–71 years with all types of invasive breast cancer was 110.5, SD: 21.6, on a scale of 0–123.[41]

Pooled effect measured from six studies presented by a Cohen's d was −0.07 (95% CI −0.14 to 0.00) with $I^2 = 82.4\%$, and −0.00 (95% CI −0.18 to 0.17) with $I^2 = 83.7\%$ for the fixed effect and random effects models, respectively (Fig. 2). The funnel plot did not show any small-study effect, as no differences between the comparison groups were found in the small studies (Appendix D, Fig. D1).

Discussion

Our review identified a mean score for long-term QoL among breast cancer survivors eligible for mammographic screening and followed for >1–10 years since diagnosis to vary from 63.0 (on a scale of 0–100) to 110.5 (on a scale of 0–123).[37,38] The studies showed better,[37,38] similar,[35,36,40] or poorer[21,39] QoL among breast cancer survivors compared with women with no history of breast cancer (the reference group). The effect size model based on six studies using a scale from 0 to 100 to measure the mean QoL did not show any statistically significant differences between breast cancer survivors and women with no history of breast cancer, eligible for mammographic screening.

The better results for breast cancer survivors could be explained by the study settings, implying that most of the women had early-stage breast cancer diagnosed in screening programmes.[37,38] Furthermore, women attending screening might be healthier and have a higher breast awareness than non-attendees.[48–51] On the other side, women usually consider screening as a check and might thus not be prepared for a diagnosis of breast cancer in contrast to women seeking mammography due to symptoms. However, the better results might also have been associated with a relatively short follow-up (1.5–5 years since diagnosis).[37,38] Furthermore, no matching by age with the reference group and the possibility of various chronic diseases in the reference group might have resulted in higher scores for QoL and the functioning components for the breast cancer survivors compared with the reference group in one of the studies.[37,52]

Similar results for breast cancer survivors and women with no history of breast cancer were found in three studies.[35,36,40] In one of these studies, the length of the follow-up might have been too short to show any differences (≥14 months since diagnosis).[35] In the other study, the data from the reference group were obtained for a long time before the study start, which might have limited health perceptions, as different health awareness, treatments and methods of care were present in that period compared with the study period.[36] Furthermore, a small number of women (n = 75) in each group and the length of follow-up of 1.5–3 years might have contributed to the lack of differences. In the other study, the differences in the disease-specific symptom burden implied a less favourable pattern for breast cancer survivors compared with the reference group.[40] However, a small number of women (n = 76) with breast cancer vs a large number of women in the reference group (n = 968), and using a 10-year follow-up with a study period 1996–1998, when the treatment recommendations differed from those used in 2000s, might have led to the lack of differences in QoL scores between the groups.[40,41] The similar results on QoL, but clinically relevant deterioration in symptoms and several QoL components, could be explained by the response shift or the adaptive mechanisms influencing the overall QoL perception, but not functioning or symptom burden.[40,53]

The poorer QoL among breast cancer survivors compared with that of women with no history of breast cancer was expected.[21,39] However, such results were shown in the study from the United States, including women aged ≥40 years, where younger women were known to have more advanced breast cancer compared with older women.[21] The main reasons for this are more aggressive treatment associated with high proliferative aggressive tumours and a stronger impact of treatment on the everyday life of women aged <50 years.[54,55] On the other side, screening of women in their 40s is more common in the United States compared with Europe and might mirror the insurance coverage.[56] The poorer results of the QoL of breast cancer survivors eligible for screening compared with the reference group in a large population-based study with a

10-year follow-up might be considered the most relevant result of this review,[39] assuming that the majority of women in the study population were in the age group 54–75 years. However, the study started in 1995 and was associated with more aggressive treatment for women with early-stage breast cancer and might have impacted the lower scores of QoL among breast cancer survivors compared with women with no history of breast cancer.[26,30]

Various study settings and periods, numbers of women and lengths of follow-up might have contributed to the results of the meta-analysis, showing no difference between breast cancer survivors and women with no history of breast cancer, eligible for screening.[21,35,36,38–40]

Limitations of the studies included in the review

The quality of the reporting in the included studies was rather low with regard to the CONSORT-PRO criteria, as the main limitations included non-reporting the baseline outcomes and underreporting the characteristics of comparison groups[21,36–41] (Appendix B). Bias due to confounding was observed in three studies and was associated with different types of treatment and therefore QoL perceptions among women with early-stage breast cancer, and not adjusting for possible comorbidities not pertaining to breast cancer.[36,38,41] Selection bias was found in all included studies and was associated with small sample sizes and differences in the age ranges between the reference groups and breast cancer survivors, different social and race status of participants and non-participants, and including solely women who participated in all follow-ups.[21,35–41] Bias due to missing data was presented in four studies and indicated low response and lack of information about loss due to follow-up, underreporting of the poorest cases, and association of the data collection methods with the respondents who could be reached by telephone and whose participation might be associated with insurance coverage.[21,35–41] Bias in measurement outcome was observed in all included studies and was associated with the lack of baseline information, using only one time point to measure the outcome, and limitations of the self-reported questionnaire and computer-assisted telephone interviews.[21,35–38,40,41] Bias in the selection of the reported results was found in three studies and included the older data collection period for the reference (1992–1996) vs the study sample (2002–2003), use of clinical but not statistical significance and comparing the findings for women diagnosed at different points of time between 1996 and 2010.[36,37,40] According to the assessment of the risk of bias, the studies by Schou et al. and by Klein et al. could be considered the most reliable, as these did not show any serious risk of bias.[35,39]

Limitations of the review and meta-analysis

Women eligible for screening were aged 21–80 years in our review and solely four studies included women of typical screening age in Europe, at diagnosis.[36,37,40,41] The overall age range of the review might have been associated with lower scores for QoL and functioning scales due to the inclusion of women aged <45 years and >75 years,[41,54,57] who might have reported poorer QoL compared with women of screening age.[58–60] However, in all the included studies, the majority of the women were of the typical screening age (45–75 years) at diagnosis, except for the study from Norway and the United States, where it was not possible to differentiate women by age groups. The inclusion of studies performed between 1995 and 2018 might have resulted in the poorer scores for breast cancer survivors in the studies, started in 1995–1996 compared with those started in the 2000s, due to improved breast cancer treatment, including reconstructive and breast conserving surgery and neoadjuvant chemotherapy.[26] Furthermore, the pure impact of participation in mammographic screening was not investigated in this review. However, based on the screening coverage in the included studies, the majority of the women might have been diagnosed due to screening.[46,47,61–65] Future research is needed to compare QoL between women with screen-detected breast cancer and women with no history of breast cancer in the areas, where mammographic screening is available.

We have not included a study using FACT-G (0–108) questionnaire in the meta-analysis, which might have contributed to the less favourable results for breast cancer survivors' QoL. SF-36/RAND and EORTC-QLQ-C30 were included in the meta-analysis on the equal basis because of the same measurement scale, 0–100, despite their content differed.[66] This could have resulted in overestimation as well as underestimation of the outcome. Furthermore, the differences in study design, length of follow-up, number of women included and periods when treatment was performed might have influenced the overall effect. Meta-regression was not performed because fewer than 10 studies were included.[67]

In conclusion, this review did not identify differences in QoL between women diagnosed with breast cancer and followed for >1–10 years compared with women with no history of breast cancer among those eligible for mammographic screening.

Author statements

Ethical approval

None declared.

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Competing interests

All the authors declare no conflict of interest.

Authors' contributions

Each author can take responsibility for the content of the article. The literature search was performed by all the authors of the article. All the authors have made substantial contribution to the conception and design of the study, acquisition of data, analyses and interpretation of findings. N.M. worked with drafting the article, and all the authors contributed to revising it critically for important intellectual content. The final approval of the version to be submitted was given by all authors.

Appendix A. Supplementary data

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