EUR Research Information Portal

Long-term health-related quality of life among adolescent and young adult breast cancer survivors

Citation for the published version (APA):
Vrancken Peeters, N. J. M. C., Kerklaan, R., Vlooswijk, C., Bijlsma, R. M., Kaal, S. E. J., Tromp, J. M., Bos, M. E. M. M., van der Hulle, T., de Boer, M., Nuver, J., Kouwenhoven, M. C. M., van der Graaf, W. T. A., & Husson, O. (2025). Long-term health-related quality of life among adolescent and young adult breast cancer survivors. *Quality of Life Research*, *34*(5), 1483-1500. Article 100255. https://doi.org/10.1007/s11136-025-03914-1

Link to publication on the EUR Research Information Portal

Erasmus University Rotterdam
Making Minds Matter

Long-term health-related quality of life among adolescent and young adult breast cancer survivors

Noelle J. M. C. Vrancken Peeters[1,2] · Roos Kerklaan[2] · Carla Vlooswijk[3] · Rhodé M. Bijlsma[4] · Suzanne E. J. Kaal[5] · Jacqueline M. Tromp[6] · Monique E. M. M. Bos[7] · Tom van der Hulle[8] · Maaike de Boer[9] · Janine Nuver[10] · Mathilde C. M. Kouwenhoven[11] · Winette T. A. van der Graaf[1,7] · Olga Husson[1,12,13]

Abstract

Purpose As the prognosis for adolescents and young adults (AYAs) with breast cancer has improved, long-term health-related quality of life (HRQoL) has become increasingly important. This study aimed to analyze the long-term HRQoL of AYA breast cancer survivors compared to an age-matched normative population and to identify factors associated with HRQoL.
Methods Secondary analyses were conducted using data from the SURVAYA study. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC QLQ-C30) was used to assess HRQoL. The Mann–Whitney U test was used to compare HRQoL scores of AYA breast cancer survivors with those of the normative population (n = 409). Linear regression models were constructed to identify patient and treatment characteristics associated with HRQoL.
Results A total of 944 female AYA breast cancer survivors were included, with a median age of 36.0 years and a median follow-up of 12.2 years. AYA breast cancer survivors scored significantly lower on five functional scales: physical, role, emotional, cognitive, and social, and higher on five symptom scales: fatigue, pain, dyspnea, insomnia, and financial impact compared to the normative population. Being in a relationship, having a positive body image, and adaptive coping were positively associated with HRQoL, while older age, chemotherapy, unemployment, and maladaptive coping were negatively associated.
Conclusion AYA breast cancer survivors experience significantly compromised long-term HRQoL compared to an age-matched normative population. These results highlight the need for tailored follow-up care and long-term support, as well as the importance of shared decision-making about the benefits and risks of treatments before initiation.

Keywords Adolescents and young adults (AYAs) · Breast cancer · Health-related quality of life (HRQoL) · Survivorship

Introduction

Adolescents and young adults (AYAs) are defined as individuals aged between 15 and 39 years at the time of their initial cancer diagnosis, according to the US National Cancer Institute [1]. However, the AYA age range may be defined differently in other healthcare systems [2]. In the Netherlands, children (0–18 years) receive treatment and support centrally in a pediatric oncology center, while adults (≥ 18 years) are treated in general and academic hospitals in the whole country. Due to this dichotomization, AYAs in the Netherlands are defined as individuals aged from 18 to 39 years at their initial cancer diagnosis [3].

Currently, the incidence of cancers in AYAs is increasing [4, 5]. AYAs are recognized as a unique population within oncology. AYAs have a long life ahead because of their prolonged survival period, with an overall 5-year relative survival rate of over 80% and 20-year relative survival of 74% [6, 7]. But most importantly, AYAs express age-specific needs as they find themselves in a developmental life phase. AYA cancer survivors are impacted by both physical issues, such as possible infertility, as well as more psychosocial matters, such as the interruption of education or career development, problems with sexuality and intimacy, and difficulties in building and maintaining mature relationships [8–10]. Furthermore, AYAs encounter more delays in their diagnosis and treatment due to failing to recognize or acknowledge the importance of their symptoms [11, 12].

Breast cancer is the most common type of cancer among female AYAs worldwide [5, 13]. Despite the increasing incidence of breast cancer among AYAs, there is a positive trend in the prognosis due to advances in various treatment modalities [4, 10, 14–16]. Although this rise in life expectancy is promising, AYA breast cancer survivors must live with the possible long-term adverse effects of breast cancer and its treatment, which can have a significant impact on their overall health-related quality of life (HRQoL) [17–19].

To date, literature on long-term HRQoL of AYA breast cancer survivors is scarce. Previous research focused either on older breast cancer survivors or on AYA cancer in general [20–24]. Yet HRQoL impairments differ by age, and breast cancer is a unique type of cancer as the breasts are regarded as one of the most important aspects of female identity and sexuality. As a result, breast cancer survivors often report lower HRQoL compared to other cancer survivors [25–28].

The primary aim of this study was to analyze the HRQoL of AYA breast cancer survivors and compare the HRQoL of AYA breast cancer survivors with that of an age-matched normative population to identify any persistent long-term HRQoL issues associated with their cancer diagnosis and treatment. The secondary aim of this study was to identify factors associated with the HRQoL of AYA breast cancer survivors. The results of this study will provide healthcare professionals with valuable insights into areas where additional long-term support may be needed to improve HRQoL of AYA breast cancer survivors in the future.

Methods

Data collection

The SURVAYA (health-related quality of life and late effects among SURVivors of cancer in Adolescence and Young Adulthood) study data was used for secondary analyses [3]. The SURVAYA study is a retrospective, population-based, observational, cross-sectional cohort questionnaire study conducted among long-term (5–20 years post-diagnosis) AYA cancer survivors (18–39 years at the time of diagnosis) in the Netherlands. AYA cancer survivors were invited to participate in the SURVAYA study from the involved cancer centers, including eight university medical centers and the Netherlands Cancer Institute (NCI), using the Netherlands Cancer Registry (NCR) [29]. The NCR collects detailed data on cancer patients in the Netherlands, including disease and treatment characteristics. Patient-reported questionnaire data of the SURVAYA study were collected using the PROFILES (Patient-Reported Outcomes Following Initial Treatment and Long-term Evaluation of Survivorship) registry and merged with the NCR data at the end of the study [30]. More detailed information concerning the SURVAYA study has previously been published elsewhere [3].

Normative population

An age-matched normative population, consisting of women from the Dutch general population without a cancer diagnosis, was obtained from CentERdata, a research institute at Tilburg University. CentERdata has an online household panel comprising more than 2000 Dutch households and is representative of the Dutch-speaking population in the Netherlands [31]. The normative data used for this study were collected in 2017.

The normative population was matched to the AYA breast cancer survivors using a frequency matching method with age at the time of filling out the EORTC QLQ-C30 strata (20–35 years, 35–50 years, and 50–65 years) [32]. A total of 409 panel members were matched to 944 AYA breast cancer survivors.

HRQoL

HRQoL was assessed using the Dutch version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC QLQ-C30, version 3) [33, 34]. The EORTC QLQ-C30 consists of 30 questions divided over 15 scales, including five functional scales (physical functioning, role functioning, cognitive functioning, emotional functioning, and social functioning), eight symptom scales (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, and diarrhea), a financial impact scale and a quality of life (QoL) scale. A four-point ordinal Likert scale was used for the functional, financial impact, and symptom scales ranging from 1 = not at all, 2 = a little, 3 = quite a bit, to 4 = very much. For the QoL scale, an ordinal scale ranging from 1 = very poor to 7 = excellent was used. All scales and item scores were linearly transformed into numeric scores (0–100). For the functional scales and the QoL scale, a higher score represents a better level of functioning. For the symptom scales and the financial impact scale, a higher score represents a higher level of symptoms/difficulties [33, 35]. A difference of 5 points was considered clinically relevant [36].

All domains of the EORTC QLQ-C30 were included in the analysis to encompass all aspects of survivorship. The hypothesis posited that while acute symptoms like nausea or dyspnea would not significantly differ between long-term AYA breast cancer survivors and the normative population, longer-term symptoms such as fatigue and cognitive issues would exhibit significant differences.

Covariates

Patient demographics (at the time of questionnaire completion), treatment modality, and tumor characteristics were obtained from the SURVAYA study and the NCR. Variables included in the analysis were selected based on literature and encompassed the following: age at diagnosis, time since diagnosis, body mass index (BMI) categorized as overweight (BMI > 25) and normal weight (BMI < 25), educational level, relationship status, employment status, chemotherapy, radiotherapy, hormonal therapy, breast and axillary surgery including breast-conserving surgery (BCS) with or without axillary lymph node dissection (ALND) and mastectomy with or without ALND, body image and coping mechanisms (maladaptive and adaptive) [26, 37–39].

Body image

Body image was assessed using the EORTC QLQ-SURV100, a questionnaire specifically developed for disease-free cancer survivors, at least one year post-treatment, covering the long-term effects of a cancer diagnosis and treatment. Body image is a functional scale consisting of two single items; "Have you felt older than your age?" and "Have you been dissatisfied with your physical appearance?". A higher score on this scale indicates a more positive body image [3, 40].

The cognitive emotion regulation questionnaire (CERQ)

The CERQ was used to measure the cognitive coping mechanisms [41]. The CERQ consists of nine scales: self-blame, other-blame, rumination, catastrophizing, positive refocusing, planning, positive reappraisal, putting into perspective, and acceptance. Each scale of the full CERQ contains four items. In this study, a condensed version utilizing two items per scale was used. For each item, the answering options ranged from 1 [(almost) never] to 5 [(almost) always]. To calculate the total scale score, the scores of the two relevant items are summed, resulting in a range from 2 to 10. A higher score represents more usage of that specific cognitive emotion regulation strategy. A maladaptive scale based on self-blame, other-blame, rumination, and catastrophizing, and an adaptive scale based on positive refocusing, planning, positive reappraisal, putting into perspective, and acceptance were constructed. The maladaptive scale ranges from 8 to 40, while the adaptive scale ranges from 10 to 50 [41, 42].

Data analysis

Descriptive statistics were used to describe patient, tumor, and treatment characteristics, as well as EORTC QLQ-C30 scores. The Mann–Whitney-U test was used to compare the HRQoL between AYA breast cancer survivors and the normative population.

Multiple linear regression models were used to identify patient and treatment characteristics associated with HRQoL of AYA breast cancer survivors, focusing on the EORTC QLQ-C30 scales that showed significant differences between AYA breast cancer survivors and the normative population (physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning, fatigue, pain, dyspnea, insomnia, and financial impact). Variables included in the multiple linear regression models were age at diagnosis, time since diagnosis, BMI, educational level, relationship status, employment status, chemotherapy, radiotherapy, hormonal therapy, breast and axillary surgery, body image, maladaptive coping, and adaptive coping. To avoid multicollinearity, the tumor stage was not included. Additionally, for the regression models of the functional scales, fatigue, pain, and insomnia from the symptom scales of the EORTC QLQ-C30 were also included.

A variance inflation factor (VIF) was calculated to check for multicollinearity. A VIF with a score < 5 was considered acceptable for analysis [43]. Normality and homoscedasticity of the residuals were tested with residual plots. A two-sided p-value of 0.05 or less was considered statistically significant. All statistical analyses were performed using R statistical software (version 4.4.3) [44].

Non-responder analysis

A non-responder analysis was conducted to assess differences in baseline characteristics between responders and non-responders. Non-responders were defined as AYA breast cancer survivors who did not answer any questions of the EORTC QLQ-C30. Numeric variables were analyzed using an unpaired Student's t-test, and categorical variables were examined using chi-squared tests. A complete case analysis was performed due to the limited amount of missing data.

Results

Patient characteristics

A total of 944 female AYA breast cancer survivors were included in the SURVAYA study. The median age at diagnosis was 36.0 years, ranging from 18.0 to 39.0 years, and the median time since diagnosis was 12.2 years, ranging from 4.41 to 21.6 years. Almost all AYA breast cancer survivors were diagnosed with tumor stage 1 (35.8%) and tumor stage 2 (47,4%). Most survivors underwent chemotherapy (85.5%), radiotherapy (77.3%), and hormonal therapy (50.7%). Additionally, BCS without ALND was the most

common treatment AYA breast cancer survivors received (39.1%, Table 1).

The baseline characteristics of the normative population (n = 409) can be found in Appendix Table 4.

No significant differences in the baseline characteristics between responders and non-responders (n = 57, 6%) were observed (p > 0.05, Appendix Table 5).

EORTC QLQ-C30 scores of AYA breast cancer survivors compared to the normative population

AYA breast cancer survivors scored significantly lower on physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning (p < 0.001). The largest difference between the groups on the functional scales was found in cognitive functioning, with AYA breast cancer survivors having a mean score of 72.4 compared to 91.4 in the normative population (p < 0.001). On the role functioning, emotional functioning, cognitive functioning, and social functioning scales, a difference of 5 points or more was observed (Fig. 1).

On the symptom scales, AYA breast cancer survivors scored significantly higher on fatigue (p < 0.001), pain (p < 0.001), dyspnea (p = 0.004), insomnia (p < 0.001), and financial impact (p < 0.001). The largest difference between the groups was observed in the fatigue scale, where AYA breast cancer survivors had a mean score of 32.8 compared to 20.1 in the normative population (p < 0.001). Differences of 5 points or more were observed on the fatigue, insomnia, and financial impact scales (Fig. 1).

The standard deviations (SD), medians, and ranges of the EORTC QLQ-C30 scales are provided in Appendix Table 6.

Factors associated with long-term HRQoL of AYA breast cancer survivors

Being in a relationship or being married compared to being single and having an adaptive coping mechanism were positively associated with HRQoL. Additionally, a higher body image score was positively associated with HRQoL on all functional and symptom scales of the EORTC QLQ-C30 (Tables 2 and 3).

An older age at diagnosis, being unemployed in comparison to being employed, having received chemotherapy, and having a maladaptive coping mechanism were negatively associated with HRQoL (Tables 2 and 3).

Being overweight compared to having a normal weight and having a higher educational level compared to an intermediate educational level had both positive and negative associations with different aspects of HRQoL. Overweight AYA breast cancer survivors scored lower on physical functioning and fatigue and higher on cognitive functioning. AYA breast cancer survivors with a high educational level

Table 1 Baseline characteristics of AYA breast cancer survivors

Characteristics	AYA breast cancer survivors (n = 944)
Age at diagnosis (years)	
Mean (SD)	34.7 (3.85)
Median [Min, Max]	36.0 [18.0, 39.0]
Time since diagnosis (years)	
Mean (SD)	12.2 (4.52)
Median [Min, Max]	12.2 [4.41, 21.6]
Age at time of filling out EORTC QLQ-C30 (years)	
Mean (SD)	47.5 (6.13)
Median [Min, Max]	47.8 [23.7, 60.0]
BMI, n (%)	
Normal weight[a]	573 (60.7)
Overweight[a]	354 (37.5)
Missing	17 (1.8)
Educational level, n (%)	
Low, no primary school	5 (0.5)
Intermediate, secondary education	377 (39.9)
High, college/university	562 (59.5)
Relationship status, n (%)	
Registered partnership/married	545 (57.7)
Relationship	247 (26.2)
Single	147 (15.6)
Missing	5 (0.5)
Employment status, n (%)	
Employed	664 (70.3)
Self employed	129 (13.7)
Unemployed	151 (16.0)
Tumor stage, n (%)	
1	338 (35.8)
2	447 (47.4)
3	153 (16.2)
4	6 (0.6)
Chemotherapy, n (%)	
Yes	807 (85.5)
No	137 (14.5)
Radiotherapy, n (%)	
Yes	730 (77.3)
No	214 (22.7)
Hormonal therapy, n (%)	
Yes	479 (50.7)
No	465 (49.3)
Targeted therapy, n (%)	
Yes	173 (18.3)
No	771 (81.7)
Breast and axillary surgery, n (%)	
BCS	369 (39.1)
BCS + ALND	133 (14.1)
Mastectomy	216 (22.9)
Mastectomy + ALND	219 (23.2)

Table 1 (continued)

Characteristics	AYA breast cancer survivors (n = 944)
Missing	7 (0.7)
Body image	
Mean (SD)	72.0 (25.7)
Median [Min, Max]	83.3 [0, 100]
Missing	59 (6.3)
Maladaptive scale	
Mean (SD)	13.1 (3.60)
Median [Min, Max]	13.0 [8.00, 27.0]
Missing	72 (7.6)
Adaptive scale	
Mean (SD)	29.9 (7.18)
Median [Min, Max]	30.0 [10.0, 50.0]
Missing	75 (7.9)

ALND axillary lymph node dissection, *BCS* breast-conserving surgery, *BMI* body mass index, *EORTC QLQ-C30* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30, SD; standard deviation

[a]BMI was categorized as overweight (BMI > 25) and normal weight (BMI < 25)

scored higher on physical functioning and cognitive functioning and lower on role functioning and social functioning (Tables 2 and 3). Moreover, fatigue, pain, and insomnia were negatively associated with HRQoL (functional scales, Table 2).

Discussion

AYA breast cancer survivors, with a median follow-up of 12.2 years, had significantly lower HRQoL than the matched normative population. AYA breast cancer survivors scored significantly lower on functional scales of the EORTC QLQ-C30 (physical, role, emotional, cognitive, and social) and higher on symptom scales (fatigue, pain, dyspnea, insomnia, and financial impact). Most differences in HRQoL were not only statistically significant but also clinically meaningful, particularly in cognitive functioning and fatigue [36]. Additionally, age at diagnosis, BMI, relationship status, educational level, employment status, chemotherapy, body image, and coping mechanisms were associated with HRQoL of AYA breast cancer survivors.

Functioning

The significant impairment in cognitive functioning among AYA breast cancer survivors compared to the normative population could be attributed to the intensive chemotherapy and long-term hormonal therapy, including ovarian ablation often required for treating the aggressive types of cancers in this group, which increases the likelihood of developing cognitive issues, such as problems with thinking, memory, and concentration [45–58]. Previous research found that self-reported cognitive problems were highest for breast cancer patients who received both chemotherapy and hormone therapy (OR = 6.33, 95% CI = 4.21, 9.54), followed by those who received only chemotherapy (OR = 5.63, 95% CI = 3.52, 9.00), and those who received only hormone therapy (OR = 1.64, 95% CI = 1.15, 2.33), compared with those reporting neither treatment [57]. Similarly, Mandelblatt et al. identified a significantly higher likelihood of accelerated cognitive decline among survivors receiving chemotherapy (with and without hormonal therapy) compared to those receiving only hormonal therapy (OR = 2.1, 95% CI = 1.3–3.5) [58]. Moreover, Schagen et al. have shown that breast cancer patients (mean age 47.1 years) treated with chemotherapy have a significantly higher risk of late cognitive impairment compared to those without chemotherapy (OR = 6.4, 95% CI = 1.5–27.6) [55]. However, Dijkshoorn et al. demonstrated that one in four breast cancer patients had cognitive impairment even before starting anticancer treatment, suggesting that psychological factors such as post-traumatic stress disorder (PTSD), which is common after a cancer diagnosis, can also play an important role [54, 59]. The linear regression analysis in the current study confirmed a negative association between chemotherapy and cognitive functioning, while no association with hormonal therapy was found. This might be explained by the fact that cognitive functioning in the current study was assessed using only the two EORTC QLQ-C30 items. Research suggests that hormonal therapy may have more pronounced effects on specific cognitive domains, such as verbal learning/memory, which were not comprehensively assessed in this study [47–50].

Furthermore, previous research among older breast cancer patients with a shorter follow-up duration showed a significant decrease in role, emotional, and social functioning scores compared to the general population; however, no statistically significant difference in physical functioning was found [60, 61]. While these findings align with those of the current study, this study also identified a significant decrease in physical functioning. This discrepancy may be explained by the fact that older cancer survivors tend to adjust their health perceptions more easily, whereas younger survivors generally have higher expectations for their physical abilities [62].

Symptoms

AYA breast cancer survivors reported statistically and clinically significant higher levels of fatigue and insomnia compared to the normative population. It is known that cancer-related fatigue is common among cancer patients and is considered one of the most burdensome symptoms experienced during and after treatment [63]. Arndt et al. demonstrated that fatigue and insomnia were more common in
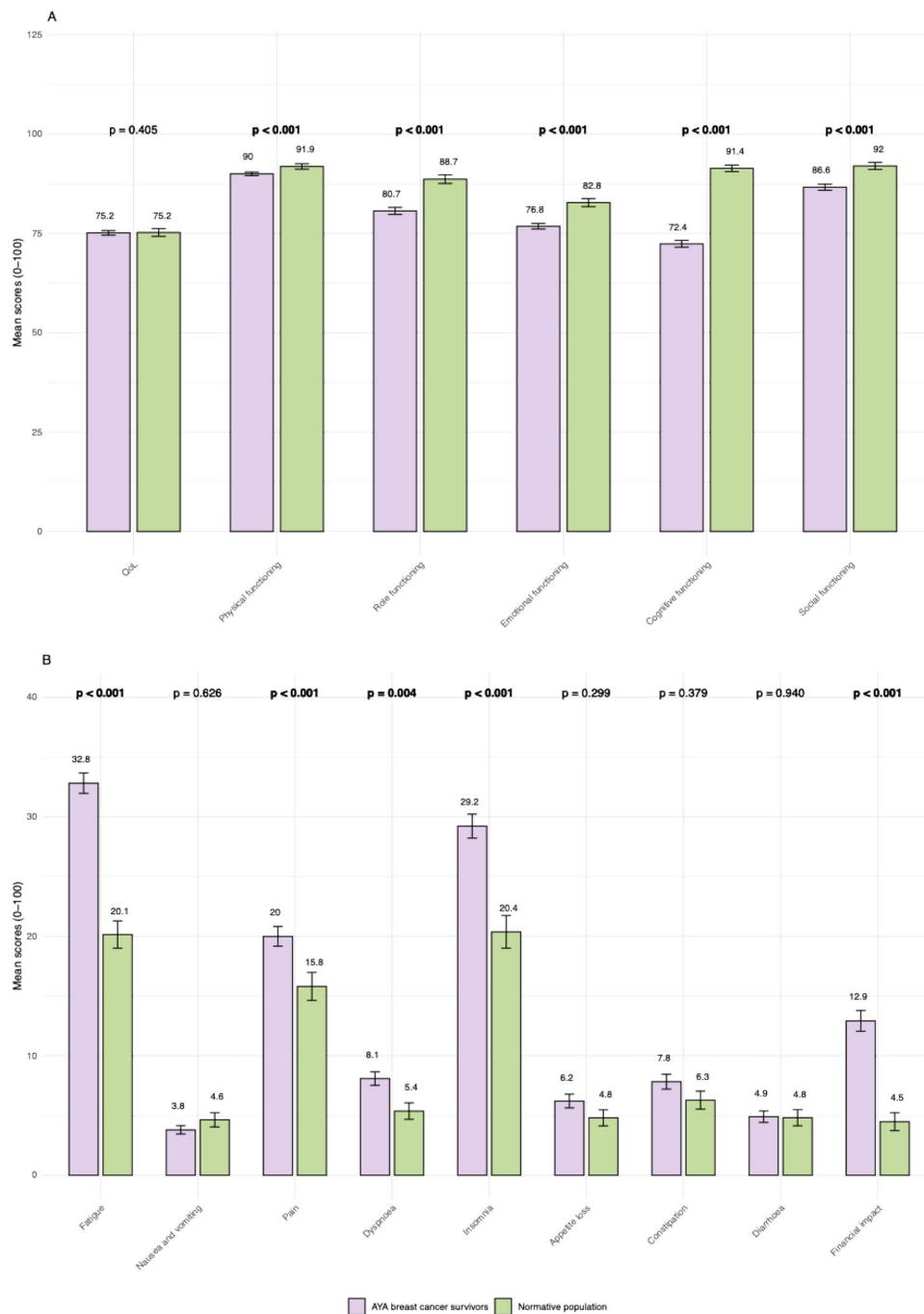
Fig. 1 Bar charts of the mean scores of EORTC QLQ-C30 functional scales (**a**) and symptom scales (**b**) for AYA breast cancer survivors (purple) and the normative population (green). A higher score on the functional scales represents a higher level of functioning, and a higher score on the symptom scales represents a higher level of symptoms. Abbreviations: *AYA* Adolescent and Young Adult, *EORTC QLQ-C30* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30, *QoL* quality of life. Error bars represent the standard error of the mean. Bold indicates P-value < 0.05

breast cancer patients (mean age 58.2 years) three years after diagnosis compared to the general population [61]. Similarly, a study with a six-year follow-up period reported that fatigue and insomnia were common in breast cancer survivors and associated with radiotherapy and hormonal therapy [64]. The current study, with a longer follow-up of 12 years, did not find any association between these symptoms and treatment characteristics. This discrepancy could be attributed to the possibility that the more immediate effects of treatment diminish over time.

Table 2 Multiple linear regression models of the functional scales of the EORTC QLQ-C30 among the AYA breast cancer survivors

Variables	Physical functioning		Role functioning		Emotional functioning		Cognitive functioning		Social functioning	
	Estimates	p	Estimates	p	Estimates	p	Estimates	p	Estimates	p
Age at diagnosis	− 0.24	**0.011**	− 0.21	0.200	0.13	0.380	− 0.43	**0.030**	− 0.21	0.199
Time since diagnosis	0.07	0.422	0.00	0.992	− 0.11	0.379	0.31	0.074	0.08	0.569
BMI										
Normal weight	Reference		Reference		Reference		Reference		Reference	
Overweight	− 1.77	**0.020**	0.52	0.692	1.56	0.174	3.07	**0.050**	1.00	0.442
Educational level										
Intermediate, secondary education	Reference		Reference		Reference		Reference		Reference	
Low, no primary school	2.57	0.666	6.17	0.546	6.49	0.469	− 8.48	0.489	6.10	0.548
High, college/university	2.03	**0.006**	− 3.47	**0.007**	0.42	0.707	5.61	**<0.001**	− 3.45	**0.007**
Relationship status										
Single	Reference		Reference		Reference		Reference		Reference	
Married/registered partnership	1.43	0.152	3.27	0.057	− 2.01	0.184	− 1.15	0.577	1.81	0.292
Relationship	2.65	**0.020**	4.48	**0.022**	− 0.59	0.729	0.29	0.903	3.74	0.055
Employment status										
Employed	Reference		Reference		Reference		Reference		Reference	
Self employed	− 1.64	0.117	− 2.37	0.187	− 1.37	0.385	− 1.20	0.577	− 0.53	0.769
Unemployed	− 5.38	**<0.001**	− 8.34	**<0.001**	− 0.51	0.744	− 3.90	0.068	− 6.43	**<0.001**
Chemotherapy										
No	Reference		Reference		Reference		Reference		Reference	
Yes	− 1.27	0.242	− 3.14	0.091	− 0.63	0.698	− 4.89	**0.028**	− 3.74	**0.043**
Radiotherapy										
No	Reference		Reference		Reference		Reference		Reference	
Yes	0.19	0.868	1.09	0.573	− 0.32	0.849	2.02	0.381	0.90	0.638
Hormonal therapy										
No	Reference		Reference		Reference		Reference		Reference	
Yes	− 1.26	0.092	− 1.52	0.235	0.67	0.550	− 0.86	0.574	− 1.41	0.268
Breast and axillary surgery										
BCS	Reference		Reference		Reference		Reference		Reference	
BCS + ALND	− 0.03	0.978	− 0.99	0.604	− 0.59	0.724	0.73	0.749	− 1.03	0.587
Mastectomy	1.31	0.278	2.20	0.289	− 2.08	0.254	− 0.50	0.840	− 0.52	0.802
Mastectomy + ALND	− 0.94	0.344	− 0.33	0.844	1.87	0.210	2.40	0.238	0.65	0.699
Body image	0.07	**<0.001**	0.11	**<0.001**	0.21	**<0.001**	0.19	**<0.001**	0.16	**<0.001**
Maladaptive scale	0.12	0.269	− 0.01	0.969	− 1.63	**<0.001**	− 0.20	0.365	− 0.52	**0.004**
Adaptive scale	0.08	0.087	0.03	0.688	0.21	**0.005**	− 0.07	0.475	0.02	0.814

Table 2 (continued)

Variables	Physical functioning		Role functioning		Emotional functioning		Cognitive functioning		Social functioning	
	Estimates	p	Estimates	p	Estimates	p	Estimates	p	Estimates	p
Fatigue	−0.16	**<0.001**	−0.30	**<0.001**	−0.20	**<0.001**	−0.33	**<0.001**	−0.23	**<0.001**
Pain	−0.16	**<0.001**	−0.46	**<0.001**	−0.02	0.415	−0.05	0.143	−0.23	**<0.001**
Insomnia	0.01	0.477	−0.02	0.414	−0.15	**<0.001**	−0.09	**0.001**	−0.06	**0.004**
Observations	851		851		851		851		850	
R^2/R^2 adjusted	0.455/0.441		0.560/0.549		0.483/0.470		0.350/0.333		0.449/0.435	

ALND axillary lymph node dissection, *BCS* breast-conserving surgery, *BMI* body mass index

Bold indicates P < 0.05

AYA breast cancer survivors also reported significantly higher, yet not clinically significant, pain and dyspnea scores. The prevalence of post-mastectomy pain syndrome, chronic pain in the breast/chest wall, axilla, or arm often of neurological origin after breast surgery, is known to be high in breast cancer survivors. A young age is an independent risk factor and may explain the high pain scores observed in this study [65–67]. Moreover, the higher dyspnea scores could be explained by the pulmonary effects of radiotherapy, as breast radiotherapy can lead to lung damage such as fibrosis [68, 69]. However, the current study did not find a direct association between dyspnea and radiotherapy. Instead, relationship status and body image were associated, suggesting that the psychosocial state of AYA breast cancer survivors could also influence the reported dyspnea.

Nausea and vomiting, appetite loss, constipation, and diarrhea symptoms were less common in the current study, which might be explained by the fact that these symptoms are more likely to be directly related to breast cancer treatment and may diminish over time [70].

Lastly, fatigue, pain, and insomnia were found to negatively impact all functional scales of the EORTC QLQ-C30, aligning with findings from De Ligt et al., which showed that health symptoms adversely affect daily functioning in early-stage breast cancer survivors (median age 62.2 ± 10.9 years) [60]. Additionally, Arndt et al. found that fatigue was the strongest predictor for functioning and overall QoL compared to other symptoms in breast cancer patients one year after diagnosis [71].

Financial impact

AYA breast cancer survivors reported statistically and clinically significant higher financial impact scores than the normative population. This difference can be explained by the fact that AYA cancer survivors often miss critical developmental milestones, such as completing their education or starting their first job, which is likely to impact their financial future [8–10, 72]. Additionally, unemployment was found to impact HRQoL negatively. The findings align with previous research showing that AYA cancer survivors are more frequently unemployed than matched controls and that a cancer diagnosis at a young age significantly impacts income levels [72, 73]. This highlights the need for financial support for AYA cancer survivors. Currently, eight members of the EU have implemented 'Rights To Be Forgotten' laws for cancer survivors to protect them from financial toxicity. There is an ongoing discussion about whether this period should be shortened for AYA cancer survivors [74].

Overall QoL

Literature on older patients demonstrated that although long-term breast cancer survivors scored lower on the functional

Table 3 Multiple linear regression models of the symptom scales of the EORTC QLQ-C30 among the AYA breast cancer survivors

Variables	Fatigue		Pain		Dyspnea		Insomnia		Financial impact	
	Estimates	p	Estimates	p	Estimates	p	Estimates	p	Estimates	p
Age at diagnosis	−0.14	0.476	0.53	**0.006**	−0.08	0.568	0.8	**0.002**	0.07	0.739
Time since diagnosis	−0.38	**0.031**	0	0.995	−0.08	0.564	0.06	0.789	−0.1	0.584
BMI										
Normal weight	Reference		Reference		Reference		Reference		Reference	
Overweight	−3.92	**0.015**	−2.4	0.122	1.46	0.221	−1.95	0.352	−1.18	0.477
Educational level										
Intermediate, secondary education	Reference		Reference		Reference		Reference		Reference	
Low, no primary school	−22.86	0.069	−6.65	0.584	−8.16	0.383	−3.53	0.83	20.78	0.11
High, college/university	1.01	0.517	−2.67	0.078	1.41	0.225	−2.56	0.21	−1.43	0.375
Relationship status										
Single	Reference		Reference		Reference		Reference		Reference	
Married/registered partnership	−4.81	**0.023**	−1.9	0.353	−5.03	**0.001**	0.61	0.826	−7.84	**<0.001**
Relationship	−4.76	**0.048**	0.79	0.733	−4.72	**0.008**	1.77	0.573	−7.01	**0.005**
Employment status										
Employed	Reference		Reference		Reference		Reference		Reference	
Self employed	1.5	0.497	2.29	0.283	1.59	0.333	3.32	0.25	4.93	**0.031**
Unemployed	7.93	**<0.001**	7.33	**<0.001**	2.77	0.086	2.75	0.331	18.16	**<0.001**
Chemotherapy										
No	Reference		Reference		Reference		Reference		Reference	
Yes	1.71	0.455	0.92	0.677	0.51	0.767	−1.82	0.542	0.44	0.851
Radiotherapy										
No	Reference		Reference		Reference		Reference		Reference	
Yes	−0.59	0.804	−1.07	0.639	1.16	0.51	4.91	0.113	−2.38	0.328
Hormonal therapy										
No	Reference		Reference		Reference		Reference		Reference	
Yes	0.18	0.907	−0.42	0.785	0.66	0.573	1.18	0.568	0.32	0.847
Breast and axillary surgery										
BCS	Reference		Reference		Reference		Reference		Reference	
BCS + ALND	−0.22	0.925	−2.57	0.257	3.47	**0.047**	−0.46	0.88	−0.36	0.882
Mastectomy	−2.5	0.325	−1.95	0.428	−1.37	0.47	1.79	0.591	−1.04	0.693
Mastectomy + ALND	0.99	0.636	−2.32	0.251	0.24	0.876	0.27	0.921	−0.68	0.753
Body image	−0.45	**<0.001**	−0.45	**<0.001**	−0.18	**<0.001**	−0.35	**<0.001**	−0.3	**<0.001**
Maladaptive scale	0.68	**0.002**	0.15	0.468	0.07	0.665	0.93	**0.001**	1.08	**<0.001**
Adaptive scale	0.08	0.435	0.16	0.122	0.04	0.629	−0.05	0.728	0.03	0.754

and higher on most symptom scales of the EORTC QLQ-C30 compared to the normative population, there was most often no significant difference on the overall QoL scale, which is in line with the current study [60, 75–78]. This is confirmed by the systematic review of Mols et al., stating that long-term breast cancer survivors experience good overall QoL but face specific functional and symptom-related problems [79]. An explanation for the overall good QoL among AYA breast cancer survivors can be the posttraumatic growth that cancer survivors develop after surviving cancer. Post-traumatic growth can result in a more positive outlook on life and is thought to improve one's perception of overall QoL despite the ongoing functional and symptom-related challenges [80, 81].

Clinical implications

It is valuable to discuss these long-term HRQoL effects with AYA breast cancer survivors during consultations and treatment decisions. Although novel treatments have enhanced breast cancer survival rates over the years, they also have negative effects [82]. Understanding these impacts can improve shared decision-making, helping patients and healthcare providers weigh the benefits and potential long-term consequences of treatment options.

Additionally, the results of the current study emphasize the importance of tailored follow-up care for AYA breast cancer survivors. While the direct supportive care for AYA cancer survivors has improved, there is a need for more comprehensive long-term support to address persistent physical and psychosocial challenges [8]. Factors such as a negative body image, maladaptive coping mechanism, unemployment and persistent fatigue, insomnia, and pain can be used to identify patients at risk for lower long-term HRQoL outcomes and are essential for effectively targeting interventions. Psychological and social interventions or support groups that enhance coping skills (with health problems) and address body image concerns should be components of survivorship care for AYAs, as highlighted by existing literature [8, 83, 84]. Furthermore, a tiered approach is essential to manage resources and ensure timely interventions efficiently. This could range from providing personalized information and accessible self-management tools through digital platforms designed for AYAs to more intensive support like regular checkups and contact with an AYA clinical nurse specialist when certain problems persist or worsen [8, 85, 86].

Strengths and limitations

To our knowledge, this is one of the first studies examining the long-term HRQoL of AYA breast cancer survivors, providing both healthcare professionals and AYA breast cancer survivors with valuable insights. The comparison with the

Table 3 (continued)

Variables	Fatigue		Pain		Dyspnea		Insomnia		Financial impact	
	Estimates	p	Estimates	p	Estimates	p	Estimates	p	Estimates	p
Observations	852		852		852		851		851	
R^2/R^2 adjusted	0.300/0.285		0.281/0.266		0.122/0.103		0.137/0.119		0.267/0.251	

ALND axillary lymph node dissection, *BCS* breast-conserving surgery, *BMI* body mass index

Bold indicates P < 0.05

normative population was essential to determine whether these survivors experience more long-term issues than typically expected, which is vital for understanding the extended impacts of their cancer diagnosis. Additionally, the comparison with the normative population enabled adjustment for the background risk of HRQoL impairments. Another key strength of this study is the availability of long-term HRQoL data and the large sample size (n = 944), which enhances the reliability of the results [3]. Moreover, the wide variety of demographic and clinical data within the SURVAYA database and the NCR allowed for the exploration of various potential associations. Furthermore, the non-responder analysis demonstrated no significant differences in baseline characteristics, which reduces the risk of selection bias.

A limitation of this study is the lack of data on several factors that can influence HRQoL. Firstly, data concerning the type of breast reconstruction was unavailable, as only primary breast surgeries were recorded within the NCR. Previous literature demonstrated that receiving a breast reconstruction has a significant positive influence on HRQoL [87]. Additionally, detailed data regarding the type and duration of hormonal therapy was missing. Breast cancer patients often undergo hormonal treatments for several years post-diagnosis (for AYA patients, often up to 10 years) to reduce the risk of recurrence. These treatments can have significant negative effects on HRQoL due to side effects such as sweating, hot flashes, and vaginal dryness. Moreover, different types of hormonal therapies, including ovarian function suppression, can have varying impacts on HRQoL [48, 49, 88–91]. Furthermore, data on menopausal status was absent. The systemic treatments that AYA breast cancer survivors receive can lead to early menopause and ovarian dysfunction, significantly affecting HRQoL [92]. Lastly, data on recurrence or distant metastasis was missing. Recurrence or distant metastasis can impact HRQoL, as they indicate a poorer prognosis and necessitate more aggressive treatments [93]. Future research should aim to include these factors to understand their distinct effects on patient outcomes. Another limitation is that only body image, which was associated with all scales of the EORTC QLQ-C30, and coping mechanisms were included as personality traits in the current study. A recent systematic review found that more personality traits such as optimism and neuroticism play an important role in the HRQoL of breast cancer patients [94]. Future research should aim to consider additional personality traits to interpret long-term HRQoL outcomes more accurately. Additionally, the assessment of cognitive functioning and pain is another limitation, as it relies on only a few questions from the EORTC QLQ-C30. Given that these scales showed large significant differences compared to the normative population, a more comprehensive examination in future studies would be valuable (e.g., issues with memory, concentration, processing speeds, and types of pain like surgical, radiative, nerve-related, or hormonal therapy-induced). Lastly,

the AYA breast cancer survivors included in the current study were treated in academic hospitals and the NCI, which likely represents a different population compared to AYA breast cancer survivors treated in general hospitals, which may limit the generalizability of the results.

Conclusion

AYA breast cancer survivors have significantly lower HRQoL, with decreased functioning and a greater burden of specific symptoms, compared to the matched normative population 5–20 years after their diagnosis. Age, BMI, relationship status, educational level, employment status, chemotherapy, body image, and coping mechanisms are all significantly associated with long-term HRQoL. The results of this study highlight the need for improvement in follow-up care and long-term support to enhance the HRQoL of AYA breast cancer survivors in the future. Furthermore, it is valuable to consider these long-term HRQoL effects during shared decision-making to support patient well-being and treatment satisfaction better.

Appendix

See Tables 4, 5 and 6.

Table 4 Baseline characteristics of the normative population

Characteristics	Overall (N = 409)
Age at time of filling out EORTC QLQ-C30 (years)	
Mean (SD)	47.6 (9.11)
Median [Min, Max]	47.0 [21.00, 64.00]
Relationship status, n (%)	
Married	234 (57.2)
Divorced	56 (13.7)
Widowed	13 (3.2)
Single	106 (25.9)
Educational level, n (%)	
Primary school	17 (4.2)
Pre-vocational secondary education	75 (18.3)
Senior general secondary education/pre-university education	37 (9.0)
Secondary vocational education	132 (32.3)
Higher professional education	100 (24.4)
University	48 (11.7)

EORTC QLQ-C30 European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30, *SD* standard deviation

Table 5 Non-responder analysis

Characteristics	Responder (n = 887)	Non-responder (n = 57)	P-value
Age at diagnosis (years)			
Mean (SD)	34.8 (3.84)	34.6 (3.99)	0.75
Median [Min, Max]	36.0 [18.0, 39.0]	36.0 [25.0, 39.0]	
Time since diagnosis (years)			
Mean (SD)	12.2 (4.49)	12.7 (4.87)	0.441
Median [Min, Max]	12.2 [4.41, 21.6]	13.6 [5.05, 20.2]	
Age at time of filling out EORTC QLQ-C30 (years)			
Mean (SD)	47.4 (6.16)	47.8 (5.77)	0.675
Median [Min, Max]	47.8 [23.7, 60.0]	18.1 [32.5, 58.9]	
BMI, n (%)			
Normal weight	547 (61.7)	26 (45.6)	0.825
Overweight	336 (37.9)	18 (31.6)	
Missing	4 (0.5)	13 (22.8)	
Relationship status, n (%)			
Registered partnership/married	509 (57.4)	36 (63.2)	0.604
Relationship	235 (26.5)	12 (21.1)	
Single	139 (15.7)	8 (14.0)	
Missing	4 (0.5)	1 (1.8)	
Educational level, n (%)			
Low, no primary school	4 (0.5)	1 (1.8)	0.329
Intermediate, secondary education	352 (39.7)	25 (43.9)	
High, college/university	531 (59.9)	31 (54.4)	
Employment status, n (%)			
Employed	629 (70.9)	35 (61.4)	0.285
Self employed	118 (13.3)	11 (19.3)	
Unemployed	140 (15.8)	11 (19.3)	
Tumor stage, n (%)			
1	320 (36.1)	18 (31.6)	0.822
2	418 (47.1)	29 (50.9)	
3	143 (16.1)	10 (17.5)	
4	6 (0.7)	0 (0)	
Chemotherapy, n (%)			
Yes	756 (85.2)	51 (89.5)	0.492
No	131 (14.8)	6 (10.5)	
Radiotherapy, n (%)			
Yes	683 (77.0)	47 (82.5)	0.429
No	204 (23.0)	10 (17.5)	
Hormonal therapy, n (%)			
Yes	452 (51.0)	27 (47.4)	0.697
No	435 (49.0)	30 (52.6)	
Targeted therapy, n (%)			
Yes	165 (18.6)	8 (14.0)	0.492
No	722 (81.4)	49 (86.0)	
Breast and axillary surgery, n (%)			
BCS	346 (39.0)	23 (40.4)	0.971
BCS + ALND	124 (14.0)	9 (15.8)	
Mastectomy	204 (23.0)	12 (21.1)	
Mastectomy + ALND	206 (23.2)	13 (22.8)	
Missing	7 (0.8)	0 (0)	

BCS breast-conserving surgery, *ALND* axillary lymph node dissection, *BMI* body mass index, *EORTC QLQ-C30* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30, *SD* standard deviation

Table 6 EORTC QLQ-C30 scores of AYA breast cancer survivors compared to the normative population

	AYA breast cancer survivors (n=887)	Normative population (n=409)	P-value
Functional scales (0–100)			
QoL			
Mean (SD)	75.2 (17.7)	75.2 (19.5)	0.405
Median [Min, Max]	75.0 [8.33, 100]	83.3 [0, 100]	
Missing, *n* (%)	8 (0.9%)	1 (0.2%)	
Physical functioning			
Mean (SD)	90.0 (13.6)	91.9 (13.7)	**<0.001**
Median [Min, Max]	93.3 [0, 100]	100 [33.3, 100]	
Missing, *n* (%)	1 (0.1%)	0 (0%)	
Role functioning			
Mean (SD)	80.7 (26.1)	88.7 (22.0)	**<0.001**
Median [Min, Max]	100 [0, 100]	100 [0, 100]	
Missing, *n* (%)	4 (0.5%)	0 (0%)	
Emotional functioning			
Mean (SD)	76.8 (21.0)	82.8 (20.4)	**<0.001**
Median [Min, Max]	83.3 [0, 100]	91.7 [0, 100]	
Missing, *n* (%)	2 (0.2%)	1 (0.2%)	
Cognitive functioning			
Mean (SD)	72.4 (25.3)	91.4 (16.5)	**<0.001**
Median [Min, Max]	83.3 [0, 100]	100 [0, 100]	
Missing, *n* (%)	2 (0.2%)	1 (0.2%)	
Social functioning			
Mean (SD)	86.6 (22.9)	92.0 (17.8)	**<0.001**
Median [Min, Max]	100 [0, 100]	100 [0, 100]	
Missing, *n* (%)	5 (0.6%)	1 (0.2%)	
Symptom scales (0–100)			
Fatigue			
Mean (SD)	32.8 (25.3)	20.1 (23.1)	**<0.001**
Median [Min, Max]	33.3 [0, 100]	11.1 [0, 100]	
Missing, *n* (%)	2 (0.2%)	0 (0%)	
Nausea and vomiting			
Mean (SD)	3.80 (10.3)	4.65 (12.1)	0.626
Median [Min, Max]	0 [0, 100]	0 [0, 83.3]	
Missing, *n* (%)	2 (0.2%)	0 (0%)	
Pain			
Mean (SD)	20.0 (24.4)	15.8 (23.7)	**<0.001**
Median [Min, Max]	16.7 [0, 100]	0 [0, 100]	
Missing, *n* (%)	1 (0.1%)	0 (0%)	
Dyspnea			
Mean (SD)	8.10 (16.9)	5.38 (13.9)	**0.004**

Table 6 (continued)

	AYA breast cancer survivors (n=887)	Normative population (n=409)	P-value
Median [Min, Max]	0 [0, 100]	0 [0, 100]	
Missing, *n* (%)	2 (0.2%)	0 (0%)	
Insomnia			
Mean (SD)	29.2 (29.8)	20.4 (27.7)	**<0.001**
Median [Min, Max]	33.3 [0, 100]	0 [0, 100]	
Missing, *n* (%)	3 (0.3%)	0 (0%)	
Appetite loss			
Mean (SD)	6.21 (17.0)	4.81 (13.7)	0.299
Median [Min, Max]	0 [0, 100]	0 [0, 66.7]	
Missing, *n* (%)	2 (0.2%)	0 (0%)	
Constipation			
Mean (SD)	7.83 (18.5)	6.29 (15.2)	0.379
Median [Min, Max]	0 [0, 100]	0 [0, 100]	
Missing, *n* (%)	2 (0.2%)	1 (0.2%)	
Diarrhea			
Mean (SD)	4.91 (14.2)	4.82 (13.7)	0.94
Median [Min, Max]	0 [0, 100]	0 [0, 66.7]	
Missing, *n* (%)	4 (0.5%)	1 (0.2%)	
Financial impact			
Mean (SD)	12.9 (25.8)	4.49 (15.1)	**<0.001**
Median [Min, Max]	0 [0, 100]	0 [0, 100]	
Missing, *n* (%)	5 (0.6%)	1 (0.2%)	

AYA Adolescent and Young Adult, *QoL* quality of life, *SD* standard deviation

Bold indicates P<0.05

Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical approval The SURVAYA study was conducted in accordance with the Declaration of Helsinki, approved and reviewed by the Netherlands Cancer Institute Institutional Review Board (IRB-IRBd18122) on 6 February 2019 and registered within clinical trial registration (NCT05379387). The Netherlands Cancer Registry (NCR) provided approval of the linkage, access, and utilization of the clinical data.

Informed consent Informed consent was obtained from all subjects (responders) involved in the study.

References

1. National Cancer Institute, & Lance Armstrong Foundation. (2006). Closing the gap: Research and care imperatives for adolescents and young adults with cancer. *Report of the Adolescent and Young Adult Oncology Progress Review Group*.

2. Smith, A. W., Seibel, N. L., Lewis, D. R., Albritton, K. H., Blair, D. F., Blanke, C. D., Archie Bleyer, W., Freyer, D. R., Geiger, A. M., Hayes-Lattin, B., Tricoli, J. V., Wagner, L. I., & Zebrack, B. J. (2016). Next steps for adolescent and young adult oncology workshop: An update on progress and recommendations for the future. *Cancer, 122*(7), 988–999. https://doi.org/10.1002/cncr.29870

3. Vlooswijk, C., van de Poll-Franse, L. V., Janssen, S. H. M., Derksen, E., Reuvers, M. J. P., Bijlsma, R., Kaal, S. E. J., Kerst, J. M., Tromp, J. M., Bos, M. E. M. M., van der Hulle, T., Lalisang, R. I., Nuver, J., Kouwenhoven, M. C. M., van der Graaf, W. T. A., & Husson, O. (2022). Recruiting adolescent and young adult cancer survivors for patient-reported outcome research: Experiences and sample characteristics of the SURVAYA study. *Current Oncology (Toronto, Ont.), 29*(8), 5407–5425. https://doi.org/10.3390/curroncol29080428

4. Trama, A., Stark, D., Bozovic-Spasojevic, I., Gaspar, N., Peccatori, F., Toss, A., Bernasconi, A., Quarello, P., Scheinemann, K., Jezdic, S., Blondeel, A., Mountzios, G., Bielack, S., Saloustros, E., & Ferrari, A. (2023). Cancer burden in adolescents and young adults in Europe. *ESMO Open, 8*(1), 100744. https://doi.org/10.1016/j.esmoop.2022.100744

5. You, L., Lv, Z., Li, C., Ye, W., Zhou, Y., Jin, J., & Han, Q. (2021). Worldwide cancer statistics of adolescents and young adults in 2019: A systematic analysis of the Global Burden of Disease Study 2019. *ESMO Open, 6*(5), 100255. https://doi.org/10.1016/j.esmoop.2021.100255

6. Berkman, A. M., Livingston, J. A., Merriman, K., Hildebrandt, M., Wang, J., Dibaj, S., McQuade, J., You, N., Ying, A., Barcenas, C., Bodurka, D., DePombo, A., Lee, H. J., de Groot, J., & Roth, M. (2020). Long-term survival among 5-year survivors of adolescent and young adult cancer. *Cancer, 126*(16), 3708–3718. https://doi.org/10.1002/cncr.33003

7. Keegan, T. H. M., Ries, L. A. G., Barr, R. D., Geiger, A. M., Dahlke, D. V., Pollock, B. H., & Bleyer, W. A. (2016). Comparison of cancer survival trends in the United States of adolescents and young adults with those in children and older adults. *Cancer, 122*(7), 1009–1016. https://doi.org/10.1002/cncr.29869

8. Janssen, S. H. M., van der Graaf, W. T. A., van der Meer, D. J., Manten-Horst, E., & Husson, O. (2021). Adolescent and young adult (AYA) cancer survivorship practices: An overview. *Cancers, 13*(19), 4847. https://doi.org/10.3390/cancers13194847

9. Jin, Z., Griffith, M. A., & Rosenthal, A. C. (2021). Identifying and meeting the needs of adolescents and young adults with cancer. *Current Oncology Reports, 23*(2), 17. https://doi.org/10.1007/s11912-020-01011-9

10. Close, A. G., Dreyzin, A., Miller, K. D., Seynnaeve, B. K. N., & Rapkin, L. B. (2019). Adolescent and young adult oncology-past, present, and future. *CA: A Cancer Journal for Clinicians, 69*(6), 485–496. https://doi.org/10.3322/caac.21585

11. Smith, E. C., Ziogas, A., & Anton-Culver, H. (2013). Delay in surgical treatment and survival after breast cancer diagnosis in young women by race/ethnicity. *JAMA Surgery, 148*(6), 516. https://doi.org/10.1001/jamasurg.2013.1680

12. Barr, R. D., Ferrari, A., Ries, L., Whelan, J., & Bleyer, W. A. (2016). Cancer in adolescents and young adults: A narrative review of the current status and a view of the future. *JAMA Pediatrics, 170*(5), 495–501. https://doi.org/10.1001/jamapediatrics.2015.4689

13. Hughes, T., Harper, A., Gupta, S., Frazier, A. L., van der Graaf, W. T., Moreno, F., Joseph, A., & Fidler-Benaoudia, M. M. (2024). The current and future global burden of cancer among adolescents and young adults: a population-based study. *The Lancet Oncology*. https://doi.org/10.1016/S1470-2045(24)00523-0

14. van der Meer, D. J., Kramer, I., van Maaren, M. C., van Diest, P. J., Linn, S. C., Maduro, J. H., Strobbe, L. J. A., Siesling, S., Schmidt, M. K., & Voogd, A. C. (2021). Comprehensive trends in incidence, treatment, survival and mortality of first primary invasive breast cancer stratified by age, stage and receptor subtype in the Netherlands between 1989 and 2017. *International Journal of Cancer, 148*(9), 2289–2303. https://doi.org/10.1002/ijc.33417

15. El Saghir, N. S., Khalil, L. E., El Dick, J., Atwani, R. W., Safi, N., Charafeddine, M., Al-Masri, A., El Saghir, B. N., Chaccour, M., Tfayli, A., Assi, H., Abbas, J., Ayoub, Z., Sbaity, E., & Moukadem, H. A. (2023). Improved survival of young patients with breast cancer 40 years and younger at diagnosis. *JCO Global Oncology, 9*, e2200354. https://doi.org/10.1200/GO.22.00354

16. Trama, A., Botta, L., Foschi, R., Ferrari, A., Stiller, C., Desandes, E., Maule, M. M., Merletti, F., Gatta, G., EUROCARE-5 Working Group. (2016). Survival of European adolescents and young adults diagnosed with cancer in 2000–07: Population-based data from EUROCARE-5. *The Lancet Oncology, 17*(7), 896–906. https://doi.org/10.1016/S1470-2045(16)00162-5

17. Javan Biparva, A., Raoofi, S., Rafiei, S., Pashazadeh Kan, F., Kazerooni, M., Bagheribayati, F., Masoumi, M., Doustmehraban, M., Sanaei, M., Zarabi, F., Raoofi, N., Chomalu, Z. B., Ahmadi, B., Talab, F. S., Hoseini, B. S., Asadollahi, E., Mir, M., Deylami, S., Zareei, M., … Ghashghaee, A. (2022). Global quality of life in breast cancer: systematic review and meta-analysis. *BMJ Supportive & Palliative Care*. https://doi.org/10.1136/bmjspcare-2022-003642

18. Epplein, M., Zheng, Y., Zheng, W., Chen, Z., Gu, K., Penson, D., Lu, W., & Shu, X.-O. (2011). Quality of life after breast cancer diagnosis and survival. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology, 29*(4), 406–412. https://doi.org/10.1200/JCO.2010.30.6951

19. Heins, M. J., de Ligt, K. M., Verloop, J., Siesling, S., Korevaar, J. C., & PSCCR group. (2022). Adverse health effects after breast cancer up to 14 years after diagnosis. *Breast (Edinburgh, Scotland), 61*, 22–28. https://doi.org/10.1016/j.breast.2021.12.001

20. Ganz, P. A., Desmond, K. A., Leedham, B., Rowland, J. H., Meyerowitz, B. E., & Belin, T. R. (2002). Quality of life in long-term, disease-free survivors of breast cancer: A follow-up study. *Journal of the National Cancer Institute, 94*(1), 39–49. https://doi.org/10.1093/jnci/94.1.39

21. Tai, E., Buchanan, N., Townsend, J., Fairley, T., Moore, A., & Richardson, L. C. (2012). Health status of adolescent and young adult cancer survivors. *Cancer, 118*(19), 4884–4891. https://doi.org/10.1002/cncr.27445

22. Harju, E., Roser, K., Dehler, S., & Michel, G. (2018). Health-related quality of life in adolescent and young adult cancer survivors. *Supportive Care in Cancer, 26*(9), 3099–3110. https://doi.org/10.1007/s00520-018-4151-z

23. Abdo, J., Ortman, H., Rodriguez, N., Tillman, R., Riordan, E. O., & Seydel, A. (2023). Quality of life issues following breast cancer treatment. *The Surgical Clinics of North America, 103*(1), 155–167. https://doi.org/10.1016/j.suc.2022.08.014

24. Carreira, H., Williams, R., Dempsey, H., Stanway, S., Smeeth, L., & Bhaskaran, K. (2021). Quality of life and mental health in breast cancer survivors compared with non-cancer controls: A study of patient-reported outcomes in the United Kingdom. *Journal of Cancer Survivorship, 15*(4), 564–575. https://doi.org/10.1007/s11764-020-00950-3

25. Quinten, C., Coens, C., Ghislain, I., Zikos, E., Sprangers, M. A. G., Ringash, J., Martinelli, F., Ediebah, D. E., Maringwa, J., Reeve, B. B., Greimel, E., King, M. T., Bjordal, K., Flechtner, H.-H., Koch, J.-V., Taphoorn, M. J. B., Weis, J., Wildiers, H., Velikova, G., & Bottomley, A. (2015). The effects of age on health-related quality of life in cancer populations: A pooled analysis of randomized controlled trials using the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 involving 6024 cancer patients. *European Journal of Cancer, 51*(18), 2808–2819. https://doi.org/10.1016/j.ejca.2015.08.027

26. Vrancken Peeters, N. J. M. C., Vlooswijk, C., Bijlsma, R. M., Kaal, S. E. J., Kerst, J. M., Tromp, J. M., Bos, M. E. M. M., van der Hulle, T., Lalisang, R. I., Nuver, J., Kouwenhoven, M. C. M., van der Ploeg, I. M. C., van der Graaf, W. T. A., & Husson, O. (2024). Sexual quality of life of adolescents and young adult breast cancer survivors. *ESMO Open, 9*(2), 102234. https://doi.org/10.1016/j.esmoop.2024.102234

27. Solvi, A. S., Foss, K., von Soest, T., Roald, H. E., Skolleborg, K. C., & Holte, A. (2010). Motivational factors and psychological processes in cosmetic breast augmentation surgery. *Journal of Plastic, Reconstructive & Aesthetic Surgery, 63*(4), 673–680. https://doi.org/10.1016/j.bjps.2009.01.024

28. Li, J., Humphreys, K., Eriksson, M., Dar, H., Brandberg, Y., Hall, P., & Czene, K. (2016). Worse quality of life in young and recently diagnosed breast cancer survivors compared with female survivors of other cancers: A cross-sectional study. *International Journal of Cancer, 139*(11), 2415–2425. https://doi.org/10.1002/ijc.30370

29. NKR. (2023). Integraal Kankercentrum Nederland. Retrieved August 23, 2023, from https://iknl.nl/nkr

30. van de Poll-Franse, L. V., Horevoorts, N., van Eenbergen, M., Denollet, J., Roukema, J. A., Aaronson, N. K., Vingerhoets, A., Coebergh, J. W., de Vries, J., Essink-Bot, M.-L., & Mols, F. (2011). The Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *European Journal of Cancer (Oxford, England: 1990), 47*(14), 2188–2194. https://doi.org/10.1016/j.ejca.2011.04.034

31. van de Poll-Franse, L. V., Mols, F., Gundy, C. M., Creutzberg, C. L., Nout, R. A., Verdonck-de Leeuw, I. M., Taphoorn, M. J., & Aaronson, N. K. (2011). Normative data for the EORTC QLQ-C30 and EORTC-sexuality items in the general Dutch population. *European Journal of Cancer, 47*(5), 667–675. https://doi.org/10.1016/j.ejca.2010.11.004

32. Gail, M. H. (2014). Frequency matching. In *Wiley StatsRef: Statistics reference online*. Wiley. https://doi.org/10.1002/9781118445112.stat05163

33. Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N. J., Filiberti, A., Flechtner, H., Fleishman, S. B., de Haes, J. C. J. M., Kaasa, S., Klee, M., Osoba, D., Razavi, D., Rofe, P. B., Schraub, S., Sneeuw, K., Sullivan, M., & Takeda, F. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute, 85*(5), 365–376. https://doi.org/10.1093/jnci/85.5.365

34. Cocks, K., Wells, J. R., Johnson, C., Schmidt, H., Koller, M., Oerlemans, S., Velikova, G., Pinto, M., Tomaszewski, K. A., Aaronson, N. K., Exall, E., Finbow, C., Fitzsimmons, D., Grant, L., Groenvold, M., Tolley, C., Wheelwright, S., Bottomley, A., European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group. (2023). Content validity of the EORTC quality of life questionnaire QLQ-C30 for use in cancer. *European Journal of Cancer (Oxford, England: 1990), 178*, 128–138. https://doi.org/10.1016/j.ejca.2022.10.026

35. Fayers, P. M., NK, A., K, B., M, G., D, C., & A, B. (2001). EORTC QLQ-C30 Scoring Manual The EORTC QLQ-C30 Introduction. *EORTC QLQ-C30 Scoring Manual, 30*, 1–67. Retrieved from http://www.eortc.be/qol/files/scmanualqlq-c30.pdf

36. Osoba, D., Rodrigues, G., Myles, J., Zee, B., & Pater, J. (2023). Interpreting the Significance of Changes in Health-Related Quality-of-Life Scores. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology, 41*(35), 5345–5350. https://doi.org/10.1200/JCO.22.02776

37. Morrow, P. K., Broxson, A. C., Munsell, M. F., Basen-Enquist, K., Rosenblum, C. K., Schover, L. R., Nguyen, L. H., Hsu, L., Castillo, L., Hahn, K. M., Litton, J. K., Kwiatkowski, D. N., & Hortobagyi, G. N. (2014). Effect of age and race on quality of life in young breast cancer survivors. *Clinical Breast Cancer, 14*(2), e21-31. https://doi.org/10.1016/j.clbc.2013.10.003

38. Paterson, C. L., Lengacher, C. A., Donovan, K. A., Kip, K. E., & Tofthagen, C. S. (2016). Body image in younger breast cancer survivors: A systematic review. *Cancer Nursing, 39*(1), E39-58. https://doi.org/10.1097/NCC.0000000000000251

39. Timperi, A. W., Ergas, I. J., Rehkopf, D. H., Roh, J. M., Kwan, M. L., & Kushi, L. H. (2013). Employment status and quality of life in recently diagnosed breast cancer survivors. *Psycho-Oncology, 22*(6), 1411–1420. https://doi.org/10.1002/pon.3157

40. van Leeuwen, M., Kieffer, J. M., Young, T. E., Annunziata, M. A., Arndt, V., Arraras, J. I., Autran, D., Hani, H. B., Chakrabarti, M., Chinot, O., Cho, J., Aloisio da Costa Vieira, R., Darlington, A.-S., Debruyne, P. R., Dirven, L., Doege, D., Eller, Y., Eichler, M., … QLG, E. (2023). Phase III study of the European Organisation for Research and Treatment of Cancer Quality of Life cancer survivorship core questionnaire. *Journal of Cancer Survivorship: Research and Practice, 17*(4), 1111–1130. https://doi.org/10.1007/s11764-021-01160-1

41. Garnefski, N., Kraaij, V., & Spinhoven, P. (2001). Negative life events, cognitive emotion regulation and emotional problems. *Personality and Individual Differences, 30*(8), 1311–1327. https://doi.org/10.1016/S0191-8869(00)00113-6

42. Garnefski, N., & Kraaij, V. (2006). Cognitive emotion regulation questionnaire—Development of a short 18-item version (CERQ-short). *Personality and Individual Differences, 41*(6), 1045–1053. https://doi.org/10.1016/j.paid.2006.04.010

43. Kim, J. H. (2019). Multicollinearity and misleading statistical results. *Korean Journal of Anesthesiology, 72*(6), 558–569. https://doi.org/10.4097/kja.19087

44. Team, R. C. (2023). *R: A Language and environment for statistical computing*. R Foundation for Statistical Computing. Retrieved from https://www.r-project.org/

45. Murphy, B. L., Day, C. N., Hoskin, T. L., Habermann, E. B., & Boughey, J. C. (2019). Adolescents and young adults with breast cancer have more aggressive disease and treatment than patients in their forties. *Annals of Surgical Oncology, 26*(12), 3920–3930. https://doi.org/10.1245/s10434-019-07653-9

46. Selamat, M. H., Loh, S. Y., Mackenzie, L., & Vardy, J. (2014). Chemobrain experienced by breast cancer survivors: A meta-ethnography study investigating research and care implications. *PLoS ONE, 9*(9), e108002. https://doi.org/10.1371/journal.pone.0108002

47. Haggstrom, L. R., Vardy, J. L., Carson, E.-K., Segara, D., Lim, E., & Kiely, B. E. (2022). Effects of endocrine therapy on cognitive function in patients with breast cancer: A comprehensive review. *Cancers, 14*(4), 920. https://doi.org/10.3390/cancers14040920

48. Lee, P. E., Tierney, M. C., Wu, W., Pritchard, K. I., & Rochon, P. A. (2016). Endocrine treatment-associated cognitive impairment in breast cancer survivors: Evidence from published studies. *Breast Cancer Research and Treatment, 158*(3), 407–420. https://doi.org/10.1007/s10549-016-3906-9

49. Schilder, C. M., Eggens, P. C., Seynaeve, C., Linn, S. C., Boogerd, W., Gundy, C. M., Beex, L. V., Van Dam, F. S., & Schagen, S. B. (2009). Neuropsychological functioning in postmenopausal breast cancer patients treated with tamoxifen or exemestane after AC-chemotherapy: Cross-sectional findings from the neuropsychological TEAM-side study. *Acta Oncologica, 48*(1), 76–85. https://doi.org/10.1080/02841860802314738

50. Underwood, E. A., Rochon, P. A., Moineddin, R., Lee, P. E., Wu, W., Pritchard, K. I., & Tierney, M. C. (2018). Cognitive sequelae of endocrine therapy in women treated for breast cancer: A meta-analysis. *Breast Cancer Research and Treatment, 168*(2), 299–310. https://doi.org/10.1007/s10549-017-4627-4

51. Gregorowitsch, M. L., Ghedri, A., Young-Afat, D. A., Bijlsma, R., Baas, I. O., van Schaik-van de Mheen, C., Agterof, M. J., Göker, E., ten Bokkel Huinink, D., van den Bongard, H. J. G. D., & Verkooijen, H. M. (2019). The effect of chemotherapy on subjective cognitive function in younger early-stage breast cancer survivors treated with chemotherapy compared to older patients. *Breast Cancer Research and Treatment, 175*(2), 429–441. https://doi.org/10.1007/s10549-019-05149-4

52. Hermelink, K. (2015). Chemotherapy and cognitive function in breast cancer patients: The so-called chemo brain. *Journal of the National Cancer Institute Monographs, 2015*(51), 67–69. https://doi.org/10.1093/jncimonographs/lgv009

53. van Dam, F. S. A. M., Boogerd, W., Schagen, S. B., Muller, M. J., Droogleever Fortuyn, M. E., Wall, E., & Rodenhuis, S. (1998). Impairment of Cognitive function in women receiving adjuvant treatment for high-risk breast cancer: High-dose versus standard-dose chemotherapy. *JNCI: Journal of the National Cancer Institute, 90*(3), 210–218. https://doi.org/10.1093/jnci/90.3.210

54. Dijkshoorn, A. B. C., van Stralen, H. E., Sloots, M., Schagen, S. B., Visser-Meily, J. M. A., & Schepers, V. P. M. (2021). Prevalence of cognitive impairment and change in patients with breast cancer: A systematic review of longitudinal studies. *Psycho-Oncology, 30*(5), 635–648. https://doi.org/10.1002/pon.5623

55. Schagen, S. B., van Dam, F. S. A. M., Muller, M. J., Boogerd, W., Lindeboom, J., & Bruning, P. F. (1999). Cognitive deficits after postoperative adjuvant chemotherapy for breast carcinoma. *Cancer, 85*(3), 640–650. https://doi.org/10.1002/(SICI)1097-0142(19990201)85:3%3c640::AID-CNCR14%3e3.0.CO;2-G

56. Wagner, L. I., Gray, R. J., Sparano, J. A., Whelan, T. J., Garcia, S. F., Yanez, B., Tevaarwerk, A. J., Carlos, R. C., Albain, K. S., Olson, J. A., Goetz, M. P., Pritchard, K. I., Hayes, D. F., Geyer, C. E., Claire Dees, E., McCaskill-Stevens, W. J., Minasian, L. M., Sledge, G. W., & Cella, D. (2020). Patient-reported cognitive impairment among women with early breast cancer randomly assigned to endocrine therapy alone versus chemoendocrine therapy: Results from TAILORx. *Journal of Clinical Oncology, 38*(17), 1875–1886. https://doi.org/10.1200/JCO.19.01866

57. Buchanan, N. D., Dasari, S., Rodriguez, J. L., Lee Smith, J., Hodgson, M. E., Weinberg, C. R., & Sandler, D. P. (2015). Post-treatment Neurocognition and Psychosocial Care Among Breast Cancer Survivors. *American Journal of Preventive Medicine, 49*(6), S498–S508. https://doi.org/10.1016/j.amepre.2015.08.013

58. Mandelblatt, J. S., Clapp, J. D., Luta, G., Faul, L. A., Tallarico, M. D., McClendon, T. D., Whitley, J. A., Cai, L., Ahles, T. A., Stern, R. A., Jacobsen, P. B., Small, B. J., Pitcher, B. N., Dura-Fernandis, E., Muss, H. B., Hurria, A., Cohen, H. J., & Isaacs, C. (2016). Long-term trajectories of self-reported cognitive function in a cohort of older survivors of breast cancer: CALGB 369901 (Alliance). *Cancer, 122*(22), 3555–3563. https://doi.org/10.1002/cncr.30208

59. Hermelink, K., Voigt, V., Kaste, J., Neufeld, F., Wuerstlein, R., Buhner, M., Munzel, K., Rjosk-Dendorfer, D., Grandl, S., Braun, M., von Koch, F. E., Hartl, K., Hasmuller, S., Bauerfeind, I., Debus, G., Herschbach, P., & Harbeck, N. (2015). Elucidating pretreatment cognitive impairment in breast cancer patients: The impact of cancer-related post-traumatic stress. *JNCI Journal of the National Cancer Institute, 107*(7), djv099. https://doi.org/10.1093/jnci/djv099

60. de Ligt, K. M., Heins, M., Verloop, J., Ezendam, N. P. M., Smorenburg, C. H., Korevaar, J. C., & Siesling, S. (2019). The impact of health symptoms on health-related quality of life in early-stage breast cancer survivors. *Breast Cancer Research and Treatment, 178*(3), 703–711. https://doi.org/10.1007/s10549-019-05433-3

61. Arndt, V., Merx, H., Stegmaier, C., Ziegler, H., & Brenner, H. (2005). Persistence of restrictions in quality of life from the first to the third year after diagnosis in women with breast cancer. *Journal of Clinical Oncology, 23*(22), 4945–4953. https://doi.org/10.1200/JCO.2005.03.475

62. Bloom, J. R., Stewart, S. L., Chang, S., & Banks, P. J. (2004). Then and now: Quality of life of young breast cancer survivors. *Psycho-Oncology, 13*(3), 147–160. https://doi.org/10.1002/pon.794

63. Prue, G., Rankin, J., Allen, J., Gracey, J., & Cramp, F. (2006). Cancer-related fatigue: A critical appraisal. *European Journal of Cancer, 42*(7), 846–863. https://doi.org/10.1016/j.ejca.2005.11.026

64. Boldyrev, L., Ghebremichael, M. S., Lotz, M. M., Kovarie, G., Kennedy, K., Keates, S., & Pories, S. E. (2022). Sleepless and spent in survivorship: Fatigue and Insomnia in breast cancer survivors. *The American Surgeon, 88*(11), 2730–2736. https://doi.org/10.1177/00031348221078949

65. Waltho, D., & Rockwell, G. (2016). Post–breast surgery pain syndrome: Establishing a consensus for the definition of post-mastectomy pain syndrome to provide a standardized clinical and research approach—A review of the literature and discussion. *Canadian Journal of Surgery, 59*(5), 342–350. https://doi.org/10.1503/cjs.000716

66. Lovelace, D. L., McDaniel, L. R., & Golden, D. (2019). Long-term effects of breast cancer surgery, treatment, and survivor care. *Journal of Midwifery & Women's Health, 64*(6), 713–724. https://doi.org/10.1111/jmwh.13012

67. De Oliveira, G. S., Chang, R., Khan, S. A., Hansen, N. M., Khan, J. H., McCarthy, R. J., & Apkarian, A. V. (2014). Factors

associated with the development of chronic pain after surgery for breast cancer: A prospective cohort from a Tertiary Center in the United States. *The Breast Journal, 20*(1), 9–14. https://doi.org/10.1111/tbj.12207

68. Karlsen, J., Tandstad, T., Steinshamn, S., Salvesen, Ø., Parlikar, N. D., Lundgren, S., & Reidunsdatter, R. J. (2023). Pulmonary function and lung fibrosis up to 12 years after breast cancer radiotherapy. *International Journal of Radiation Oncology*Biology*Physics.* https://doi.org/10.1016/j.ijrobp.2023.10.026

69. Davis, S. D., Yankelevitz, D. F., & Henschke, C. I. (1992). Radiation effects on the lung: Clinical features, pathology, and imaging findings. *American Journal of Roentgenology, 159*(6), 1157–1164. https://doi.org/10.2214/ajr.159.6.1442375

70. Shapiro, C. L., & Recht, A. (2001). Side effects of adjuvant treatment of breast cancer. *New England Journal of Medicine, 344*(26), 1997–2008. https://doi.org/10.1056/NEJM200106283442607

71. Arndt, V., Stegmaier, C., Ziegler, H., & Brenner, H. (2006). A population-based study of the impact of specific symptoms on quality of life in women with breast cancer 1 year after diagnosis. *Cancer, 107*(10), 2496–2503. https://doi.org/10.1002/cncr.22274

72. Siebinga, T. M., Janssen, S. H. M., Boumans, A. W., Van Eenbergen, M. C., Siflinger, B., Van Der Graaf, W. T. A., & Husson, O. (2023). Financial outcomes of adolescent and young adult cancer survivors: a longitudinal population-based registry study. *JNCI: Journal of the National Cancer Institute, 115*(11), 1294–1301. https://doi.org/10.1093/jnci/djad107

73. Janssen, S. H. M., van der Meer, D. J., van Eenbergen, M. C. H. J., Manten-Horst, E., van der Graaf, W. T. A., & Husson, O. (2022). Short- and long-term impact of cancer on employment and financial outcomes of adolescents and young adults (AYAs): A large population-based case-control registry study in the Netherlands. *ESMO Open, 7*(4), 100521. https://doi.org/10.1016/j.esmoop.2022.100521

74. European Cancer Organisation (ECO). (2024). Time to accelerate: The right to be forgotten. Retrieved May 10, 2024, from https://www.europeancancer.org/resources/355:time-to-accelerate-the-right-to-be-forgotten-a-position-paper-of-the-european-cancer-organisation.html

75. Koch, L., Jansen, L., Herrmann, A., Stegmaier, C., Holleczek, B., Singer, S., Brenner, H., & Arndt, V. (2013). Quality of life in long-term breast cancer survivors—A 10-year longitudinal population-based study. *Acta Oncologica, 52*(6), 1119–1128. https://doi.org/10.3109/0284186X.2013.774461

76. Doege, D., Thong, M.-Y., Koch-Gallenkamp, L., Bertram, H., Eberle, A., Holleczek, B., Pritzkuleit, R., Waldeyer-Sauerland, M., Waldmann, A., Zeissig, S. R., Jansen, L., Brenner, H., & Arndt, V. (2019). Health-related quality of life in long-term disease-free breast cancer survivors versus female population controls in Germany. *Breast Cancer Research and Treatment, 175*(2), 499–510. https://doi.org/10.1007/s10549-019-05188-x

77. Maurer, T., Thöne, K., Obi, N., Jung, A. Y., Behrens, S., Becher, H., & Chang-Claude, J. (2021). Health-related quality of life in a cohort of breast cancer survivors over more than 10 years post-diagnosis and in comparison to a control cohort. *Cancers, 13*(8), 1854. https://doi.org/10.3390/cancers13081854

78. Gao, Y., Rosas, J. C., Fink, H., Behrens, S., Chang-Claude, J., & Seibold, P. (2023). Longitudinal changes of health-related quality of life over 10 years in breast cancer patients treated with radiotherapy following breast-conserving surgery. *Quality of Life Research, 32*(9), 2639–2652. https://doi.org/10.1007/s11136-023-03408-y

79. Mols, F., Vingerhoets, A. J. J. M., Coebergh, J. W., & van de Poll-Franse, L. V. (2005). Quality of life among long-term breast cancer survivors: A systematic review. *European Journal of Cancer, 41*(17), 2613–2619. https://doi.org/10.1016/j.ejca.2005.05.017

80. İnan, F. Ş், & Üstün, B. (2014). Breast cancer and posttraumatic growth. *The Journal of Breast Health, 10*(2), 75–78. https://doi.org/10.5152/tjbh.2014.1778

81. Greup, S. R., Kaal, S. E. J., Jansen, R., Manten-Horst, E., Thong, M. S. Y., van der Graaf, W. T. A., Prins, J. B., & Husson, O. (2018). Post-traumatic growth and resilience in adolescent and young adult cancer patients: An overview. *Journal of Adolescent and Young Adult Oncology, 7*(1), 1–14. https://doi.org/10.1089/jayao.2017.0040

82. Caswell-Jin, J. L., Sun, L. P., Munoz, D., Lu, Yu., Li, Y., Huang, H., Hampton, J. M., Song, J., Jayasekera, J., Schechter, C., Alagoz, O., Stout, N. K., Trentham-Dietz, A., Lee, S. J., Huang, X., Mandelblatt, J. S., Berry, D. A., Kurian, A. W., & Plevritis, S. K. (2024). Analysis of breast cancer mortality in the US—1975 to 2019. *JAMA, 331*(3), 233. https://doi.org/10.1001/jama.2023.25881

83. Belpame, N., Kars, M. C., Deslypere, E., Rober, P., Van Hecke, A., & Verhaeghe, S. (2021). Coping strategies of adolescent and young adult survivors of childhood cancer. *Cancer Nursing, 44*(6), E395–E403. https://doi.org/10.1097/NCC.0000000000000865

84. Drabbe, C., Van der Graaf, W. T. A., De Rooij, B. H., Grünhagen, D. J., Soomers, V. L. M. N., Van de Sande, M. A. J., Been, L. B., Keymeulen, K. B. M. I., van der Geest, I. C. M., Van Houdt, W. J., & Husson, O. (2021). The age-related impact of surviving sarcoma on health-related quality of life: data from the SURVSARC study. *ESMO Open, 6*(1), 100047. https://doi.org/10.1016/j.esmoop.2021.100047

85. Husson, O., Ligtenberg, M. J. L., van de Poll-Franse, L. V., Prins, J. B., van den Bent, M. J., van Eenbergen, M. C., Fles, R., Manten-Horst, E., Gietema, J. A., & van der Graaf, W. T. A. (2021). Comprehensive assessment of incidence, risk factors, and mechanisms of impaired medical and psychosocial health outcomes among adolescents and young adults with cancer: Protocol of the prospective observational COMPRAYA cohort study. *Cancers, 13*(10), 2348. https://doi.org/10.3390/cancers13102348

86. Gupta, A. A., Papadakos, J. K., Jones, J. M., Amin, L., Chang, E. K., Korenblum, C., Mina, D. S., McCabe, L., Mitchell, L., & Giuliani, M. E. (2016). Reimagining care for adolescent and young adult cancer programs: Moving with the times. *Cancer, 122*(7), 1038–1046. https://doi.org/10.1002/cncr.29834

87. Howes, B. H. L., Watson, D. I., Xu, C., Fosh, B., Canepa, M., & Dean, N. R. (2016). Quality of life following total mastectomy with and without reconstruction versus breast-conserving surgery for breast cancer: A case-controlled cohort study. *Journal of plastic, Reconstructive & Aesthetic Surgery: JPRAS, 69*(9), 1184–1191. https://doi.org/10.1016/j.bjps.2016.06.004

88. Pagani, O., Regan, M. M., Walley, B. A., Fleming, G. F., Colleoni, M., Láng, I., Gomez, H. L., Tondini, C., Burstein, H. J., Perez, E. A., Ciruelos, E., Stearns, V., Bonnefoi, H. R., Martino, S., Geyer, C. E., Pinotti, G., Puglisi, F., Crivellari, D., Ruhstaller, T., … Francis, P. A. (2014). Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. *New England Journal of Medicine, 371*(2), 107–118. https://doi.org/10.1056/NEJMoa1404037

89. Alnaim, L. (2022). Health-related quality of life in women with breast cancer undergoing treatment with hormonal therapy—A review study. *European Journal of Breast Health, 18*(4), 292–298. https://doi.org/10.4274/ejbh.galenos.2022.2022-5-8

90. Johnsson, A., Fugl-Meyer, K., Bordas, P., Åhman, J., & Von Wachenfeldt, A. (2023). Side effects and its management in adjuvant endocrine therapy for breast cancer: A matter of communication and counseling. *Breast Cancer: Basic and Clinical Research, 17*, 117822342211454. https://doi.org/10.1177/11782234221145440

91. Phillips, K.-A., Regan, M. M., Ribi, K., Francis, P. A., Puglisi, F., Bellet, M., Spazzapan, S., Karlsson, P., Budman, D. R., Zaman,

K., Abdi, E. A., Domchek, S. M., Feng, Y., Price, K. N., Coates, A. S., Gelber, R. D., Maruff, P., Boyle, F., Forbes, J. F., … Bernhard, J. (2016). Adjuvant ovarian function suppression and cognitive function in women with breast cancer. *British Journal of Cancer, 114*(9), 956–964. https://doi.org/10.1038/bjc.2016.71

92. Treatment-induced ovarian insufficiency and early menopause in breast cancer survivors. (2023). *Clinical Journal of Oncology Nursing*. https://doi.org/10.1188/23.CJON.7-12

93. Park, J., Rodriguez, J. L., O'Brien, K. M., Nichols, H. B., Hodgson, M. E., Weinberg, C. R., & Sandler, D. P. (2021). Health-related quality of life outcomes among breast cancer survivors. *Cancer, 127*(7), 1114–1125. https://doi.org/10.1002/cncr.33348

94. Wintraecken, V. M., Vulik, S., de Wild, S., Dirksen, C., Koppert, L. B., de Vries, J., & Smidt, M. L. (2022). A descriptive systematic review of the relationship between personality traits and quality of life of women with non-metastatic breast cancer. *BMC Cancer, 22*(1), 426. https://doi.org/10.1186/s12885-022-09408-4

Authors and Affiliations

Noelle J. M. C. Vrancken Peeters[1,2] · **Roos Kerklaan[2]** · **Carla Vlooswijk[3]** · **Rhodé M. Bijlsma[4]** · **Suzanne E. J. Kaal[5]** · **Jacqueline M. Tromp[6]** · **Monique E. M. M. Bos[7]** · **Tom van der Hulle[8]** · **Maaike de Boer[9]** · **Janine Nuver[10]** · **Mathilde C. M. Kouwenhoven[11]** · **Winette T. A. van der Graaf[1,7]** · **Olga Husson[1,12,13]**

✉ Olga Husson
o.husson@nki.nl

Noelle J. M. C. Vrancken Peeters
n.vranckenpeeters@erasmusmc.nl

Roos Kerklaan
r.kerklaan@erasmusmc.nl

Carla Vlooswijk
C.Vlooswijk@iknl.nl

Rhodé M. Bijlsma
R.M.Bijlsma@umcutrecht.nl

Suzanne E. J. Kaal
Suzanne.Kaal@radboudumc.nl

Jacqueline M. Tromp
j.m.tromp@amsterdamumc.nl

Monique E. M. M. Bos
m.bos@erasmusmc.nl

Tom van der Hulle
t.van_der_hulle@lumc.nl

Maaike de Boer
maaike.de.boer@mumc.nl

Janine Nuver
j.nuver@umcg.nl

Mathilde C. M. Kouwenhoven
m.kouwenhoven@amsterdamumc.nl

Winette T. A. van der Graaf
w.vd.graaf@nki.nl

1 Department of Medical Oncology, Netherlands Cancer Institute-Antoni Van Leeuwenhoek, 1066 CX Amsterdam, The Netherlands

2 Department of Plastic and Reconstructive Surgery, Erasmus MC Cancer Institute, Erasmus University Medical Centre, 3015 GD Rotterdam, The Netherlands

3 Research and Development, Netherlands Comprehensive Cancer Organisation, 3511 CV Utrecht, The Netherlands

4 Department of Medical Oncology, University Medical Centre, 3584 CX Utrecht, The Netherlands

5 Department of Medical Oncology, Radboud University Medical Centre, 6525 GA Nijmegen, The Netherlands

6 Department of Medical Oncology, Amsterdam University Medical Centres, 1105 AZ Amsterdam, The Netherlands

7 Department of Medical Oncology, Erasmus MC Cancer Institute, Erasmus University Medical Centre, 3015 GD Rotterdam, The Netherlands

8 Department of Medical Oncology, Leiden University Medical Centre, 2333 ZA Leiden, The Netherlands

9 Department of Medical Oncology, Maastricht University Medical Center, 6202 AZ Maastricht, The Netherlands

10 Department of Medical Oncology, University Medical Centre Groningen, 9713 GZ Groningen, The Netherlands

11 Department of Neurology, Amsterdam UMC, Amsterdam University Medical Centres, Location VUmc, 1081 HV Amsterdam, The Netherlands

12 Department of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, 1066 CX Amsterdam, The Netherlands

13 Department of Surgical Oncology, Erasmus MC Cancer Institute, Erasmus University Medical Centre, 3015 GD Rotterdam, The Netherlands