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Long-term quality of life and quality adjusted life years after breast cancer: Impact of detection mode, tumor characteristics and treatment

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ABSTRACT

Background: Health-related quality of life (HRQoL) of breast cancer survivors has been extensively evaluated. However, HRQoL differences for women diagnosed by organized mammographic screening and women diagnosed due to symptoms have been sparsely described. We aimed to compare self-reported long-term HRQoL and quality adjusted life years (QALYs) between women with screen-detected breast cancer and women with symptomatic breast cancer, adjusting for histopathologic tumor characteristics and treatment.

Methods: This study was nested within a cohort of women diagnosed with breast cancer by organized mammographic screening or due to symptoms 2006–2017 who responded a questionnaire measuring HRQoL (VAS, 0–100) and EQ-5D-5L 2019–2020. Responses to EQ-5D-5L were transformed into health utility values using a tariff based on preferences elicited in a national survey. Multivariable linear regression models were used to compare VAS-scores adjusting for tumor characteristics and treatment. QALYs were estimated by summing up the health utility values between the third and the fifth year since breast cancer diagnosis adjusting for breast cancer survival.

Results: Mean HRQoL (VAS) was 66.2 (standard deviation, SD: 21.1) for women with screen-detected breast cancer (n = 1141) and 62.5 (SD: 21.2) for women with symptomatic breast cancer (n = 1561). Women with screen-detected breast cancer had 3.8 (95 % confidence interval, CI, 2.3, 5.4) and 3.7 (95 %CI 2.1, 5.2) higher HRQoL VAS-scores compared to women with symptomatic breast cancer in the models adjusted for tumor characteristics and treatment, respectively. Women with screen-detected breast cancer and women with symptomatic breast cancer accrued 2.30 and 2.06 QALYs, respectively.

Conclusion: Women with screen-detected breast cancer demonstrated higher estimates of long-term HRQoL and QALYs compared to women with symptomatic cancer.

Policy Summary: More favorable long-term quality of life outcomes were shown for women diagnosed with breast cancer by organized mammographic screening compared to women diagnosed due to symptoms.

1. Background

Breast cancer is the most common cancer and the leading cause of cancer death among women in Norway and worldwide [1,2]. Screening and improved treatment have contributed to breast cancer mortality reduction, receiving substantial international attention during the last

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decades [3,4]. However, less attention has been devoted to quality of life among breast cancer survivors in association with detection mode, i.e. detection by screening or due to symptoms [5,6].

Individual's physical and mental health over time determines health-related quality of life (HRQoL) [7]. The combination of health related quality and length of life indicates quality-adjusted life years (QALYs), and reflects the person's ability to perform the activities of daily living without pain and mental disturbance during a certain period of life [8]. If the HRQoL during one year is measured on a scale where 0 represents 'death' and 1 'perfect health', the number of QALYs experienced is estimated by multiplying the expected length of life by the expected HRQoL [8].

Symptomatic breast cancers are associated with less favorable histopathologic tumor characteristics compared to screen-detected cancers [9]. Women with symptomatic cancer are thus expected to receive more aggressive treatment and to have a lower HRQoL and possibly experience fewer QALYs compared to women with screen-detected cancer [10]. Few studies investigating HRQoL by detection mode reported better outcomes for women with breast cancer detected by screening [5,6,11]. However, whether the better HRQoL in women with screen-detected cancer persisted in a long term and was solely due to more favorable histopathologic tumor characteristics and less aggressive treatment remains unclear.

With the underlying goal to elucidate the association between long-term HRQoL and detection mode, we compared HRQoL and QALYs between women with screen-detected and symptomatic breast cancer diagnosed in Norway 2006–2017 and examined how the difference in HRQoL and QALYs between these groups of women was affected by histopathologic tumor characteristics and treatment.

2. Methods

2.1. Study design and participants

This case-control study was nested within a cohort of women diagnosed with breast cancer [11]. We received information about breast cancer from the Cancer Registry of Norway, Norwegian Institute of Public Health, which collects data on all cancer cases diagnosed in the country [12]. The Cancer Registry administers BreastScreen Norway, the organized screening program for breast cancer, offering all female residents aged 50–69 biennial two-view mammographic screening [13]. BreastScreen Norway started in 1996 in four counties and became nationwide in 2005. The program targeted about 670,000 women in 2024. The annual participation rate is 75 %.

Women aged 50–69 at invitation to screening or histological diagnosis of primary invasive breast cancer, diagnosed 2006–2017, were eligible for inclusion. Women with symptomatic cancer were defined as women invited to the screening program, but never attended, last attended more than two years prior to their diagnosis, or attended the program and were diagnosed with interval cancer within 24 months after a negative screening examination or 6–24 month after a false positive screening result [13]. A random sample of 2500 women with screen-detected cancer and 5000 women with symptomatic cancer was considered eligible for the study. Women with screen-detected cancer were considered controls, while women with symptomatic cancer were cases.

A paper-based self-administered questionnaire, including EQ-5D-5L [14], was sent to the eligible women between December 2019 and April 2020. Detailed information on the questionnaire can be found elsewhere [11]. We excluded women with incorrect addresses, those who did not return the questionnaire, refused to participate, died before receiving the questionnaire, and women with detrimental health conditions not related to breast cancer, and missing information on HRQoL or histopathologic tumor characteristics.

2.2. Variables and data measurement

The questionnaire collected self-reported information about height (cm), weight (kg), education (no/primary school; secondary school; university/college), physical activity (no/<2 h a week; 2–3 h a week; >3 h a week), treatment of primary breast cancer (surgery [breast conserving; mastectomy], chemotherapy [no; yes], radiotherapy [no; yes], and hormone therapy [no; yes]), and relapse (self-reported statement of breast cancer relapse on the same site after received treatment [no; yes]). Data on height and weight were used to calculate body mass index (BMI, kg/m^2).

Information about age, detection mode, date of diagnosis, tumor diameter (mm), histologic grade (1−3) [15], lymph node status (positive; negative), stage (I to IV, based on TNM classification) [16], and hormone receptor (HR) status (estrogen receptor (ER) and progesterone receptor (PR) [positive; negative]) was extracted from the Cancer Registry database. The variable HR was considered positive if ER or PR status or both were positive, and negative if ER and PR status was negative. Histopathologic tumor characteristics were grouped into favorable (tumor diameter <14.45 mm, negative lymph node status, histologic grade 1 or 2 and HR positive tumors) and unfavorable (tumor diameter ≥14.44 mm, positive lymph node status, histologic grade 3 or HR negative tumors). Primary breast cancer treatment was categorized as local treatment (solely surgery and/or radiotherapy) and systemic treatment (surgery and/or radiotherapy, chemotherapy and/or hormone therapy). The variable Nottingham Prognostic Index (NPI) was calculated as NPI = [0.2 x S] + N + G, where S is the diameter of the index lesion in centimeters; N is the node status: 0 involved nodes = 1, 1–3 involved nodes = 2, > 3 involved nodes = 3; and G is the histologic grade: grade 1 = 1, grade 2 = 2, grade 3 = 3 [17].

EQ-5D-5L consists of five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) with five levels of severity (1, best - 5, worst), and a visual analog scale (VAS) to report present health status, indicating a score for self-reported current HRQoL (0, low, worst health imaginable – 100, high, the best health imaginable) [14]. The response about five dimensions was used to obtain health utility values, representing the HRQoL values on the day women responded to the questionnaire [14,18]. We used ordinal regression to impute the missing responses on the levels of severity. Sensitivity analysis for the imputations have been published [11]. In the absence of Norwegian health utility values, responses of the women were scored using the Danish value set for the EQ-5D-5L [14,19].

3. Ethics

This study had a legal basis in accordance with Articles 6 (1a and e) and 9 (2a and j) of the GDPR [20]. The data was disclosed with a legal basis in the Cancer Registry Regulations (§§ 1–9 and 1–7) and the Act on Health Registries and Processing of Health Information (Health Registry Act) § 19e [21,22]. The study was approved by the Regional Committees for Medical and Health Research Ethics (N28484) and registered at Clinical.Trials.gov (NCT03877029, registration date March 13th, 2019, last updated October 28th, 2024). The data were de-identified prior to the analyses.

3.1. Statistical methods

Means and standard deviations (SD) for continuous variables, and frequencies and percentages for categorical variables were presented by detection mode. To compare the self-reported HRQoL score (VAS, 0–100) by detection mode, we performed a set of linear regression analyses adjusted and stratified by potential confounders. In model A, we adjusted for tumor characteristics (diameter, histologic grade, lymph node and HR status), and other factors (age, time since diagnosis, BMI, education, and physical activity). In model B, treatment was used instead of tumor characteristics. Further, we stratified analyses by

favorable and unfavorable tumor characteristics (model C1-C2), NPI 1–4 (model D1-D4), unfavorable tumor characteristics and histologic grade 1–3 (model E1-E3), and unfavorable tumor characteristics and stage 1–4 (model F1-F4). Relapse was considered the intermediary step in the pathway from detection mode to HRQoL and was not adjusted for. Missing values of BMI (n = 164) were imputed using multiple imputation via linear regression, while missing values for education and physical activity were included as a dummy variable. Interaction between detection mode and stage (continuous) was analyzed using adjusted linear regression models including tumor characteristics and treatment, separately.

To analyze the scores of the EQ-5D-5L by detection mode, an ordered probit regression model controlling for tumor characteristics and other factors, and two separate ordered probit regression models for women with favorable and unfavorable tumor characteristics adjusted for other factors, were used [23].

Health utility values with standard errors were obtained using a margin function (partial derivatives of the regression equation with respect to each variable in the model for each unit in the data) for time since diagnosis after performing a linear regression model adjusted for tumor characteristics and other factors, and graphically presented from the third to the 14th year since diagnosis by detection mode. Crude breast cancer-specific survival in Norwegian women aged 50–69 at diagnosis by detection mode was solely available for the maximum period of six years since diagnosis (2005–2011) [24]. Therefore, QALYs from the third to the fifth year since diagnosis were calculated by summing up the adjusted health utility values multiplied by the percentage of survival for women with screen-detected and symptomatic breast cancer [24]. Data on QALYs from women who have never been diagnosed with breast cancer based on the Danish population EQ-5D-5L norms were the reference [25]. Stata MP Version 16.1 (Stata, Texas, College Station) was used.

4. Results

Among 7500 women with breast cancer, 4798 were excluded, leaving 1141 women with screen-detected cancer and 1561 with symptomatic cancer for the study (Figure A1).

Women excluded due to missing histopathologic tumor characteristics were on average younger at diagnosis (57.4 versus 59.0 years, respectively) and had more favorable tumor characteristics (mean tumor diameter 18.7 versus 19.3 mm; lymph node positive 34.1 versus 35.2 %; and hormone receptor positive 100 versus 86.2 %, respectively) compared to those included in the analyses (Table A1), while women excluded due to other reasons (refusal to participate, missing HRQoL, etc.) were on average one year younger at diagnosis compared to included women [11].

Among included participants, women with screen-detected cancer were on average older at diagnosis (59.9 versus 58.8 years), had a longer time since diagnosis (7.5 versus 7.2 years), higher BMI (26.5 versus 25.6 kg/m^2), and lower proportions of unfavorable tumor characteristics (63.3 versus 82.6 %) and systemic treatment (64.9 versus 82.8 %) compared to women with symptomatic cancer (Table 1). Mean HRQoL score and health utility value were higher for women with screen-detected breast cancer compared to women with symptomatic cancer (66.2 versus 62.5 and 0.80 versus 0.78, respectively).

Compared to women with symptomatic cancer, women with screen-detected cancer had a 3.8 (95 % CI 2.2, 5.4) higher HRQoL score after adjustment for tumor characteristics (Model A, Table 2, and Table A2A) and a 3.7 (95 % CI 2.1, 5.2) higher score after adjustment for treatment (Model B, Table 2, and Table A2B).

Women with lymph node positive tumors had a 2.4 (95 %CI −4.1, −0.7) lower HRQoL score compared to women with lymph node negative tumors (Table A2A). Women who underwent systemic treatment had a 5.9 lower HRQoL score (95 %CI −7.7, −4.1) compared to women who underwent local treatment (Table A2B).

Table 1
Descriptive characteristics of women invited to BreastScreen Norway and diagnosed with screen-detected (n = 1141) or symptomatic (n = 1561) cancer 2006–2017.

	Screen-detected cancer n = 1141	Symptomatic cancer n = 1561	Total N = 2702
Age at recruitment, mean (SD), years	67.4 (6.4)	66.0 (6.6)	66.6 (6.5)
Age at diagnosis, mean (SD), years	59.9 (5.7)	58.8 (5.9)	59.0 (5.9)
Time since diagnosis, mean (SD), years	7.5 (3.4)	7.2 (3.2)	7.3 (3.3)
Body mass index, mean (SD), kg/m^2	26.5 (4.3)	25.6 (4.2)	25.9 (4.3)
Education			
No or primary school, n (%)	224 (19.8)	250 (16.0)	474 (17.5)
Secondary school, n (%)	450 (39.8)	561 (36.6)	1011 (37.9)
University/college, n (%)	456 (40.4)	740 (47.4)	1196 (44.6)
Missing, n	11	10	21
Physical activity			
No or < 2 h a week, n (%)	209 (18.5)	247 (15.9)	456 (17.0)
2–3 h a week, n (%)	499 (44.2)	633 (40.9)	1132 (42.3)
> 3 h a week, n (%)	421 (37.3)	669 (43.2)	1090 (40.7)
Missing, n	12	12	24
Tumor diameter, mean (SD), mm	17.3 (14.3)	21.3 (13.9)	19.2 (14.2)
Grade			
1, n (%)	324 (28.4)	224 (14.3)	548 (20.3)
2, n (%)	570 (50.0)	766 (49.1)	1336 (49.4)
3, n (%)	247 (21.7)	571 (36.6)	818 (30.3)
Positive lymph nodes, n (%)	339 (29.7)	612 (39.2)	951 (35.2)
HR positive, n (%)	1038 (91.0)	1292 (82.8)	2330 (86.2)
Unfavorable characteristics*	722 (63.3)	1289 (82.6)	2011 (74.4)
Stage at diagnosis			
I, n (%)	671 (58.8)	579 (37.1)	1250 (46.3)
II, n (%)	275 (24.1)	693 (44.4)	968 (35.8)
III, n (%)	176 (15.4)	224 (14.3)	400(14.8)
IV, n (%)	19 (1.7)	65 (4.2)	84 (3.1)
Surgery			
Breast conserving, n (%)	834 (73.1)	865 (55.4)	1699 (62.9)
Mastectomy, n (%)	307 (26.9)	696 (44.6)	1003 (37.1)
Chemotherapy, n (%)	562 (49.3)	1059 (67.8)	1621 (60.0)
Radiotherapy, n (%)	982 (86.1)	1282 (82.1)	2264 (83.8)
Hormone therapy, n (%)	529 (46.4)	880 (56.4)	1409 (52.1)
Local treatment**, n (%)	400 (35.1)	269 (17.2)	669 (24.8)
Systemic treatment***, n (%)	741 (64.9)	1292 (82.8)	2033 (75.2)
Relapse, n (%)	74 (6.5)	98 (6.3)	172 (6.4)
HRQoL (0, low – 100, high), mean (SD)	66.2 (21.1)	62.5 (21.2)	64.1 (21.2)
Health utility value (−0.107, low – 1, high), mean (SD)	0.80 (0.14)	0.78 (0.15)	0.79 (0.15)
Mobility (1, best – 5, worst), mean (SD)	1.46 (0.76)	1.50 (0.82)	1.48 (0.80)
Self-care (1, best – 5, worst), mean (SD)	1.10 (0.33)	1.10 (0.39)	1.10 (0.36)
Usual activities (1, best – 5, worst), mean (SD)	1.55 (0.77)	1.67 (0.89)	1.62 (0.84)
Pain/discomfort (1, best – 5, worst), mean (SD)	2.00 (0.82)	2.18 (0.90)	2.11 (0.88)
Anxiety/depression (1, best – 5, worst), mean (SD)	1.54 (0.75)	1.59 (0.76)	1.57 (0.76)

SD - Standard deviation
HR - Hormone receptor status (positive if estrogen and/or progesterone positive and negative if estrogen and progesterone negative)
HRQoL - Health related quality of life, VAS (EQ-5D-5L)
* Tumor diameter ≥ 14.44 mm, positive lymph node status, grade 3 or HR negative
** Local treatment - solely surgery and/or radiotherapy as primary treatment
*** Systemic treatment - surgery and/or radiotherapy and systemic treatment as primary treatment

Table 2
The association of a self-reported health-related quality of life score (0, low – 100, high) and detection mode, screen-detected (SDC) and symptomatic breast cancer diagnosed 2006–2017.

Model	Coefficient of detection mode for SDC using symptomatic cancer as reference*	95 % confidence interval	P-value
A: Tumor diameter, lymph node status, histologic grade, and HR status** (SDC: n = 1141; Symptomatic: n = 1561)***	3.8	2.3; 5.4	< 0.01
B: Treatment (SDC: n = 1141; Symptomatic: n = 1561)***	3.7	2.1; 5.2	< 0.01
C: Model stratified by histopathologic tumor characteristics (n = 2702)			
C1: Favorable# histopathologic tumor characteristics (SDC: n = 419; Symptomatic: n = 272)	2.5	−0.7; 5.7	0.13
C2: Unfavorable## histopathologic tumor characteristics (SDC: n = 722; Symptomatic: n = 1289)	4.5	2.7; 6.3	< 0.01
D: Model stratified by NPI (n = 2702)			
D1: NPI 1 (SDC: n = 252; Symptomatic: n = 136)	3.1	−1.2; 7.5	0.15
D2: NPI 2 (SDC: n = 354; Symptomatic: n = 376)	1.8	−1.6; 4.5	0.35
D3: NPI 3 (SDC: n = 422; Symptomatic: n = 832)	4.4	2.1; 6.7	< 0.01
D4: NPI 4 (SDC: n = 113; Symptomatic: n = 217)	6.9	2.2; 11.5	< 0.01
E: Model for women with unfavorable histopathologic tumor characteristics stratified by histologic grade (n = 2011)			
E1: Grade 1 (SDC: n = 105; Symptomatic: n = 132)	2.5	−2.7; 7.6	0.35
E2: Grade 2 (SDC: n = 370; Symptomatic: n = 586)	4.4	1.8; 7.0	< 0.01
E3: Grade 3 (SDC: n = 247; Symptomatic: n = 571)	5.3	2.3; 8.3	< 0.01
F: Model for women with unfavorable histopathologic tumor characteristics stratified by stage (n = 2011)			
F1: Stage 1 (SDC: n = 258; Symptomatic: n = 322)	2.3	−1.1; 5.8	0.18
F2: Stage 2 (SDC: n = 273; Symptomatic: n = 689)	4.2	1.5; 6.8	< 0.01
F3: Stage 3 (SDC: n = 175; Symptomatic: n = 218)	7.8	3.5; 12.0	< 0.01
F4: Stage 4 (SDC: n = 16; Symptomatic: n = 60)	3.0	−9.8; 15.8	0.64

SDC – screen-detected breast cancer
HR – hormone receptor
NPI – Nottingham Prognostic Index
* Linear regression models adjusted for age, time since diagnosis, body mass index, education, and physical activity
** Hormone receptor status was positive if estrogen and/or progesterone positive and negative if estrogen and progesterone negative
*** Details are presented in Table A2
# tumor diameter < 14.45 mm, negative lymph node status, grade < 3 and estrogen and/or progesterone positive
tumor diameter ≥ 14.44 mm, positive lymph node status, grade 3 or estrogen and progesterone negative

HRQoL scores did not differ by detection mode among women with favorable tumor characteristics, NPI 1 and 2, and in women with unfavorable tumor characteristics and histologic grade 1 and stage 1 (Model C2, D1, D2, E1, and F1, Table 2; Table A2, Table A3A, Table A4AB, Table A5A, Table A6A). The scores were higher in women with screen-detected cancer among those with NPI 3 and 4, unfavorable tumor characteristics and histologic grade 2 and 3 and stage 2 and 3 (Model D3, D4, E2, E3, F2, and F3, Table 2; Table A4CD, Table A5BC, Table A6BC). Interaction between stage and detection mode was observed for the model including local versus systemic treatment (Table A7B).

Studying the five dimensions of the EQ-5D-5L (1, best – 5, worst) separately, we observed that women with screen-detected cancer had significantly lower scores for usual activities (-0.14, 95 %CI −0.24, −0.05) and pain/discomfort (-0.21, 95 %CI −0.29, −0.12) compared to women with symptomatic cancer (Table 3, Table A8).

Pain/discomfort scores were lower in women with screen-detected breast cancer among those with favorable (-0.29, 95 %CI −0.46, −0.12) and unfavorable (-0.18, 95 %CI −0.28, −0.08) tumor characteristics ($p < 0.01$ for both) (Table A9).

Adjusted health utility values varied between 0.79 and 0.82 for women with screen-detected cancer and between 0.77 and 0.80 for women with symptomatic cancer (Figure A2).

Women with screen-detected breast cancer and women with symptomatic breast cancer accrued on average 2.30 and 2.06 QALYs, respectively, from the third to the fifth year since diagnosis (Fig. 1). Women without underlying diseases aged 50–70 + accrued on average 2.67 QALYs during the three-year period [25].

5. Discussion

Women with screen-detected cancer had an about 4-point higher long-term HRQoL score compared to women with symptomatic cancer when adjusted for histopathologic tumor characteristics and treatment. The difference was more prominent in women with more advanced disease. We estimated average QALYs of 2.30 for women with screen-detected cancer and 2.06 for women with symptomatic cancer between the third and fifth year since diagnosis when accounting for differences in breast cancer-specific survival between the groups.

Various tumor characteristics and treatment types were associated with differences in HRQoL scores, implying that favorable tumor characteristics and treatment were crucial for determining higher HRQoL in our study. Interaction between stage at diagnosis and HRQoL scores indicated that the difference by detection mode increased by increasing disease severity. However, the difference by detection mode might also be associated with other reasons than disease severity. One possible explanation might be linked to sociodemographic and cultural aspects. Women who did not attend screening and were diagnosed with symptomatic cancer might have been represented by groups associated with socioeconomic marginality, lower health literacy, and/or negative cultural perceptions of healthcare institutions [26–29]. As shown in previous studies, these factors might determine lower quality of life and breast cancer survival [30,31]. Furthermore, the lower HRQoL for women diagnosed outside of the screening program could have been related to the perception of the breast cancer diagnosis and treatment as

Table 3
The association of the score for five dimensions of EQ-5D-5L (1, best – 5, worst) and detection mode, for 2702 women with screen-detected (SDC) or symptomatic cancer 2006–2017.

	Coefficient for detection mode for SDC using symptomatic cancer as reference in the ordered log-odds scale*	95 % confidence interval	p-value
Mobility	−0.10	−0.20; 0.00	0.06
Self-care	−0.06	−0.21; 0.10	0.47
Usual activities	−0.14	−0.24; −0.05	< 0.01
Pain/discomfort	−0.21	−0.29; −0.12	< 0.01
Anxiety/depression	−0.06	−0.15; 0.03	0.20

* Adjusted for histopathologic tumor characteristics, age, time since diagnosis, body mass index, education, and physical activity

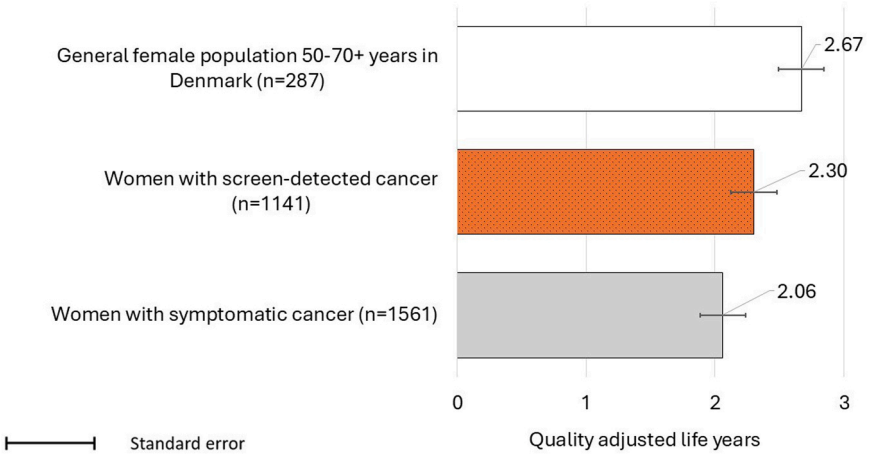

Fig. 1. Quality adjusted life years for women diagnosed and treated for screen-detected and symptomatic breast cancer 2006–2017 based on self-reported information using EQ-5D-5L from the 3rd to the 5th year since diagnosis, breast cancer-specific survival data for Norwegian women for 6 years since diagnosis, and data from Danish population health measured by EQ-5D-5L.

unanticipated health events, resulting in a larger psychological burden for these women compared to women with screen-detected cancer [32]. Another explanation can be biological features associated with tumor growth, including proliferation index and immunohistochemical subtypes, which were not investigated in this study [33–35].

Less pain/discomfort was reported by women with screen-detected versus symptomatic cancer also in stratified analyses for the EQ-5D-5L responses, emphasizing that pain/discomfort could have been a significant reason for reduced HRQoL among women with symptomatic cancer. Furthermore, women with symptomatic cancer had a lower mean health utility value and lower range of adjusted health utility values compared to women with screen-detected cancer. The differences in health utility values per year since diagnosis by detection mode were low but statistically significant in the adjusted regression model (data not shown). The reasons for these low differences per year might be the non-transformed presentation and decreased disease impact over time.

The difference in QALYs for the two groups of women was rather small, 0.24 [25]. A higher proportion of survivors among women with screen-detected cancer versus women with symptomatic cancer might be expected during the first two years and over five years since diagnosis [24,36]. As our comparison was conditional on surviving three to five years, the actual difference could be larger [37].

Previous studies on breast cancer survivors' self-reported HRQoL by detection mode favored detection by screening [6,11]. Studies comparing HRQoL of breast cancer survivors of screening age and women without breast cancer showed inconsistent results [37–40]. QALYs for survivors of the disease stratified by detection mode have never been compared based on data reported by the women, but rather from opinions of health care professionals [5,41,42]. The results of our study are in line with an Australian study, reporting that, on average, women with community-detected (analogous to symptomatic) and interval-detected cancers were estimated to have a slightly larger treatment-related QALY loss than those with screen-detected breast cancer [5]. Further, our findings are corroborated by the results from the Netherlands, indicating that women with screen-detected cancer showed better outcomes in general health compared to women with clinically detected breast cancer [6].

Our results suggest that mammographic screening provides a benefit of preserving the long-term post-diagnosis well-being. The results are valuable in policy discussions on balancing benefits and harms of mammographic screening [43] and imply the importance of resource allocation for screening continuation and development.

Limitations

We did not use a breast cancer-specific questionnaire, as the study did not intend to investigate disease-specific domains of HRQoL. Further, information on possible confounding factors (race, ethnicity, immunohistochemical subtypes, and sociodemographic status) was not reported by the women. HRQoL might have been overestimated for the participated women as those women might have been in a better health condition to respond to the questionnaire, while women who refused to participate were unable to respond as their health was poor and therefore HRQoL was too low. The cutoff for tumor diameter for favorable versus unfavorable tumor characteristics was 14.45 mm, as this division more closely reflected the corresponding groups of local and systemic treatment, and the differences in survival were shown for tumor diameter < 14.45 versus ≥ 14.44 mm [44]. Using a dummy variable for the missing values of the categorical variables might be associated with biased impact estimates and potentially lead to misspecification of the functional form of the analysis model [45]. However, as the study was based on complete data of the existing factors, inclusion of all covariates in a correctly specified impact model could help increase the precision of the estimates.

Further, the Danish EQ-5D-5L value set was chosen for the analyses due the comparable to Norway situation on breast cancer screening in Denmark, as women aged 50–69 years are invited to the Danish screening program [46]. The heteroscedastic censored hybrid model combining composite time trade-off and discrete-choice experiment data was more robust compared to other models for obtaining value sets based on data from other countries [19,25,47,48].

Information bias was inevitable as the outcome was subjective. A previous study from Norway showed that the association of appearance and body functioning, general pain, fatigue, and lymphedema with HRQoL score was rather strong. Since the study included a high number of women in the compared groups, the clinical relevance of the difference of 4 points for HRQoL on a VAS-scale might be questioned. However, as the results from stratified analyses and five dimensions of EQ-5D-5L, specifically on usual activities and pain/discomfort, and QALYs, were consistent with the findings on VAS, the difference by detection mode should be considered clinically important. Finally, the ideal study design would include a prospective study comparing HRQoL and QALYs by detection mode over decades.

Conclusions

The self-reported HRQoL was higher for women with screen-detected

breast cancer compared to women with symptomatic breast cancer during the period from the third to 14th year since diagnosis. The results favor organized mammographic screening.

Ethics approval

This study had a legal basis in accordance with Articles 6 (1a and e) and 9 (2a and j) of the GDPR [20]. The data was disclosed with a legal basis in the Cancer Registry Regulations (§§ 1–9 and 1–7) and the Act on Health Registries and Processing of Health Information (Health Registry Act) § 19e [21,22]. The study was approved by the Regional Committees for Medical and Health Research Ethics (N28484).

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CRediT authorship contribution statement

Giske Ursin: Writing – review & editing, Validation, Supervision, Methodology, Formal analysis, Conceptualization. **Akslen Lars:** Writing – review & editing, Validation, Methodology, Formal analysis, Conceptualization. **Marthe Larsen:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Edoardo Botteri:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Solveig Hofvind:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Cairns John:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Falk Ragnhild:** Writing – review & editing, Validation, Methodology, Formal analysis, Conceptualization. **Nataliia Moshina:** Writing – original draft, Validation, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Nataliia Moshina reports financial support was provided by Stiftelsen Dam. Solveig Hofvind is the head of BreastScreen Norway but has an independent fixed position at the Cancer Registry of Norway. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Disclaimer

Data from the Cancer Registry of Norway (CRN) has been used in this publication. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by CRN is intended nor should be inferred.

Consent to participate and publish

The consent to participate in the study and consequently publish the results of the study was obtained from all participants included in the study. The questionnaire was sent to participants by post and included a page with an informed consent regarding privacy and participation in the study. Women, who did not sign the informed consent, were not included in the study.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jcpo.2025.100631.

Data availability

Data used in the analyses can be made available on request to https://helsedata.no/, given legal basis in Articles 6 and 9 of the GDPR and that the processing is in accordance with Article 5 of the GDPR.

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