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Clinical and Surgical Correlates of Quality of Life and Fatigue During Breast Cancer Chemotherapy in Indonesia: A Cross-Sectional Study

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ABSTRACT

Background: Health-related quality of life (HRQoL) and fatigue during chemotherapy for breast cancer are poorly described in Indonesia. Most women present late and undergo extensive surgery.

Objective: To describe HRQoL and fatigue and their clinical, surgical and sociodemographic correlates in Indonesian women receiving chemotherapy.

Methods: In this cross-sectional study, 102 consecutive women at a tertiary hospital in Palembang (June–July 2025) completed the FACT-G and FACIT-F. Analyses comprised group comparisons, correlations and a four-block hierarchical regression, and an exploratory identification (bounds) analysis.

Results: Stage III–IV disease was present in 62.7%, mastectomy in 75.5% and axillary lymph node dissection (ALND) in 68.6%. Mean FACIT-F was 98.5 (SD 21.2), FACT-G 76.8 (SD 18.5). The derived Fatigue Subscale mean (21.7/52) was far below the German population norm (43.5). FACIT-F fell from 115.6 in stage II to 61.2 in stage IV (η^2 0.70; 0.60 after reconciling the stage means). It was lower after mastectomy (−17.3 points; Hedges g = 0.83) and ALND (−22.1; g = 1.12). In the final model (adjusted R^2 0.58), stage (β = −0.41), mastectomy (β = −0.28), ALND (β = −0.25) and chemotherapy cycles (β = −0.19) were associated with lower scores. Sociodemographic variables were not ($|p| \leq 0.15$). The surgical associations were attainable only if mastectomy and ALND were nearly uncorrelated, which was not reported.

Conclusion: Fatigue was severe. HRQoL declined steeply with stage, surgical extent and cumulative chemotherapy. Fatigue screening, lymphedema surveillance and rehabilitation merit evaluation in routine chemotherapy care. Prospective studies must confirm the independent contribution of surgery.

1. Introduction

Breast cancer is the most frequently diagnosed cancer in women worldwide. In 2022 it accounted for 11.6% of all new cancers and 6.9% of cancer deaths¹. The Global Burden of Disease 2023 analysis estimated 2.30 million new cases, 764,000 deaths and 24.1 million disability-adjusted life-years among women in 2023. Age-standardized mortality was highest in low-income settings, despite their lower incidence². Late presentation shapes the burden in Indonesia. In the national surgical-oncology registry, one in five women already had distant metastases at diagnosis, and lower education and rural residence were associated with metastatic disease, and lower education and residence outside Java and Bali with late-stage disease³. Even in a university setting on Java, more than 40% of patients wait three months or longer between first symptoms and presentation⁴. Effective multimodal treatment now prolongs survival at every stage. How women feel and function during that treatment has therefore become an outcome in its own right. Where most patients receive curative or palliative treatment for advanced disease, it is a leading patient-centered outcome during the months of active therapy.

Chemotherapy remains central to the treatment of locally advanced and metastatic breast cancer in Indonesia, and it may be given before surgery to downstage the tumor, after surgery to treat micrometastatic disease, or to control metastatic disease. Its most pervasive symptomatic cost is cancer-related fatigue (CRF). This is a persistent, distressing sense of physical,

emotional and cognitive exhaustion that is out of proportion to activity and is not relieved by rest. Meta-analyses estimate that 43–52% of patients with cancer experience CRF. One-third of those on active treatment report severe fatigue, and chemotherapy carries about 1.5 times the prevalence of severe fatigue associated with surgery^{5,6}. Low-grade inflammation is one likely common pathway. C-reactive protein and interleukin-6 were associated with fatigue in breast cancer survivors, although not independently of other risk factors⁷, and a cluster of patients with high tumor necrosis factor- α , interleukin-1 β and interleukin-6 concentrations has a mainly physical fatigue phenotype⁸. Chemotherapy-induced anemia was present in 61% of patients in one series and was associated with much higher fatigue scores (65.9 vs 37.8 on a 0–100 symptom scale)⁹. Fatigue during chemotherapy also follows distinct trajectories linked to exercise capacity and neuromuscular fatigue¹⁰.

Surgery adds a separate and lasting burden. Breast-conserving surgery (BCS) is associated with better body image, psychosocial and sexual well-being than mastectomy, in high-income settings¹¹ and in low- and middle-income countries^{12,13}. Breast reconstruction recovers only part of the deficit¹⁴. Axillary lymph node dissection (ALND) increases the prevalence of lymphedema by about 14 percentage points and of chronic pain by about 24 points compared with sentinel lymph node biopsy (SLNB)¹⁵. Together with mastectomy, it is also a primary risk factor for patient-reported arm symptoms¹⁶. Randomized trials of axillary de-escalation have confirmed that less extensive axillary surgery reduces arm and breast symptoms^{17,18}.

Mastectomy with ALND remains the usual operation for locally advanced disease in Indonesia. Surgical morbidity is therefore expected to coexist with the systemic toxicity of chemotherapy in the same patients.

Evidence on health-related quality of life (HRQoL) during breast cancer treatment in Indonesia is limited and heterogeneous. Studies have shown moderate WHOQOL-BREF scores, with physical activity as the dominant modifiable correlate¹⁹, and fatigue and insomnia were associated with lower quality of life before palliative treatment²⁰. Health utility fell steeply from metastasis-free to distant metastatic disease in postmenopausal women with hormone-responsive, HER2-negative cancer²¹, and body image was better after surgery in locally advanced disease²². Across Asian low- and middle-income countries, scores on the Functional Assessment of Cancer Therapy-General (FACT-G) range from about 61 to 82, and income is the most consistent sociodemographic correlate, whereas the effects of age, education, marital status and stage are inconsistent²³. The national health insurance scheme finances most treatment, and its chemotherapy tariffs fall well below hospital costs²⁴. Validated Indonesian patient-reported outcome instruments are available²⁵. No study from Sumatra has reported FACT-G and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scores during chemotherapy. None has asked how far published summary data can establish the independent contribution of surgery when stage, surgery and chemotherapy are so closely intertwined.

This study had three aims. The first was to describe HRQoL and fatigue, with their precision and against external benchmarks, in women receiving chemotherapy for breast cancer at a tertiary referral hospital in Palembang, South Sumatra. The second was to quantify the associations of disease stage, breast and axillary surgery, cumulative chemotherapy and sociodemographic characteristics with these outcomes, using effect sizes and confidence intervals. The third was to determine which of the adjusted associations hold when the co-occurrence of the clinical predictors is unreported. We hypothesized that disease stage, surgical extent and chemotherapy exposure would each be associated with lower HRQoL and more fatigue. Sociodemographic characteristics were expected to show weaker associations.

2. Methods

Study design and setting

This was an analytical cross-sectional study with prospective data collection. It is reported in accordance with the STROBE statement for cross-sectional studies. The study took place in the outpatient Surgical Oncology Clinic of Dr. Mohammad Hoesin General Hospital, Palembang, South Sumatra, Indonesia, between 1 June and 31 July 2025. The hospital is the national tertiary referral and teaching hospital for South Sumatra and the main center for multimodal breast cancer care in the province. It receives patients from urban Palembang and from rural districts. Most treatment is financed through the national health insurance scheme (Jaminan Kesehatan Nasional, administered by BPJS Kesehatan).

Participants and eligibility

All women attending the clinic during the study period who met the eligibility criteria were invited consecutively. Inclusion criteria were female sex and age ≥ 18 years; histopathologically confirmed breast cancer of any stage; at least one completed cycle of chemotherapy, with the most recent administration within three months of the survey; the ability to understand and complete questionnaires in Bahasa Indonesia; and written

informed consent. Exclusion criteria were severe cognitive impairment or psychiatric illness precluding reliable self-report, and physical incapacity preventing questionnaire completion. Women with severe uncontrolled systemic illness likely to dominate quality of life independently of the cancer were also excluded (for example, New York Heart Association class IV heart failure or end-stage kidney disease), as were those who refused. In total, 102 women were enrolled and all were analyzed (Figure 1).

Sample size

The planned analysis was a multiple linear regression with up to eight predictors. For a medium effect ($f^2 = 0.15$), two-sided $\alpha = 0.05$ and 80% power, the required sample is 103 participants for seven predictors and 109 for eight. The 102 enrolled patients give 79.5% power for the seven-predictor final model and 77% for an eight-predictor model. For a single predictor tested within the final model, they give 80% power to detect $f^2 \geq 0.083$ (semipartial r^2 of about 0.03). For correlations, the minimum detectable $|r|$ at 80% power is 0.27. For the two-group surgical comparisons, the minimum detectable standardized difference is $d = 0.65$ (breast surgery, 25 vs 77) and $d = 0.60$ (axillary surgery, 32 vs 70).

Clinical and sociodemographic variables

A standardized extraction form was used to obtain clinical data from the medical records. These data were stage according to the American Joint Committee on Cancer (AJCC) 8th edition (I–IV); the number of chemotherapy cycles received up to the survey date; and treatment intent (neoadjuvant, chemotherapy before surgery; adjuvant, chemotherapy after surgery; palliative, chemotherapy for metastatic disease). They also included the type of breast surgery (breast-conserving surgery, BCS, or mastectomy) and the type of axillary surgery (sentinel lymph node biopsy, SLNB, or axillary lymph node dissection, ALND). For description, cycles were grouped as 1–4, 5–10 and >10 . Sociodemographic data were obtained by structured interview. These covered age in years (also grouped as <40 , 40–59 and ≥ 60), highest completed education (no schooling or elementary; junior or senior high school; university), monthly household income in bands defined by the regional minimum wage (low, <1.5 million; medium, 1.5–3.5 million; high, >3.5 million Indonesian rupiah) and marital status (married or not married).

Outcome measures

Health-related quality of life (HRQoL) was measured with the officially translated Bahasa Indonesia versions of instruments from the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system. The Functional Assessment of Cancer Therapy-General (FACT-G, version 4) has 27 items in four domains: physical (seven items), social/family (seven), emotional (six) and functional well-being (seven). Each item is rated on a five-point scale from 0 ('not at all') to 4 ('very much'), and the total ranges from 0 to 108, while the FACIT-Fatigue version (FACIT-F, version 4) adds the 13-item Fatigue Subscale (FS, 0–52) to the FACT-G, giving a total of 0–160. Negatively worded items are reverse-scored. Higher scores therefore always indicate better HRQoL and less fatigue. The FACIT-Fatigue scale is unidimensional, has high internal consistency in population samples (Cronbach α 0.92) and has published general-population norms. It is also among the few fatigue instruments in breast cancer with an established minimal clinically important difference^{26,27}. The FACIT-F total is the sum of the FACT-G total and the FS for every respondent, so the mean FS of any group equals the difference between its FACIT-F and

FACT-G means. This identity was used to obtain FS means. FS standard deviations could not be derived.

Statistical analysis

The patient-level data were analyzed with SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). We calculated frequencies and percentages for categorical variables, and means, standard deviations and ranges for continuous variables. Spearman rank correlations were computed between the FACT-G and FACIT-F totals and the ordinal variables (stage, number of chemotherapy cycles, age, education, income) and marital status. A sensitivity analysis of the stage correlation excluded the two patients with stage I disease. A four-block hierarchical linear regression of the FACIT-F total was then fitted. Block 1 contained age, education and income (each entered as a single term, education and income as three-level ordinal scores). Block 2 added cancer stage, Block 3 breast surgery (mastectomy vs BCS) and axillary surgery (ALND vs SLNB), and Block 4 the number of chemotherapy cycles. Standardized coefficients (β) were used to compare predictors. Collinearity was checked with the variance inflation factor ($VIF < 5$).

All further analyses were deterministic functions of the subgroup sizes, means, standard deviations, correlations and regression output. They were run in Python 3 (NumPy 2.4, SciPy 1.18). Proportions are reported with 95% Wilson score intervals, and precision was expressed as the interval half-width and as the sample size needed for ± 10 and ± 5 percentage points. Proportions were compared with external benchmarks by exact binomial tests with Cohen's h , and means by Welch t tests computed from summary statistics. The derived FS mean was compared with the German general-population norm (mean 43.5, SD 8.3)²⁶ by a one-sample t test. This test used the largest standard deviation that a 0–52 score with the observed mean can have (the Bhatia–Davis bound), so the result is the least extreme value compatible with the data.

Subgroup differences were tested exactly from summary statistics. We used Fisher and Welch one-way analysis of variance (ANOVA) with η^2 and ω^2 , linear-trend contrasts with Welch degrees of freedom and centered integer scores, and Games–Howell pairwise comparisons. Welch t tests were used for the two surgical comparisons because group variances differed up to 4.4-fold. Standardized differences are Hedges g with exact confidence intervals from the non-central t distribution. Point-biserial correlations for the surgical variables were derived from the subgroup means and the cohort standard deviation. Confidence intervals for Spearman coefficients used the Fisher z transformation with the Bonett–Wright variance. The p values were recomputed from the reported coefficients and adjusted by the Holm method across the 12 coefficients. Stage I ($n = 2$) contributed to omnibus tests only.

For the hierarchical regression, R^2 , model F and the F -change of each block were computed from the adjusted R^2 values, together with Cohen's f^2 for each block. For the final model, the t statistic of each predictor was recovered from its exact two-sided p value with 94 residual degrees of freedom, and from it the standard error, 95% confidence interval, semipartial r^2 (sr^2), f^2 and VIF of each standardized coefficient were derived. For stage, which was reported only as $p < 0.001$, the outer limits of the interval were derived.

The cross-classification of the predictors (for example, how many patients with mastectomy also had ALND) is not reported in this article. The extent to which the summary data (subgroup margins, means and correlations) identify the adjusted associations was therefore examined by an identification

(bounds) analysis. An admissible configuration assigns stage, breast surgery, axillary surgery and chemotherapy band to the 102 patients so that every observed margin is preserved. For each configuration, the standardized coefficients of the four-predictor clinical model follow from the predictor correlation matrix and the observed predictor–outcome correlations ($\beta = R^{-1}r$). Three scenarios were examined. S_0 allowed any configuration giving a valid correlation structure. S_1 kept configurations whose model R^2 lies within 0.55–0.614, the range compatible with the fitted final model. S_2 added clinically expected positive associations to S_1 : stage with mastectomy, ALND and chemotherapy cycles, and mastectomy with ALND. Typical values were summarized over 20,000 configurations (independent label permutations in S_0 ; a random walk restricted to the admissible region in S_1 and S_2). The most extreme attainable coefficients were sought by penalized simulated annealing from 14 starting configurations for each bound. A range that includes zero was interpreted as showing that the summary data cannot identify the direction of that adjusted association. No outcome value was generated for any patient, because outcomes entered only through the observed correlations.

The stage-specific means are not fully consistent with the cohort means. Their weighted average is 94.8 for FACIT-F and 74.5 for FACT-G, against cohort means of 98.5 and 76.8, whereas the surgical and chemotherapy subgroups reproduce the cohort means to within 0.4 points. Stage results are therefore reported as recorded. A reconciliation sensitivity analysis keeps the within-stage standard deviations and imposes the total variance implied by the cohort standard deviation. Wherever stage is combined with other variables, the Spearman coefficient (-0.68) that agrees with the regression output was used. FACIT-F, the outcome of the regression, was designated the primary outcome. Because the FACT-G forms 27 of the 40 items of the FACIT-F, FACT-G results are secondary and are not counted as independent confirmation. Games–Howell p values are adjusted within each family of pairwise comparisons, and Spearman p values across the 12 coefficients. Omnibus tests are not adjusted across outcomes. Because group variances differed, standardized differences were also expressed as Glass's Δ , using the standard deviation of the less-treated reference group. Statistical significance was set at two-sided $\alpha = 0.05$, and p values are reported to three decimals.

To determine which co-occurrence of mastectomy and ALND would be required for the coefficients estimated in the patient-level model to be attainable, we searched for admissible configurations whose four clinical coefficients lay within rounding distance of the estimated values (Euclidean ≤ 0.015 , and ≤ 0.030 as a sensitivity margin). The attainable range of each predictor–predictor correlation among them was mapped. A further 64,000 admissible configurations from a restricted random walk described how the adjusted mastectomy coefficient varies with the mastectomy–ALND correlation. The Pearson correlation between stage and FACIT-F is not reported. The bounds were therefore repeated with stage–FACIT-F correlations of -0.72 and -0.76 .

Ethical approval

The protocol was reviewed and approved by CMHC Research Center Indonesia (approval number 2024/8456) before data collection began. The study followed the Declaration of Helsinki. A trained research assistant who was not involved in the patients' clinical care explained the study in the clinic waiting area. Each patient received a written information sheet and gave written informed consent before any data were collected. Questionnaires and extraction forms carried a study code only.

3. Results

Participants

All 102 enrolled women completed both questionnaires and were included in the analysis (Figure 1). Their characteristics are summarized in Table 1 and Figure 2. The mean age was 48.7 years (SD 9.2); 28 women (27.5%; 95% CI 19.7–36.8) were younger than 40 years and 17 (16.7%) were 60 or older. Eighty (78.4%) had not progressed beyond secondary school and 80 (78.4%) reported low or medium household income. Stage III was the most frequent stage (43 women, 42.2%; 95% CI 33.0–51.9), followed by stage II (36, 35.3%) and stage IV (21, 20.6%;

95% CI 13.9–29.4); only two women (2.0%) had stage I disease, so that 64 (62.7%; 95% CI 53.1–71.5) had stage III–IV disease. Chemotherapy was adjuvant in 67 women (65.7%) and neoadjuvant or palliative in 35 (34.3%). Every woman had undergone breast and axillary surgery: 77 (75.5%; 95% CI 66.3–82.8) mastectomy and 25 (24.5%) BCS; 70 (68.6%; 95% CI 59.1–76.8) ALND and 32 (31.4%) SLNB. Seventy women (68.6%) had received 1–4 cycles, 26 (25.5%) 5–10 cycles and six (5.9%) more than 10 cycles. The intervals around these proportions were wide: the half-width of a 95% interval was 7.8–9.2 percentage points, and 252–360 patients would be needed to estimate the same proportions within ± 5 points.

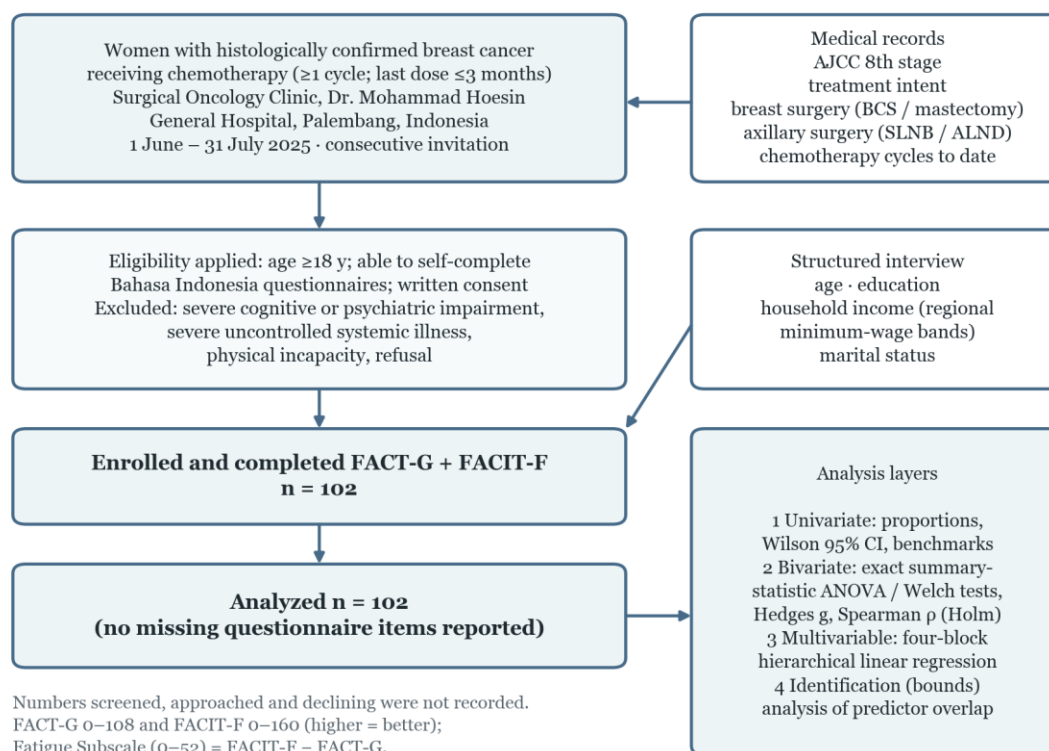


Figure 1. Study design, participant selection and analytic framework. Women receiving chemotherapy for breast cancer were invited consecutively during two months; all 102 enrolled patients completed both instruments and were analyzed. Clinical variables came from medical records and sociodemographic variables from a structured interview. The numbers screened and declining were not recorded.

Table 1. Characteristics of the 102 women receiving chemotherapy for breast cancer.

Characteristic	n	%	95% CI, %
Age, years	Mean 48.7 (SD 9.2)		
Age group			
<40 years	28	27.5	19.7–36.8
40–59 years	57	55.9	46.2–65.1
≥60 years	17	16.7	10.7–25.1
Education			
No schooling or elementary	39	38.2	29.4–47.9
Junior or senior high school	41	40.2	31.2–49.9
University	22	21.6	14.7–30.5
Monthly household income			
Low (<1.5 million IDR)	37	36.3	27.6–45.9
Medium (1.5–3.5 million IDR)	43	42.2	33.0–51.9
High (>3.5 million IDR)	22	21.6	14.7–30.5
AJCC 8th-edition stage			

Characteristic	n	%	95% CI, %
I	2	2.0	0.5–6.9
II	36	35.3	26.7–44.9
III	43	42.2	33.0–51.9
IV	21	20.6	13.9–29.4
III–IV combined	64	62.7	53.1–71.5
Treatment intent			
Adjuvant	67	65.7	56.1–74.2
Neoadjuvant or palliative	35	34.3	25.8–43.9
Breast surgery			
Breast-conserving surgery	25	24.5	17.2–33.7
Mastectomy	77	75.5	66.3–82.8
Axillary surgery			
Sentinel lymph node biopsy	32	31.4	23.2–40.9
Axillary lymph node dissection	70	68.6	59.1–76.8
Chemotherapy cycles received			
1–4	70	68.6	59.1–76.8
5–10	26	25.5	18.0–34.7
>10	6	5.9	2.7–12.2

CI, Wilson score confidence interval; IDR, Indonesian rupiah. Income bands follow the regional minimum wage. Marital status was recorded but its distribution was not tabulated. Treatment intent was recorded as adjuvant, neoadjuvant or palliative; the neoadjuvant and palliative groups are reported together. Every patient had undergone breast and axillary surgery at the time of the survey.

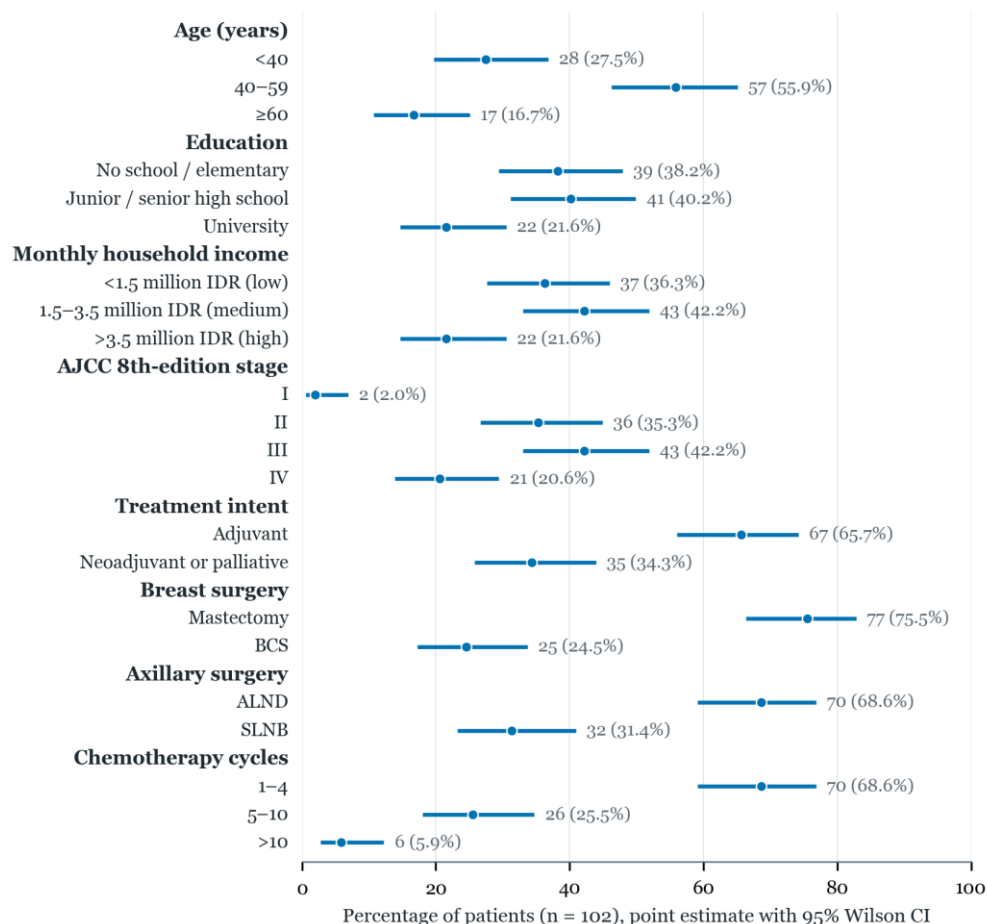


Figure 2. Cohort profile. Points are percentages of the 102 patients and horizontal bars their 95% Wilson confidence intervals; counts and percentages are shown beside each interval. Chemotherapy cycles are the number received to date.

Against external benchmarks (Table 2), the proportion with stage IV disease was almost identical to the 20.1% recorded in the Indonesian national surgical-oncology registry ($h = 0.01$; $p = 0.902$). Compared with a tertiary cohort from Bangladesh of

similar age ($p = 0.473$), stage II disease was less frequent (35.3% vs 53.0%; $h = -0.36$; $p < 0.001$) and mastectomy more frequent (75.5% vs 58.5%; $h = 0.36$; $p < 0.001$).

Table 2. Comparison of the cohort with external benchmarks.

Quantity	This cohort	Benchmark (source)	Difference / effect size	p
Stage IV at diagnosis	21/102 (20.6%)	20.1% of 4,959 women, Indonesian national surgical-oncology registry ³	+0.5 points; Cohen's h 0.01	0.902
Stage II	36/102 (35.3%)	53.0% of 200 women, tertiary cohort in Bangladesh ²⁸	-17.7 points; h -0.36	<0.001
Mastectomy	77/102 (75.5%)	58.5%, same Bangladeshi cohort ²⁸	+17.0 points; h 0.36	<0.001
Age, years	48.7 (SD 9.2)	49.5 (SD 9.02), same Bangladeshi cohort ²⁸	-0.8 years; Welch t -0.72	0.473
FACT-G total	76.8 (SD 18.5)	60.8–82.2: range of means across Asian LMIC studies ²³	Within the regional range (upper half)	—
Fatigue Subscale	21.7 (derived)	43.5 (SD 8.3), German general population, n = 2,426 ²⁶	-21.8 points; one-sample t ≤ -8.59 at the largest attainable SD (25.6)	<0.001

Proportions were compared with the benchmark by exact binomial tests and means by Welch t tests from summary statistics. For the Fatigue Subscale, whose standard deviation was not available, the test used the largest standard deviation that a 0–52 score with a mean of 21.7 can have (Bhatia–Davis bound), so the reported statistic is the least extreme value compatible with the data. LMIC, low- and middle-income countries.

Quality of life and fatigue

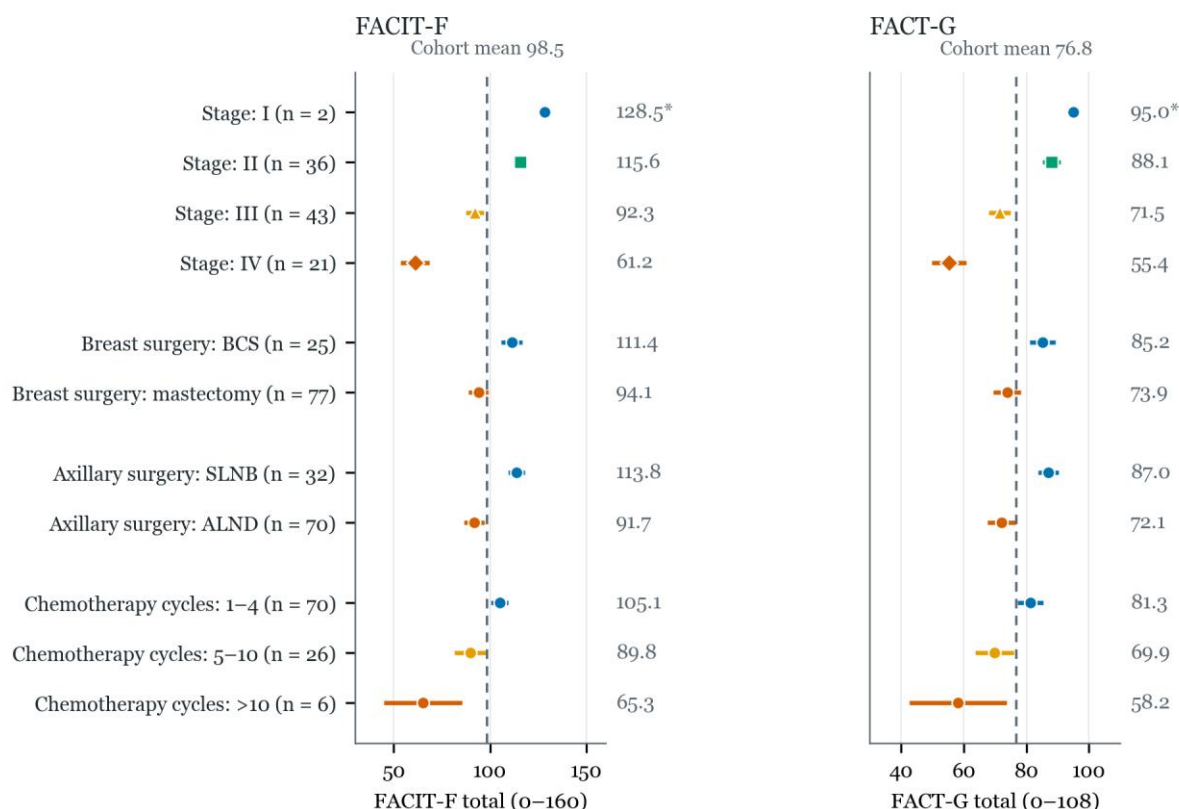
The mean FACIT-F score was 98.5 (SD 21.2; 95% CI 94.3–102.7) and the mean FACT-G score 76.8 (SD 18.5; 95% CI 73.2–80.4) (Table 3). The mean derived Fatigue Subscale score was 21.7 of a possible 52. Scores were lower at each successive stage, in women who had undergone mastectomy or ALND and in women who had received more chemotherapy cycles (Figure 3). FACIT-

F means were 115.6 (95% CI 112.1–119.1) in stage II, 92.3 (87.7–96.9) in stage III and 61.2 (53.7–68.7) in stage IV; the corresponding FACT-G means were 88.1, 71.5 and 55.4. The two women with stage I disease had a mean FACIT-F of 128.5 and FACT-G of 95.0. The derived FS mean fell from 27.5 in stage II to 20.8 in stage III and 5.8 in stage IV, from 26.2 after BCS to 20.2 after mastectomy, from 26.8 after SLNB to 19.6 after ALND, and from 23.8 after 1–4 cycles to 7.1 after more than 10 cycles.

Table 3. FACIT-F, FACT-G and Fatigue Subscale scores by clinical subgroup.

Subgroup	n	FACIT-F, mean (SD)	95% CI	FACT-G, mean (SD)	95% CI	FS, mean
Stage						
I	2	128.5 (5.1)	—	95.0 (4.2)	—	33.5
II	36	115.6 (10.2)	112.1–119.1	88.1 (8.5)	85.2–91.0	27.5
III	43	92.3 (14.8)	87.7–96.9	71.5 (11.3)	68.0–75.0	20.8
IV	21	61.2 (16.5)	53.7–68.7	55.4 (12.1)	49.9–60.9	5.8
Breast surgery						
Breast-conserving surgery	25	111.4 (13.3)	105.9–116.9	85.2 (9.8)	81.2–89.2	26.2
Mastectomy	77	94.1 (22.6)	89.0–99.2	73.9 (19.6)	69.5–78.3	20.2
Axillary surgery						
Sentinel lymph node biopsy	32	113.8 (12.1)	109.4–118.2	87.0 (9.1)	83.7–90.3	26.8
Axillary lymph node dissection	70	91.7 (22.1)	86.4–97.0	72.1 (19.0)	67.6–76.6	19.6
Chemotherapy cycles						
1–4	70	105.1 (18.9)	100.6–109.6	81.3 (16.7)	77.3–85.3	23.8
5–10	26	89.8 (20.5)	81.5–98.1	69.9 (15.4)	63.7–76.1	19.9
>10	6	65.3 (19.3)	45.0–85.6	58.2 (14.8)	42.7–73.7	7.1
All patients	102	98.5 (21.2)	94.3–102.7	76.8 (18.5)	73.2–80.4	21.7

FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue (0–160); FACT-G, Functional Assessment of Cancer Therapy–General (0–108); FS, Fatigue Subscale (0–52), obtained as the difference of the FACIT-F and FACT-G means (FACIT-F = FACT-G + FS for every patient). Higher scores indicate better quality of life and less fatigue. CIs use the t distribution; they are not shown for stage I (n = 2), where they are not estimable. The weighted mean of the stage rows (FACIT-F 94.8; FACT-G 74.5) differs from the cohort means, whereas the surgical and chemotherapy rows reproduce them to within 0.4 points (see Methods, Statistical analysis).



Points: group means; bars: 95% CI (t distribution). Dashed line: cohort mean. *Stage I (n = 2): confidence interval not estimable and not shown.

Figure 3. FACIT-F (left) and FACT-G (right) scores by disease stage, breast surgery, axillary surgery and number of chemotherapy cycles. Points are group means and bars 95% confidence intervals (t distribution); the dashed line is the cohort mean and group means are listed at the right of each panel. Higher scores indicate better health-related quality of life and less fatigue. The stage I interval (n = 2) is not shown because it is not estimable.

The cohort FACT-G mean lay in the upper half of the range reported across Asian low- and middle-income countries (60.8–82.2), whereas the derived FS mean was 21.8 points below the German general-population norm of 43.5; even at the largest

standard deviation a 0–52 score with this mean can have, the one-sample t statistic was –8.59 ($p < 0.001$), and every subgroup mean lay below the lower limit of one population standard deviation (Table 2, Figure 4).

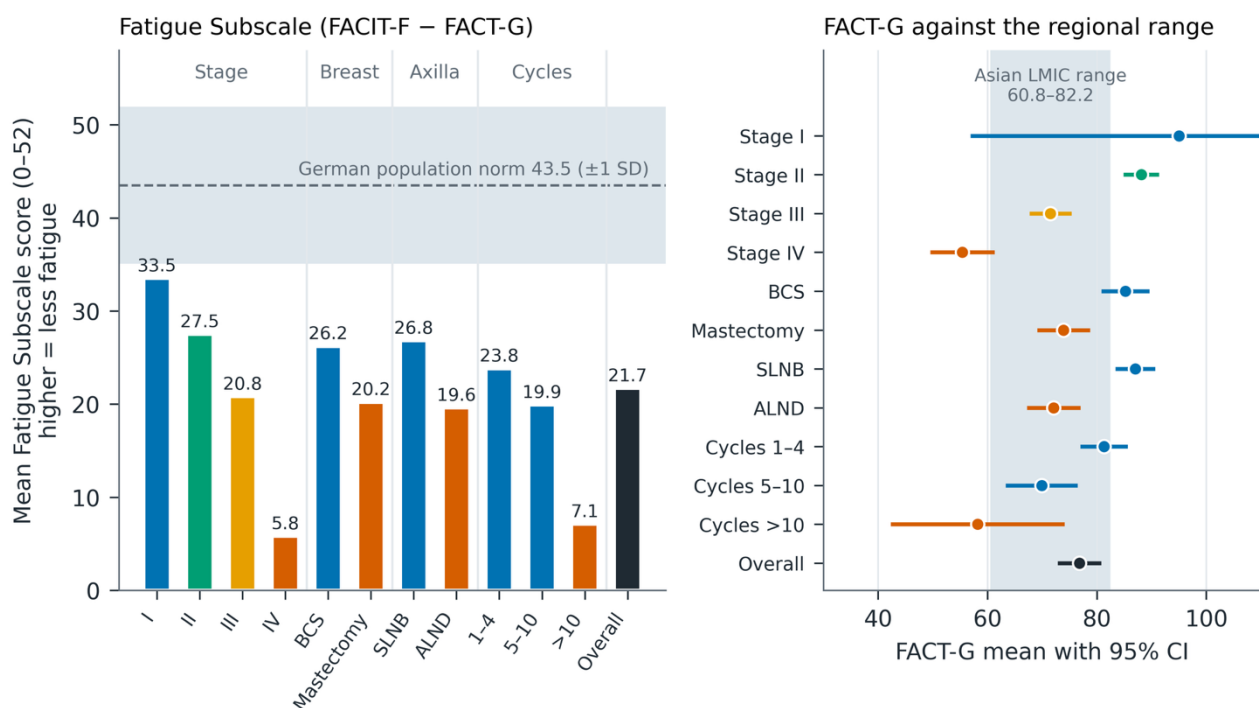


Figure 4. Fatigue and quality of life against external benchmarks. Left: mean Fatigue Subscale score of each subgroup, obtained as the difference between the FACIT-F and FACT-G means (subgroup standard deviations of the subscale were not available); the dashed line and band show the German general-population mean ± 1 SD (43.5 ± 8.3). Right: FACT-G means with 95% confidence intervals against the range of FACT-G means reported across studies from Asian low- and middle-income countries (shaded, 60.8–82.2).

Differences between clinical subgroups

Stage was strongly associated with both outcomes (Table 4). For FACIT-F, stage explained 69.5% of the variance ($\eta^2 = 0.695$; $\omega^2 = 0.684$; Welch $F(3, 5.9) = 70.9$; $p < 0.001$), and 68.4% among stages II–IV, with a linear decline across stages II to IV (Welch $t(29.1) = -13.66$; $p < 0.001$). Every pairwise difference among stages II–IV was large: stage II vs III, 23.3 points ($g = 1.79$, 95% CI 1.26 to 2.30); stage III vs IV, 31.1 points ($g = 2.00$, 1.37 to 2.62); and stage II vs IV, 54.4 points ($g = 4.17$, 3.23 to 5.11), all with Games–Howell $p < 0.001$. The FACT-G pattern was similar but smaller ($\eta^2 = 0.589$; stage II vs IV $g = 3.24$). In the reconciliation sensitivity analysis stage still explained 59.7% of FACIT-F variance and 58.9–68.6% of FACT-G variance.

Women who had undergone mastectomy scored 17.3 FACIT-F points lower than those treated with BCS (95% CI 9.9 to 24.7; Welch $t(70.5) = 4.67$; $p < 0.001$; $g = 0.83$, 95% CI 0.36 to 1.29), and those who had undergone ALND scored 22.1 points lower than those with SLNB (95% CI 15.4 to 28.8; $p < 0.001$; $g = 1.12$,

0.68 to 1.56). The corresponding FACT-G differences were 11.3 points ($g = 0.63$; $p < 0.001$) and 14.9 points ($g = 0.89$; $p < 0.001$). Scores were also more variable after the more extensive procedures (standard deviations 22.6 vs 13.3 for mastectomy vs BCS and 22.1 vs 12.1 for ALND vs SLNB). Expressed relative to the reference-group standard deviation (Glass's Δ), the FACIT-F differences were 1.30 for mastectomy and 1.83 for ALND (FACT-G 1.15 and 1.64), larger than the pooled-SD estimates because the reference groups were more homogeneous.

FACIT-F decreased with the number of chemotherapy cycles ($\eta^2 = 0.239$; Welch $F(2, 13.2) = 14.7$; $p < 0.001$; linear trend $p = 0.003$). The difference between 1–4 and 5–10 cycles was 15.3 points ($g = 0.78$; Games–Howell $p = 0.005$) and that between 1–4 and more than 10 cycles 39.8 points ($g = 2.08$; $p = 0.007$); the difference between 5–10 and more than 10 cycles (24.5 points) did not reach significance ($p = 0.058$), reflecting the six patients in the highest band. Standardized differences for all contrasts are shown in Figure 5.

Table 4. Differences in FACIT-F and FACT-G between clinical subgroups (exact tests from summary statistics).

Contrast	FACIT-F difference (95% CI) or variance explained	FACIT-F test	FACIT-F Hedges g (95% CI)	FACT-G difference (95% CI) or variance explained	FACT-G test	FACT-G Hedges g (95% CI)
Stage (I–IV), omnibus	$\eta^2 0.695$; $\omega^2 0.684$	$F(3, 98) = 74.6$; Welch $F(3, 5.9) = 70.9$; $p < 0.001$	—	$\eta^2 0.589$; $\omega^2 0.574$	$F(3, 98) = 46.9$; Welch $F(3, 5.8) = 45.8$; $p < 0.001$	—
Stage II–IV only	$\eta^2 0.684$	Welch $F(2, 48.5) = 103.9$; $p < 0.001$	—	$\eta^2 0.576$	Welch $F(2, 49.8) = 68.2$; $p < 0.001$	—
Linear trend, II→IV	—	$t(29.1) = -13.66$; $p < 0.001$	—	—	$t(31.7) = -10.91$; $p < 0.001$	—
Stage II vs III	23.3	$t(74.4) = 8.25$; Games–Howell $p < 0.001$	1.79 (1.26 to 2.30)	16.6	$t(76.2) = 7.44$; Games–Howell $p < 0.001$	1.62 (1.11 to 2.13)
Stage III vs IV	31.1	$t(36.1) = 7.32$; Games–Howell $p < 0.001$	2.00 (1.37 to 2.62)	16.1	$t(37.4) = 5.11$; Games–Howell $p < 0.001$	1.38 (0.80 to 1.94)
Stage II vs IV	54.4	$t(29.1) = 13.66$; Games–Howell $p < 0.001$	4.17 (3.23 to 5.11)	32.7	$t(31.7) = 10.91$; Games–Howell $p < 0.001$	3.24 (2.43 to 4.03)
BCS vs mastectomy	17.3 (9.9 to 24.7)	Welch $t(70.5) = 4.67$; $p < 0.001$	0.83 (0.36 to 1.29)	11.3 (5.4 to 17.2)	Welch $t(82.7) = 3.80$; $p < 0.001$	0.63 (0.17 to 1.09)
SLNB vs ALND	22.1 (15.4 to 28.8)	Welch $t(96.7) = 6.50$; $p < 0.001$	1.12 (0.68 to 1.56)	14.9 (9.4 to 20.4)	Welch $t(99.7) = 5.35$; $p < 0.001$	0.89 (0.46 to 1.32)
Chemotherapy cycles, omnibus	$\eta^2 0.239$; $\omega^2 0.222$	$F(2, 99) = 15.5$; Welch $F(2, 13.2) = 14.7$; $p < 0.001$	—	$\eta^2 0.152$; $\omega^2 0.134$	$F(2, 99) = 8.9$; Welch $F(2, 13.7) = 9.4$; $p = 0.003$	—
Linear trend	—	$t(5.9) = -4.86$; $p = 0.003$	—	—	$t(6.1) = -3.63$; $p = 0.011$	—
1–4 vs 5–10 cycles	15.3	$t(41.8) = 3.32$; Games–Howell $p = 0.005$	0.78 (0.32 to 1.24)	11.4	$t(48.3) = 3.15$; Games–Howell $p = 0.008$	0.69 (0.23 to 1.15)
5–10 vs >10 cycles	24.5	$t(7.8) = 2.77$; Games–Howell $p = 0.058$	1.18 (0.25 to 2.08)	11.7	$t(7.7) = 1.73$; Games–Howell $p = 0.254$	0.75 (–0.15 to 1.62)
1–4 vs >10 cycles	39.8	$t(5.9) = 4.86$; Games–Howell $p = 0.007$	2.08 (1.18 to 2.97)	23.1	$t(6.1) = 3.63$; Games–Howell $p = 0.025$	1.38 (0.52 to 2.23)

Differences are the score of the first-named (less advanced or less extensive) group minus the second; positive values and positive g indicate lower scores with more advanced disease, more extensive surgery or more cycles. Omnibus tests: Fisher and Welch one-way ANOVA; pairwise: Welch t with Games–Howell adjustment; linear trend: Welch-type contrast with centered integer scores. Stage I ($n = 2$) contributes to the omnibus I–IV test only. BCS, breast-conserving surgery; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection. With three groups, the linear-trend contrast with centered integer scores reduces to the contrast between the two extreme groups and equals the corresponding pairwise Welch t .

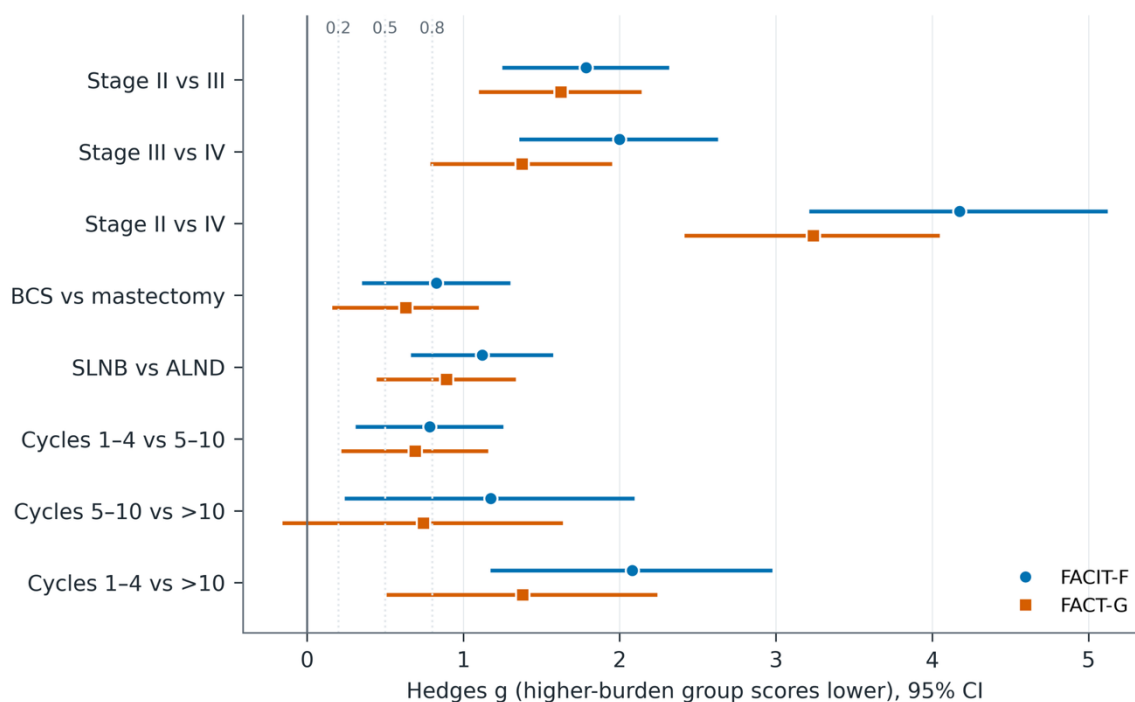


Figure 5. Standardized mean differences (Hedges g with 95% confidence intervals) for each contrast, oriented so that positive values indicate lower scores in the group with more advanced disease, more extensive surgery or more chemotherapy cycles. Circles: FACIT-F; squares: FACT-G. Dotted lines mark conventional small (0.2), medium (0.5) and large (0.8) effects. Stage I (n = 2) is not included.

Correlations

Stage correlated strongly and negatively with FACIT-F ($\rho = -0.68$, 95% CI -0.78 to -0.54) and FACT-G ($\rho = -0.65$, -0.76 to -0.51), and the correlation was unchanged when the two stage I patients were excluded ($\rho = -0.66$, -0.77 to -0.52) (Table 5, Figure 6). The number of chemotherapy cycles correlated moderately with both outcomes (FACIT-F $\rho = -0.42$; FACT-G $\rho = -0.40$), and the derived point-biserial correlations were -0.35

for mastectomy and -0.49 for ALND (FACIT-F). The Spearman coefficients for stage and cycles remained significant after Holm adjustment (adjusted $p < 0.001$); the point-biserial correlations were not adjusted. No sociodemographic variable correlated significantly with either outcome; the coefficients ranged from -0.15 to 0.11 and their confidence intervals excluded correlations stronger than about $|0.34|$, but did not exclude small correlations in either direction.

Table 5. Correlations of clinical and sociodemographic variables with FACIT-F and FACT-G.

Variable	FACIT-F, coefficient (95% CI)	p	Holm p	FACT-G, coefficient (95% CI)	p	Holm p
Cancer stage (AJCC), ρ	$-0.68 (-0.78 \text{ to } -0.54)$	<0.001	<0.001	$-0.65 (-0.76 \text{ to } -0.51)$	<0.001	<0.001
Chemotherapy cycles, ρ	$-0.42 (-0.57 \text{ to } -0.24)$	<0.001	<0.001	$-0.40 (-0.56 \text{ to } -0.22)$	<0.001	<0.001
Mastectomy (vs BCS), r_{pb}	$-0.35 (-0.51 \text{ to } -0.17)$	<0.001	—	$-0.26 (-0.44 \text{ to } -0.07)$	0.007	—
ALND (vs SLNB), r_{pb}	$-0.49 (-0.62 \text{ to } -0.32)$	<0.001	—	$-0.38 (-0.53 \text{ to } -0.20)$	<0.001	—
Age, ρ	$0.08 (-0.12 \text{ to } 0.27)$	0.424	1.000	$0.11 (-0.09 \text{ to } 0.30)$	0.271	1.000
Education level, ρ	$-0.09 (-0.28 \text{ to } 0.11)$	0.368	1.000	$-0.12 (-0.31 \text{ to } 0.08)$	0.230	1.000
Income level, ρ	$-0.14 (-0.33 \text{ to } 0.06)$	0.160	1.000	$-0.15 (-0.34 \text{ to } 0.05)$	0.132	1.000
Marital status, ρ	$-0.02 (-0.21 \text{ to } 0.18)$	0.842	1.000	$0.03 (-0.17 \text{ to } 0.22)$	0.765	1.000
Cancer stage, ρ , stage I excluded (n = 100)	$-0.66 (-0.77 \text{ to } -0.52)$	<0.001	—	—	—	—

ρ , Spearman rank correlation (confidence interval by Fisher z with the Bonett–Wright variance); r_{pb} , point-biserial correlation derived from the subgroup means in Table 3 and the cohort standard deviation. Holm adjustment across the 12 Spearman coefficients. The minimum correlation detectable with 80% power at $n = 102$ is $|r| = 0.27$.

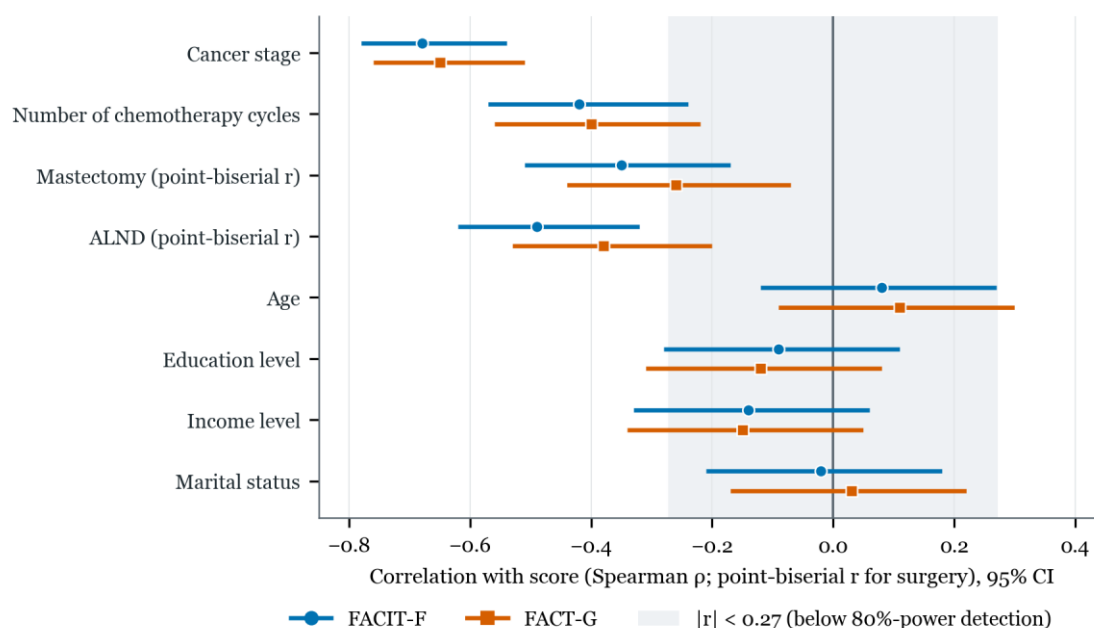


Figure 6. Correlations of clinical and sociodemographic variables with FACIT-F (circles) and FACT-G (squares), with 95% confidence intervals. Spearman ρ for ordinal and sociodemographic variables; point-biserial r for breast and axillary surgery. The shaded band marks correlations smaller than the minimum detectable at 80% power with $n = 102$.

Hierarchical regression

In the hierarchical regression (Table 6, Figure 7), the sociodemographic block explained 4.9% of the variance in FACIT-F (adjusted R^2 0.02; $p = 0.175$). Adding stage increased R^2 by 0.442 (F -change(1, 97) = 84.2; $p < 0.001$; $f^2 = 0.87$), with a stage coefficient of $\beta = -0.64$. The surgical block added 0.086 (F -change(2, 95) = 9.62; $p < 0.001$; $f^2 = 0.20$), and chemotherapy cycles a further 0.032 (F -change(1, 94) = 7.79; $p = 0.006$). The final model explained 60.9% of the variance (adjusted R^2 0.58;

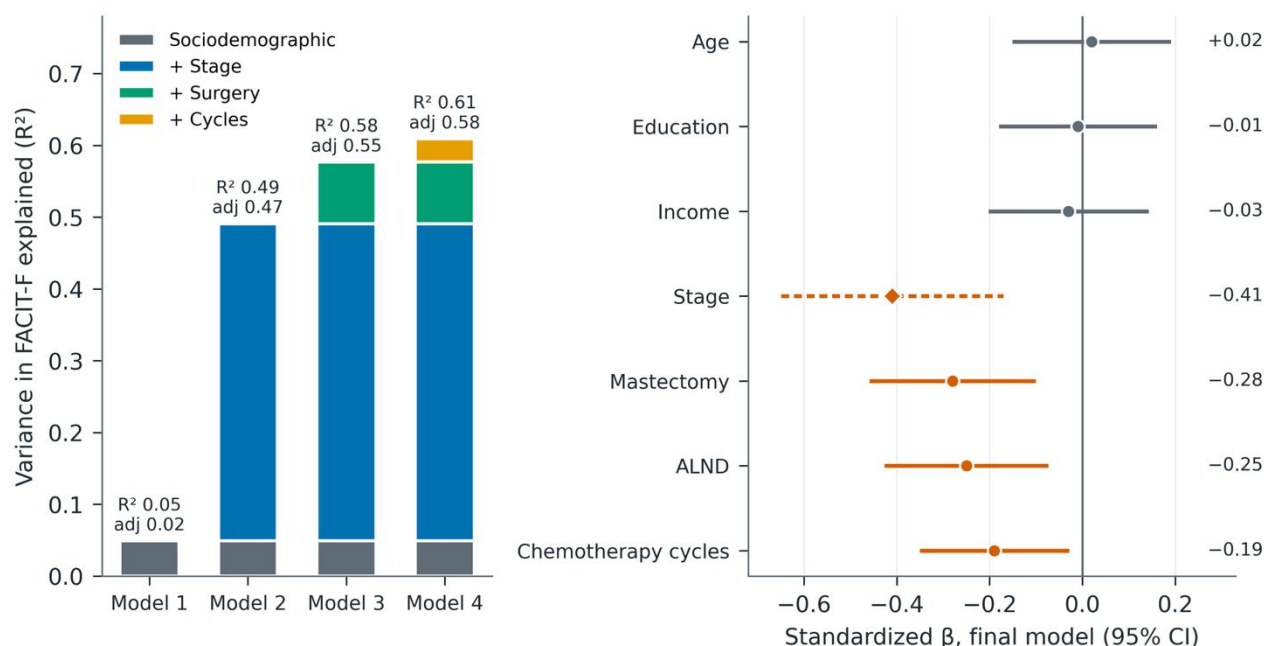
$F(7, 94) = 20.9$; $p < 0.001$). In this model stage ($\beta = -0.41$; $p < 0.001$), mastectomy ($\beta = -0.28$, 95% CI -0.45 to -0.11 ; $p = 0.002$; $sr^2 = 0.042$), ALND ($\beta = -0.25$, -0.42 to -0.08 ; $p = 0.005$; $sr^2 = 0.034$) and chemotherapy cycles ($\beta = -0.19$, -0.35 to -0.03 ; $p = 0.018$; $sr^2 = 0.024$) were each independently associated with lower FACIT-F scores, whereas age, education and income were not (all $p \geq 0.724$). The derived VIFs ranged from 1.50 to 1.87. The stage coefficient fell from -0.64 to -0.45 when the surgical variables were added, indicating that part of the stage gradient was shared with the extent of surgery.

Table 6. Hierarchical linear regression of FACIT-F: model summaries and standardized coefficients.

Model	Block added	R^2	Adjusted R^2	Model F	ΔR^2	F-change	Cohen's f^2 (block)
Model 1	Age, education, income	0.049	0.02	$F(3, 98) = 1.69$; $p = 0.175$	0.049	$F(3, 98) = 1.69$; $p = 0.175$	0.052
Model 2	+ Stage	0.491	0.47	$F(4, 97) = 23.39$; $p < 0.001$	0.442	$F(1, 97) = 84.21$; $p < 0.001$	0.868
Model 3	+ Mastectomy, ALND	0.577	0.55	$F(6, 95) = 21.57$; $p < 0.001$	0.086	$F(2, 95) = 9.62$; $p < 0.001$	0.203
Model 4	+ Chemotherapy cycles	0.609	0.58	$F(7, 94) = 20.93$; $p < 0.001$	0.032	$F(1, 94) = 7.79$; $p = 0.006$	0.083

Predictor	β , Model 1	β , Model 2	β , Model 3	β , Model 4	95% CI (Model 4)	p (Model 4)	sr^2 (Model 4)	VIF
Age	0.07	0.04	0.03	0.02	-0.15 to 0.19	0.812	0.000	1.69
Education level	-0.10	-0.05	-0.02	-0.01	-0.18 to 0.16	0.905	0.000	1.68
Income level	-0.15	-0.08	-0.04	-0.03	-0.20 to 0.14	0.724	0.001	1.73
Cancer stage	—	-0.64	-0.45	-0.41	(within -0.65 to -0.17)	<0.001	≥ 0.048	—
Mastectomy (vs BCS)	—	—	-0.31	-0.28	-0.45 to -0.11	0.002	0.042	1.87
ALND (vs SLNB)	—	—	-0.27	-0.25	-0.42 to -0.08	0.005	0.034	1.82
Chemotherapy cycles	—	—	—	-0.19	-0.35 to -0.03	0.018	0.024	1.50

Standardized coefficients (β) from the patient-level models ($n = 102$); categorical predictors coded mastectomy = 1, ALND = 1; stage I–IV, education and income as ordinal scores; chemotherapy cycles as the number received. R^2 , F and F -change are computed from the adjusted R^2 values; the 95% CI, semipartial r^2 (sr^2) and variance inflation factor (VIF) of the final model are derived from each β and its exact p value ($t = t^{-1}(1 - p/2; 94 \text{ df})$, $SE = \beta/t$, $sr^2 = t^2(1 - R^2)/94$, $VIF = 94 \cdot SE^2 / (1 - R^2)$); for stage, reported as $p < 0.001$, only the outer limits of the interval are derivable. Derived quantities inherit the rounding of β to two decimals.



Dashed interval for stage: outer limit implied by $p < 0.001$ (exact CI not derivable).

Figure 7. Four-block hierarchical linear regression of FACIT-F. Left: variance explained (R^2) by each successive block. Right: standardized coefficients of the final model with 95% confidence intervals derived from the reported coefficients and exact p values; for stage, reported only as $p < 0.001$, the dashed interval is the widest interval compatible with that p value.

Identification analysis

With the observed predictor–outcome correlations the four clinical predictors could not have been independent of one another: under independence the implied R^2 would be about 1.00, so substantial positive co-occurrence of advanced stage, extensive surgery and more cycles is required by the data. Within that constraint, the summary data did not determine the direction of any adjusted association (Table 7, Figure 8). In scenario S1, the most extreme admissible configurations gave coefficients from -0.97 to 0.38 for stage, -0.48 to 0.79 for mastectomy, -0.59 to 0.56 for ALND and -0.43 to 0.38 for chemotherapy cycles; imposing clinically expected directions

(S2) narrowed but did not close these ranges. In typical admissible configurations, however, all four coefficients were negative (100% of 20,000 configurations), with medians of -0.50 , -0.16 , -0.25 and -0.21 ; stage, ALND and chemotherapy cycles reached significance in 100.0%, 99.5% and 94.8% of configurations, but mastectomy in only 72.9%. The coefficients estimated in the patient-level model were attainable (closest configuration within 0.006 of the estimated vector). When the stage-specific means were used in place of the Spearman coefficient, no configuration was compatible with the fitted model, because stage alone would then explain at least 68% of the variance.

Table 7. Identification analysis: attainable standardized coefficients of the clinical predictors across all predictor configurations consistent with the observed data.

Predictor	Estimated β (Model 4)	S0: typical configurations, 95% band	S1: median (95% band)	S1: most extreme values found	S1: % negative / % significant	S2: most extreme values found
Cancer stage	-0.41	-0.73 to -0.55	-0.50 (-0.54 to -0.46)	-0.97 to 0.38	100.0 / 100.0	-0.95 to 0.25
Mastectomy	-0.28	-0.46 to -0.16	-0.16 (-0.24 to -0.07)	-0.48 to 0.79	100.0 / 72.9	-0.43 to 0.67
ALND	-0.25	-0.56 to -0.31	-0.25 (-0.32 to -0.18)	-0.59 to 0.56	100.0 / 99.5	-0.54 to 0.53
Chemotherapy cycles	-0.19	-0.51 to -0.23	-0.21 (-0.28 to -0.12)	-0.43 to 0.38	100.0 / 94.8	-0.43 to 0.38

Each admissible configuration assigns stage, breast surgery, axillary surgery and chemotherapy band to the 102 patients so that every observed margin is preserved; correlations with FACIT-F are fixed at their observed values (stage -0.68 , chemotherapy -0.42 , mastectomy -0.35 , ALND -0.49), and the four-predictor standardized coefficients follow as $\beta = R^{-1}r$. S0: any valid configuration; S1: model R^2 within 0.55–0.614, the range compatible with the fitted final model; S2: S1 plus positive associations of stage with mastectomy, ALND and cycles, and of mastectomy with ALND. Typical values: 20,000 configurations (independent permutations in S0; restricted random walk in S1). Extremes: penalized simulated annealing from 14 starting configurations per bound; they are lower bounds on the attainable range. % significant: coefficient negative with $|t|$ above the two-sided 5% critical value at 97 residual degrees of freedom. No outcome value was generated for any patient.

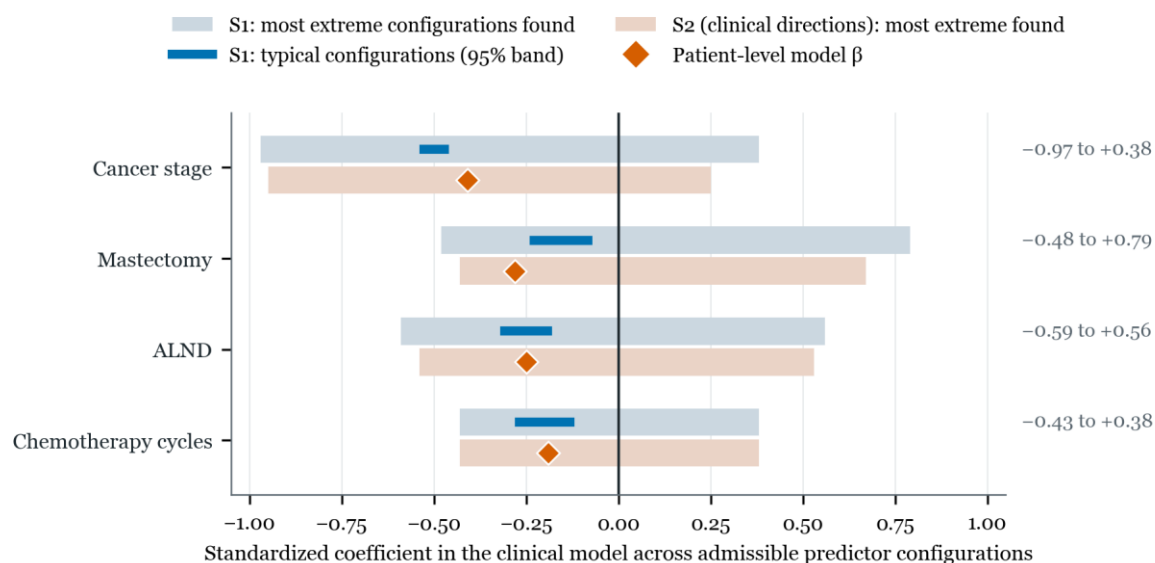


Figure 8. Identification analysis. For the four clinical predictors, the attainable standardized coefficients across all joint configurations of the predictors that preserve every observed margin and the fit of the patient-level model (scenario S1: R^2 0.55–0.614). Light bars: most extreme configurations found by optimization; dark bars: 95% band of typical admissible configurations; lower bars: scenario S2, which additionally imposes clinically expected positive associations among stage, surgery and chemotherapy; diamonds: coefficients estimated in the patient-level model.

The estimated coefficients were compatible only with a narrow co-occurrence structure (Figure 9). Among configurations that reproduced all four clinical coefficients within rounding, the correlation between mastectomy and ALND ranged from -0.14 to 0.11 (-0.19 to 0.30 with the wider margin), while stage correlated 0.16 to 0.33 with mastectomy and 0.41 to 0.63 with ALND. A correlation of 0.11 corresponds, for example, to ALND in about 71% of the women with mastectomy and 60% of those with BCS. Across 64,000 admissible configurations, the adjusted mastectomy coefficient

moved towards zero as the mastectomy–ALND correlation increased: at correlations of 0.4 or more its median was -0.11 and its most negative value -0.23 , and no configuration came within 0.13 of the estimated coefficient vector. When the stage–FACIT-F correlation was set at -0.72 , the stage coefficient remained negative in every configuration found (maximum -0.09), whereas the surgical and chemotherapy coefficients still spanned zero; at -0.76 the mastectomy range narrowed to -0.22 to 0.26 but still included zero.

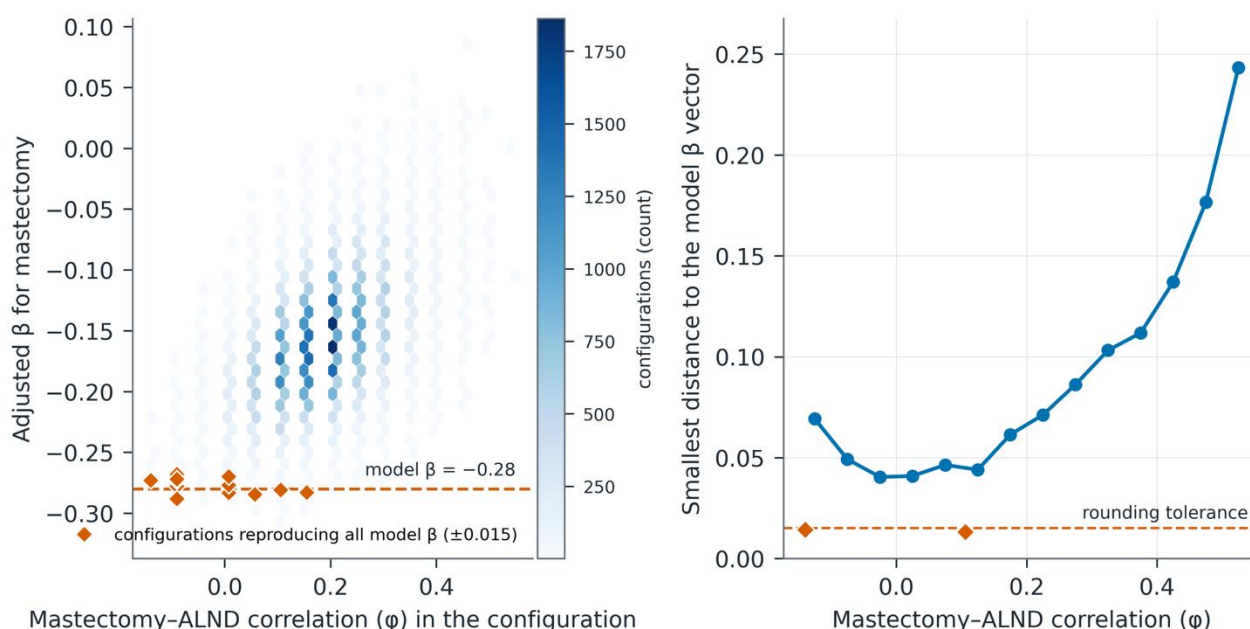


Figure 9. Compatibility of the estimated coefficients with the co-occurrence of mastectomy and axillary lymph node dissection. Left: adjusted mastectomy coefficient against the mastectomy–ALND correlation (ϕ) across 64,000 admissible configurations (hexagons; darker = more configurations) and configurations that reproduce all four estimated clinical coefficients within rounding (diamonds). Right: smallest distance to the estimated coefficient vector found at each level of ϕ (an upper bound on the true minimum); diamonds mark the optimized compatible configurations.

4. Discussion

Principal findings

In 102 women receiving chemotherapy for breast cancer at Dr. Mohammad Hoesin General Hospital, Palembang, fatigue was severe. Health-related quality of life fell steeply with advancing

stage, and women who had undergone mastectomy, ALND or more chemotherapy cycles reported much lower scores. Stage alone accounted for well over half of the variance in FACIT-F. In the patient-level multivariable model, surgery and cumulative chemotherapy added further variance, and no sociodemographic characteristic showed an association large

enough to be detected. The identification analysis added a qualification: the summary data alone cannot establish that the surgical associations are independent of stage and

chemotherapy, and that inference rests on the patient-level model and on how mastectomy and ALND co-occurred in this cohort (Figure 10).

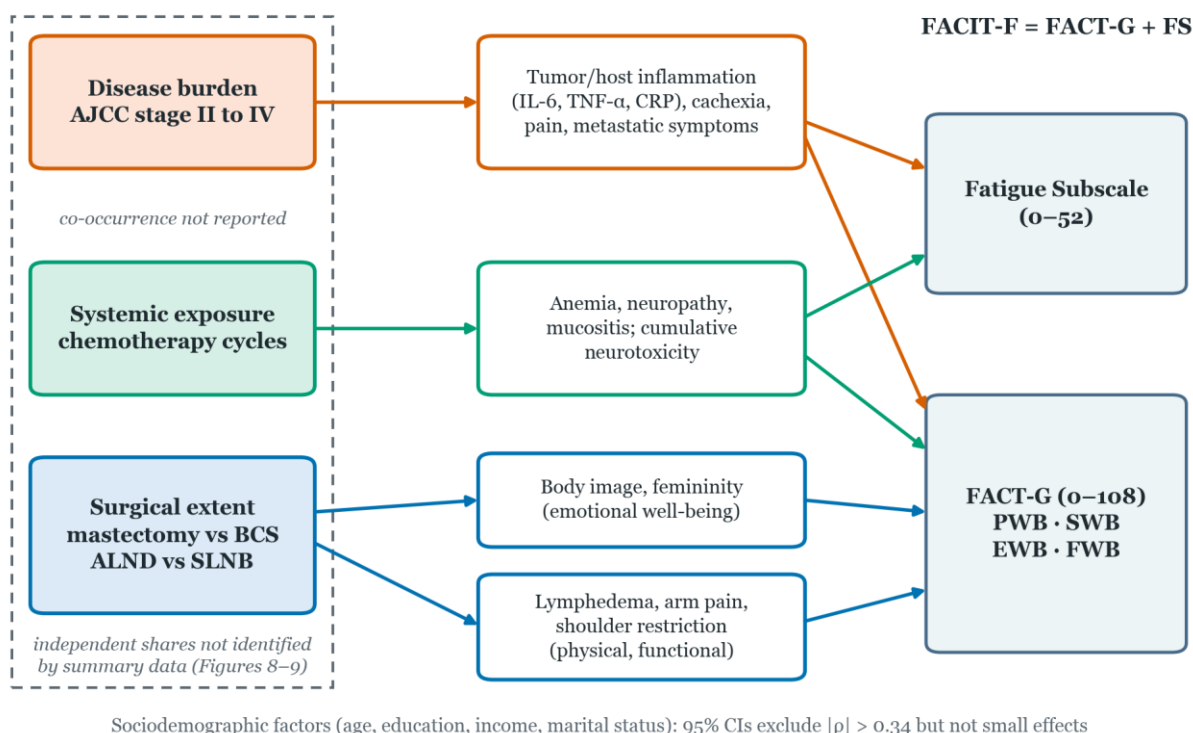


Figure 10. Conceptual model linking disease burden, surgical extent and systemic exposure to fatigue and health-related quality of life. Mechanistic pathways are drawn from the literature and were not measured in this study. The dashed box indicates that the co-occurrence of stage, surgery and chemotherapy was not reported, which limits how far the independent contribution of each domain can be identified from summary data.

Disease stage and the magnitude of the gradient

The association between stage and quality of life agrees in direction with the comparable studies cited here. In Yogyakarta, among postmenopausal women with hormone-responsive, HER2-negative disease, EQ-5D utility fell from 0.87 in metastasis-free disease to 0.77 with locoregional and 0.58 with distant metastases²¹. At the national cancer hospital, emotional functioning, fatigue, insomnia and pain were associated with global quality of life in women with stage III-IV disease before palliative treatment²⁰. In Malaysian survivors, fatigue, pain and insomnia predicted global health after chemotherapy²⁹. The magnitude observed here is, however, unusually large. A standardized difference of about four between stage II and stage IV is one sign of this. So is a mean Fatigue Subscale score of 5.8 of 52 in stage IV, which corresponds to an average item score below 0.5 on the 0-4 scale. Women with metastatic disease therefore sit close to the most severe response option on most fatigue items. Part of this may be genuine, because all women with stage IV disease were receiving palliative chemotherapy, had undergone locoregional surgery and were assessed within three months of a cycle, a combination that concentrates disease and treatment burden. Part may reflect the internal inconsistency of the stage-specific means, which do not reproduce the cohort mean, although the reconciliation analysis showed that the conclusion does not depend on it, because stage explained 60-70% of the FACIT-F variance under either reading. The point estimates for individual stages should still be interpreted with that caveat. A systematic review of Asian low- and middle-income countries found inconsistent associations between stage and HRQoL across 28 studies²³. This suggests that the strength of the gradient depends on the stage mix and treatment phase of each cohort. In a sample in which 63% had

stage III-IV disease and all were on active treatment, a strong gradient is expected.

A stage gradient in fatigue has strong biological support. Tumor burden drives systemic inflammation. Inflammatory markers such as C-reactive protein and interleukin-6 are associated with fatigue in breast cancer⁷, and the subgroup with high pro-inflammatory cytokine concentrations shows mainly physical fatigue⁸. In the present data, the stage gradient was steeper for FACIT-F (η^2 0.70) than for FACT-G (η^2 0.59). The derived fatigue subscale fell almost fivefold from stage II to stage IV, so fatigue rather than general well-being carried much of the gradient. This fits meta-analytic evidence that poor performance status is the strongest risk factor for CRF⁶, and it also fits the finding that CRF during chemotherapy is accompanied by reduced exercise capacity and neuromuscular fatigue¹⁰.

Fatigue during chemotherapy

The mean derived Fatigue Subscale score of 21.7 was less than half the German general-population mean of 43.5²⁶. Every subgroup scored below the population mean minus one standard deviation, including women with stage I-II disease and those treated with BCS or SLNB, and because fatigue reporting is culturally shaped and no Indonesian or Asian population norms exist, the size of the gap should be interpreted with caution. Even so, a difference of more than two population standard deviations is less likely to be explained by cultural response style alone. Pooled data indicate that 43% of patients with cancer report fatigue, and one-third of those on active treatment report severe fatigue⁵, so the present cohort may sit toward the severe end of that distribution, although a mean subscale score and a prevalence of severe fatigue are not directly comparable. The steep decline with the number of cycles, from 23.8 after 1-4 cycles to 7.1 after more than 10, would fit the cumulative nature of chemotherapy toxicity. Persistent taxane-

induced neuropathy impairs global quality of life in proportion to its severity³⁰, its sensory and motor profile depends on the taxane used³¹, and it affects about two-thirds of Indonesian patients, in whom baseline inflammation predicts its occurrence³². Neuropathy also raises the subsequent risk of depression and anxiety³³. Chemotherapy-induced anemia is strongly associated with fatigue³. In Malaysia, fatigue correlated with lower FACT-B scores in survivors³⁴, and in the present data the FACT-G and FACIT-F gradients moved together across every clinical subgroup. Neither hemoglobin nor neuropathy was recorded, so these mechanisms remain hypotheses for this cohort. They do, however, identify measurable targets for future work.

The six women who had received more than 10 cycles deserve separate comment. They probably had metastatic disease treated with successive palliative lines, so their very low scores likely reflect the combined effect of disease burden and treatment, rather than cycle count alone. For the same reason, the bivariate gradient across cycle bands is partly a stage gradient. Only the regression addresses this overlap. Cycles remained associated with FACIT-F there after adjustment for stage and surgery. The 24.5-point difference between 5–10 and more than 10 cycles was not significant, which illustrates the imprecision of such small groups, since the confidence interval of the highest band spanned 40 points.

Breast and axillary surgery

The differences between surgical groups were large. They agree with the literature. Women treated by mastectomy scored 17.3 FACIT-F points and 11.3 FACT-G points lower than those treated with BCS. In a large North American cohort, mastectomy with reconstruction was associated with worse psychosocial (–3.80) and sexual (–5.41) well-being than BCS with radiotherapy nine years after diagnosis¹¹. In India, BCS was associated with better physical functioning, less fatigue and better body image at six months, and better global health at one year, than modified radical mastectomy¹³. In Pakistan, Mexico, Saudi Arabia and the United Arab Emirates, mastectomy was associated with poorer quality of life or cosmetic satisfaction^{12,35–37}, and qualitative work in South Asia identifies mastectomy-related disfigurement, distress, stigma and social withdrawal as central concerns³⁸. Reconstruction improves body image and physical health compared with mastectomy alone¹⁴, but it is rarely available to Indonesian women undergoing mastectomy for locally advanced disease. An Indonesian study of locally advanced disease found that women who had undergone surgery had better body image than those who had not²², an apparent contrast that probably reflects the comparison groups, since women with locally advanced disease who have not undergone surgery may still carry bulky or ulcerated tumors. For most patients in the present cohort, the relevant comparison is mastectomy against BCS. It is not surgery against none.

The axillary contrast was the largest surgical difference (22.1 FACIT-F points; $g = 1.12$). A meta-analysis of 67 studies found that ALND increased the prevalence of lymphedema by 13.7 percentage points and of pain by 24.2 points compared with SLNB¹⁵. Pooled risk ratios for lymphedema after ALND range from 3.67 to 5.41^{16,39}. In the SENOMAC trial, women randomized to completion ALND reported more pain and arm symptoms and worse physical function and mobility one year after surgery, although global HRQoL did not differ¹⁷. In INSEMA, arm and breast symptom scores favored omission of axillary surgery at every assessment¹⁸. Once lymphedema is established, its burden appears similar after either procedure⁴⁰. ALND may therefore affect quality of life mainly through its higher incidence of lymphedema, which was not measured here. The larger variance

after ALND and mastectomy in the present cohort fits this interpretation: a subset of women may develop disabling arm morbidity while others recover well. Women were assessed at different intervals after surgery. These contrasts therefore also mix the effect of the procedure with that of recovery time, which a cross-sectional design cannot separate.

Whether these surgical associations are independent of stage and chemotherapy is the central inferential question. The answer depends on information that summary tables do not contain. In the patient-level regression, mastectomy and ALND remained associated with lower FACIT-F after adjustment for stage and sociodemographic factors, and the surgical block explained a further 8.6% of the variance. The identification analysis showed that this is one admissible reading of the data but not the only one. Across all predictor configurations that preserve the observed margins and the fit of the patient-level model, the adjusted coefficients of mastectomy and ALND could take either sign, and mastectomy reached significance in only about 73% of typical configurations. The two surgical variables are clinically linked, since mastectomy and ALND are frequently performed together as modified radical mastectomy. Their individual coefficients are therefore sensitive to their overlap. The prudent conclusion is that more extensive surgery is associated with poorer quality of life in this cohort and that the patient-level model supports an independent contribution. Confirmation requires the cross-classification of stage and surgery or, better, a prospective design.

The compatibility analysis made this condition explicit. The estimated coefficients could be reproduced only by configurations in which mastectomy and ALND were nearly uncorrelated (correlation between –0.14 and 0.11), that is, configurations in which ALND was performed in a similar proportion of women after mastectomy and after BCS. If ALND was concentrated among women undergoing mastectomy, as is common in Indonesian practice, the independent mastectomy coefficient would be smaller than reported. At correlations of 0.4 or more, no admissible configuration came close to the estimated values, and the median adjusted mastectomy coefficient was about –0.11. Reporting the stage-by-surgery cross-tabulation alongside such models is the most direct way to make the surgical inference verifiable.

Sociodemographic characteristics

None of the sociodemographic variables correlated significantly with either outcome, and together they explained 4.9% of the variance. This finding should be read as the absence of large associations rather than the absence of any, because the confidence intervals excluded correlations stronger than about |0.34| but allowed small effects, and the study had 80% power only for correlations of 0.27 or more. Elsewhere in Asia, income has been the most consistent sociodemographic correlate of HRQoL²³. Education, employment and income have been associated with better quality of life in Saudi Arabia, India, the United Arab Emirates and Bangladesh^{28,36,37,41}. In Iraq, age, marital status and disease duration were the main correlates⁴², and in China social constraints, stigma and support explained a large share of the variance⁴³. Two features of the present setting may attenuate direct sociodemographic effects. First, the national registry shows that lower education is associated with metastatic presentation³. Socioeconomic disadvantage may therefore act on quality of life indirectly through stage, an effect that adjustment for stage removes by design. Second, national health insurance finances most treatment in this hospital and standardizes access to core therapy, although its chemotherapy tariffs do not cover hospital costs²⁴ and institutional resources shape arm symptoms and financial difficulty in other universal-

coverage systems⁴⁴. Whether social support, which was not measured, buffers the association between marital status and quality of life remains a hypothesis for future work.

Locoregional surgery in stage IV disease

All 21 women with stage IV disease had undergone breast and axillary surgery. Randomized evidence shows that early locoregional therapy does not improve overall survival in de novo metastatic breast cancer^{45,46}, and a meta-analysis found lower quality of life at 18 months among women who received locoregional treatment⁴⁷. In Indonesia, surgery for metastatic disease is often performed to control fungating or bleeding tumors. Some women in the present cohort may also have been found to have metastases after surgery planned with curative intent. Whatever the reason, these women carried the morbidity of surgery in addition to that of metastatic disease and palliative chemotherapy. All of them had surgery and no comparison group exists, so their very low scores cannot be attributed to surgery here, but together with the external evidence above they argue for careful selection of locoregional surgery in stage IV disease and for proactive palliative care when it is performed.

Clinical implications

Three practical implications follow from the cited evidence, not from the present cross-sectional data. First, fatigue should be screened routinely at every chemotherapy visit, because it was severe across all subgroups. Resistance training during anticancer therapy improves fatigue by about four FACIT-Fatigue points⁴⁸. Second, women undergoing ALND or mastectomy should enter structured rehabilitation from the first postoperative day. Early tailored exercise improves shoulder range of motion and strength⁴⁹, a physiotherapy-led program improved upper-limb function and pain at 12 months in the UK PROSPER trial⁵⁰, and prospective surveillance with early management reduces chronic lymphedema by about 70%⁵¹. Third, axillary surgery should be de-escalated wherever current evidence allows. Omission of completion ALND in women with limited sentinel-node involvement, and omission of SLNB in selected low-risk patients, are oncologically safe^{52,53}. These trials enrolled women with early, clinically node-negative disease treated by primary surgery. They apply directly only to the minority of Indonesian patients who present early. For the majority with locally advanced disease, the applicability of axillary de-escalation after neoadjuvant chemotherapy needs to be established in local studies.

Regional context

These findings sit within a regional pattern of late presentation and treatment-intensive care. One year after diagnosis, survivors in eight Southeast Asian countries reported a mean global health score of 66 of 100, with anxiety in 37% and depression in 46%⁵⁴. Malaysian survivors had low global health one to three years after chemotherapy²⁹. In Indonesia, presentation delays⁴ and late-stage disease³ translate directly into the stage mix seen here. The gap between chemotherapy costs and insurance reimbursement²⁴ limits the resources available for supportive care. The FACT-G mean of 76.8 lies in the upper half of the regional range²³, which suggests that general well-being is relatively preserved in many women, whereas the very low fatigue scores identify fatigue as the domain most in need of attention. Validated Indonesian instruments now allow breast-specific and arm-specific symptoms to be measured alongside the FACIT system²⁵.

Methodological contribution

This study illustrates how the analytical value of a cross-sectional report can be maximized without access to the full dataset. Group means and standard deviations permit exact

analysis of variance, Welch tests and standardized effect sizes, and reported coefficients with exact p values permit recovery of confidence intervals, semipartial r^2 and variance inflation factors. An identification analysis makes explicit which multivariable conclusions depend on unreported joint distributions. The four clinical predictors could not have been mutually independent. The surgical coefficients are attainable only under specific overlap structures, which is a property of the reported numbers that any reader can verify. We suggest that reports of correlated clinical predictors routinely include their cross-tabulation. Adjusted associations can then be appraised independently.

Research agenda

Four studies would resolve the questions left open. First, a prospective cohort enrolling women before surgery and following them through chemotherapy would separate the contributions of surgery and chemotherapy in time. It would use FACT-B, FACIT-Fatigue and arm-specific measures at baseline, after surgery and after every second cycle. To detect an independent surgical association explaining 2% of the variance (semipartial r^2 0.02, smaller than the 3–4% implied here) with 80% power in an eight-predictor model, 156 participants are required. Second, a comparison of BCS with mastectomy in women with stage II–III disease, matched on stage and nodal status, would need about 66 women treated with BCS and 198 with mastectomy to detect a standardized difference of 0.4 at the 1:3 ratio observed here. Third, a study of sociodemographic correlates able to estimate correlations of 0.1–0.2 with a confidence-interval half-width of ± 0.10 would require about 360–380 participants, ideally across several provinces. Fourth, a trial of supervised resistance training integrated into chemotherapy visits would test the most promising intervention in the population that needs it most. FACIT-Fatigue would be the primary outcome, with hemoglobin, neuropathy and inflammatory markers as mediators.

Strengths and limitations

The study has several strengths. It used validated instruments with population norms in a consecutively recruited sample during active chemotherapy, a treatment phase in which HRQoL is rarely measured in Indonesia. Every subgroup comparison was analyzed exactly, with effect sizes and confidence intervals. The multivariable model was supplemented by an analysis that quantifies its dependence on unreported data. The benchmarks were drawn from verified national and regional sources. The internal inconsistency of the stage-specific means was reported and tested rather than ignored.

Treatment intent deserves specific mention. Women receiving neoadjuvant chemotherapy are, by definition, assessed before their final surgery, yet every woman in the cohort had already undergone breast and axillary surgery. Neoadjuvant patients were therefore either assessed after completing neoadjuvant therapy and surgery, or the intent was recorded at a different time point. Intent was reported only as adjuvant versus neoadjuvant or palliative combined, so its association with HRQoL could not be examined. It may partly explain the overlap between stage, surgery and cycle count that limits identification. Reliability coefficients for the Bahasa Indonesia FACIT instruments were not calculated in this sample, although the instruments are the official translations and the FACIT-Fatigue scale has shown high internal consistency elsewhere²⁶.

The limitations are considerable. The cross-sectional design precludes causal inference. It cannot separate the effect of surgery from that of time since surgery or of the treatment

phase in which each woman was assessed. The study was conducted at a single tertiary hospital during two months. The numbers screened and declining were not recorded, so selection cannot be assessed. Performance status, comorbidity, hemoglobin, neuropathy, chemotherapy regimen, radiotherapy, reconstruction, psychological morbidity and social support were not measured, and residual confounding is likely. The stage-specific means are internally inconsistent with the cohort means. The stage I group contained only two patients and the highest chemotherapy band only six. Unstandardized regression coefficients and residual diagnostics are not reported, and the identification analysis showed that the independence of the surgical associations cannot be confirmed from the summary data. Finally, the Fatigue Subscale standard deviations were not available, so fatigue could be compared with population norms only through a conservative bound.

5. Conclusion

In women receiving chemotherapy for breast cancer at a tertiary referral hospital in South Sumatra, fatigue was severe, with a mean Fatigue Subscale score of less than half the population norm. Health-related quality of life declined steeply with advancing stage (FACIT-F 115.6 in stage II vs 61.2 in stage IV), after mastectomy (−17.3 points) and ALND (−22.1 points), and with more chemotherapy cycles, whereas sociodemographic characteristics showed no association large enough to detect. The patient-level multivariable model supports independent contributions of stage, surgery and chemotherapy. The summary data alone cannot confirm the independence of the surgical associations, which holds only if mastectomy and ALND were nearly uncorrelated in this cohort. Routine fatigue screening, prospective lymphedema surveillance, early rehabilitation after axillary surgery and de-escalation of axillary surgery where evidence allows merit evaluation as part of chemotherapy care in Indonesian referral hospitals. A prospective cohort is needed to establish the independent association of surgical extent on quality of life. It should enroll women before surgery, include arm-specific outcomes and have at least 156 participants.

6. Declarations

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki. The protocol was reviewed and approved by CMHC Indonesia (approval number 2024/8456), before data collection began. Every participant received a verbal and written explanation of the study from a research assistant who was not involved in her clinical care and provided written informed consent before completing the questionnaires. Participation was voluntary, refusal had no consequence for treatment, and questionnaires and extraction forms were coded without names or medical-record numbers.

Consent for Publication

Not applicable. The article contains only aggregate data; no individual patient data, images or other identifying information are reported.

Availability of Data and Materials

All summary data analyzed in this article are reported in Tables 1–7. The de-identified patient-level dataset is held by the corresponding author and is available on reasonable request, subject to approval by the ethics committee.

Artificial Intelligence Use Statement

None.

Author Contribution Statement

M.Y.R.F.: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing – original draft. M.U.: Conceptualization, Supervision, Validation, Writing – review & editing. T.: Methodology, Formal analysis, Supervision, Writing – review & editing. All authors read and approved the final manuscript.

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Conflict of Interest / Competing Interests

The authors declare no competing interests.

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7. References

- Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024;74(3):229-63. doi:10.3322/caac.21834
- GBD 2023 Breast Cancer Collaborators. Global, regional, and national burden of breast cancer among females, 1990–2023, with forecasts to 2050: a systematic analysis for the Global Burden of Disease Study 2023. *Lancet Oncol.* 2026;27(3):302-26. doi:10.1016/S1470-2045(25)00730-2
- Setyawan IB, Kurnia D, Setiaji K, et al. Sociodemographic disparities associated with advanced stages and distant metastatic breast cancers at diagnosis in Indonesia: a cross-sectional study. *Ann Med Surg (Lond).* 2023;85(9):4211-7. doi:10.1097/MS9.0000000000001030
- Hutajulu SH, Prabandari YS, Bintoro BS, et al. Delays in the presentation and diagnosis of women with breast cancer in Yogyakarta, Indonesia: A retrospective observational study. *PLoS One.* 2022;17(1):e0262468. doi:10.1371/journal.pone.0262468
- Kang YE, Yoon JH, Park NH, et al. Prevalence of cancer-related fatigue based on severity: a systematic review and meta-analysis. *Sci Rep.* 2023;13(1):12815. doi:10.1038/s41598-023-39046-0
- Ma Y, He B, Jiang M, et al. Prevalence and risk factors of cancer-related fatigue: A systematic review and meta-analysis. *Int J Nurs Stud.* 2020;111:103707. doi:10.1016/j.ijnurstu.2020.103707
- Maurer T, Jaskulski S, Behrens S, et al. Tired of feeling tired - The role of circulating inflammatory biomarkers and long-term cancer related fatigue in breast cancer survivors. *Breast.* 2021;56:103-9. doi:10.1016/j.breast.2021.02.008
- Schmidt ME, Maurer T, Behrens S, et al. Cancer-related fatigue: Towards a more targeted approach based on classification by biomarkers and psychological factors. *Int J Cancer.* 2024;154(6):1011-8. doi:10.1002/ijc.34791
- Batool R, Hayat T, Butt HR, et al. Prevalence of chemotherapy-induced anemia and its impact on quality of life in breast cancer patients. *J Complement Integr Med.* 2026;23(3):506-12. doi:10.1515/jcim-2026-0231
- Mallard J, Hucteau E, Schott R, et al. Tracking cancer-related fatigue during chemotherapy: Insights from a comparative cohort study of early breast cancer patients. *Int J Cancer.* 2025;157(8):1625-36. doi:10.1002/ijc.35508
- Diao K, Lei X, He W, et al. Patient-reported Quality of Life After Breast-conserving Surgery With Radiotherapy Versus Mastectomy and Reconstruction. *Ann Surg.* 2023;278(5):e1096-e1102. doi:10.1097/SLA.0000000000005920
- Vohra LM, Javed SM, Jabeen D, et al. Quality of life of breast cancer survivors: a comparison of breast conserving surgery versus total mastectomy with and without immediate reconstruction: a prospective cohort study. *Ann Med Surg (Lond).* 2023;85(5):1513-7. doi:10.1097/MS9.0000000000000607
- Cherian K, Acharya NR, Bhargavan RV, et al. Quality of Life Post Breast Cancer Surgery: Comparison of Breast Conservation

- Surgery versus Modified Radical Mastectomy in a Developing Country. *South Asian J Cancer*. 2022;11(3):183-9. doi:10.1055/s-0042-1743420
14. Zehra S, Doyle F, Barry M, et al. Health-related quality of life following breast reconstruction compared to total mastectomy and breast-conserving surgery among breast cancer survivors: a systematic review and meta-analysis. *Breast Cancer*. 2020;27(4):534-66. doi:10.1007/s12282-020-01076-1
 15. Che Bakri NA, Kwasnicki RM, Khan N, et al. Impact of Axillary Lymph Node Dissection and Sentinel Lymph Node Biopsy on Upper Limb Morbidity in Breast Cancer Patients: A Systematic Review and Meta-Analysis. *Ann Surg*. 2023;277(4):572-80. doi:10.1097/SLA.0000000000005671
 16. Liang Y, Zhou Y, Houben R, et al. A systematic review and meta-analysis of risk factors influencing patient-reported arm symptoms post-breast cancer treatment: Accounting for radiotherapy impact. *Breast*. 2024;78:103812. doi:10.1016/j.breast.2024.103812
 17. Appelgren M, Sackey H, Wengström Y, et al. Patient-reported outcomes one year after positive sentinel lymph node biopsy with or without axillary lymph node dissection in the randomized SENOMAC trial. *Breast*. 2022;63:16-23. doi:10.1016/j.breast.2022.02.013
 18. Reimer T, Stachs A, Veselinovic K, et al. Patient-reported outcomes for the Intergroup Sentinel Mamma study (INSEMA): A randomised trial with persistent impact of axillary surgery on arm and breast symptoms in patients with early breast cancer. *EClinicalMedicine*. 2023;55:101756. doi:10.1016/j.eclinm.2022.101756
 19. Sukarno A, Dewi R, Kurnia MP, et al. Quality of Life Determinants among Breast Cancer Women Undergoing Treatment in Indonesia: A Cross-Sectional Study. *Indian J Palliat Care*. 2024;30(3):215-21. doi:10.25259/IJPC.344_2023
 20. Gayatri D, Efremov L, Mikolajczyk R, et al. Quality of Life Assessment and Pain Severity in Breast Cancer Patients Prior to Palliative Oncology Treatment in Indonesia: A Cross-Sectional Study. *Patient Prefer Adherence*. 2021;15:2017-26. doi:10.2147/PPA.S320972
 21. Etikasari R, Andayani TM, Endarti D, et al. Health related quality of life among postmenopausal woman with hormone responsive HER2- breast cancer in Indonesia. *J Basic Clin Physiol Pharmacol*. 2021;32(4):561-5. doi:10.1515/jbcp-2020-0427
 22. Priyono SH, Budiwinata W, Tedjowitono B, et al. Sociodemographic factors and treatment effects on quality of life in locally advanced breast cancer: a cross-sectional study. *Ecanermedalscience*. 2025;19:1965. doi:10.3332/ecancer.2025.1965
 23. Ngo NTN, Nguyen HT, Nguyen PTL, et al. Health-related quality of life in breast cancer patients in low-and-middle-income countries in Asia: a systematic review. *Front Glob Womens Health*. 2023;4:1180383. doi:10.3389/fgwh.2023.1180383
 24. Kurniawan MD, Abdissalam E, Ariawan MW, et al. Cost Disparities Between Hospital Expenditures and Reimbursement Schemes in Indonesia: A Study on Chemotherapy for Breast Cancer. *Asian Pac J Cancer Prev*. 2026;27(3):999-1005. doi:10.31557/APJCP.2026.27.3.999
 25. Solikhah S, Perwitasari DA, Rejeki DSS. Cross-cultural adaptation and psychometric properties of the Indonesian version for quality of life among breast cancer patients. *Front Public Health*. 2023;11:1069422. doi:10.3389/fpubh.2023.1069422
 26. Montan I, Löwe B, Cella D, et al. General Population Norms for the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale. *Value Health*. 2018;21(11):1313-21. doi:10.1016/j.jval.2018.03.013
 27. Amarsheda S, Bhise AR. Systematic review of cancer-related fatigue instruments in breast cancer patients. *Palliat Support Care*. 2022;20(1):122-8. doi:10.1017/S1478951521000444
 28. Rahman R, Ishika A, Ali TY, et al. Influence of age, body mass index and family income on the health Quality of Life among the breast cancer patients in Bangladesh: a cross-sectional study. *Front Oncol*. 2026;16:1817273. doi:10.3389/fonc.2026.1817273
 29. Syed Alwi SM, Narayanan V, Mohd Taib NA, et al. Predictors of health-related quality of life after completion of chemotherapy among Malaysian early-stage breast cancer survivors. *Support Care Cancer*. 2022;30(3):2793-801. doi:10.1007/s00520-021-06686-9
 30. Engvall K, Gréen H, Fredrikson M, et al. Impact of persistent peripheral neuropathy on health-related quality of life among early-stage breast cancer survivors: a population-based cross-sectional study. *Breast Cancer Res Treat*. 2022;195(3):379-91. doi:10.1007/s10549-022-06670-9
 31. Mo H, Yan X, Zhao F, et al. Association of Taxane Type With Patient-Reported Chemotherapy-Induced Peripheral Neuropathy Among Patients With Breast Cancer. *JAMA Netw Open*. 2022;5(11):e2239788. doi:10.1001/jamanetworkopen.2022.39788
 32. Wiranata JA, Astari YK, Ucce M, et al. Predictive Factors of Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer: A Decision Tree Model Approach. *JCO Glob Oncol*. 2024;10:e2400160. doi:10.1200/GO.24.00160
 33. McNeish BL, Richardson JK, Whitney DG. Chemotherapy-induced peripheral neuropathy onset is associated with early risk of depression and anxiety in breast cancer survivors. *Eur J Cancer Care (Engl)*. 2022;31(6):e13648. doi:10.1111/ecc.13648
 34. Rahman ANA, Ooi FK, Justine M, et al. Components of Physical Activity and Their Relationships with Quality of Life and Cancer-Related Fatigue in Breast Cancer Survivors in Malaysia. *Malays J Med Sci*. 2025;32(3):120-31. doi:10.21315/mjms-12-2024-996
 35. Alvarez-Pardo S, Romero-Pérez EM, Camberos-Castañeda N, et al. Quality of Life in Breast Cancer Survivors in Relation to Age, Type of Surgery and Length of Time since First Treatment. *Int J Environ Res Public Health*. 2022;19(23):16229. doi:10.3390/ijerph192316229
 36. Al-Karni MAT, Omar MTA, Al-Dhwayan NM, et al. Factors Associated with Health-Related Quality of Life Among Breast Cancer Survivors in Saudi Arabia: Cross-Sectional Study. *Asian Pac J Cancer Prev*. 2024;25(3):951-61. doi:10.31557/APJCP.2024.25.3.951
 37. Smail L, Jassim G, Khan S, et al. Quality of Life of Emirati Women with Breast Cancer. *Int J Environ Res Public Health*. 2022;20(1):570. doi:10.3390/ijerph20010570
 38. Malawaraarachchi BP, Abeysinghe C, Seneviwickrama M, et al. Body image concerns among women diagnosed with breast cancer in a South Asian setting: a phenomenology approach. *BMC Cancer*. 2025;25(1):1819. doi:10.1186/s12885-025-15288-1
 39. Lin Y, Xu Y, Wang C, et al. Loco-regional therapy and the risk of breast cancer-related lymphedema: a systematic review and meta-analysis. *Breast Cancer*. 2021;28(6):1261-72. doi:10.1007/s12282-021-01263-8
 40. Poulsen L, Kaur M, Jacobsen AL, et al. Comparison of upper extremity lymphedema after sentinel lymph node biopsy and axillary lymph node dissection: patient-reported outcomes in 3044 patients. *Breast Cancer Res Treat*. 2022;191(1):87-96. doi:10.1007/s10549-021-06414-1
 41. Gupta N, Pandey AK, Dimri K, et al. Health-related quality of life among breast cancer patients in India. *Support Care Cancer*. 2022;30(12):9983-90. doi:10.1007/s00520-022-07395-7
 42. Alsdan RM, Abdul Kadir A, Mohd Noor N, et al. Quality of Life and Its Associated Factors Among Breast Cancer Women in Iraq: A Cross-Sectional Study. *Asian Pac J Cancer Prev*. 2025;26(1):339-45. doi:10.31557/APJCP.2025.26.1.339
 43. Cui C, Wang L, Wang X. Health-related quality of life and social constraints among Chinese breast cancer patients: a cross-sectional study. *Health Qual Life Outcomes*. 2021;19(1):238. doi:10.1186/s12955-021-01871-0
 44. Laperche-Santos D, Assad-Suzuki D, Resende H, et al. Impact of public vs. private insurance coverage on quality of life of women with early-stage estrogen receptor-positive breast cancer. *Breast Cancer Res Treat*. 2025;215(1):26. doi:10.1007/s10549-025-07866-5
 45. Khan SA, Zhao F, Goldstein LJ, et al. Early Local Therapy for the Primary Site in De Novo Stage IV Breast Cancer: Results of a Randomized Clinical Trial (EA2108). *J Clin Oncol*. 2022;40(9):978-87. doi:10.1200/JCO.21.02006

46. Tosello G, Riera R, Torloni MR, et al. Breast surgery for metastatic breast cancer. *Cochrane Database Syst Rev.* 2025;11(11):CD011276. doi:10.1002/14651858.CD011276.pub3
47. Weiss C, Trens P, Schmitt M, et al. Quality of Life After Locoregional Treatment in Women with De Novo Metastatic Breast Cancer: A Systematic Review and Meta-Analysis. *Cancers (Basel).* 2025;17(5):751. doi:10.3390/cancers17050751
48. Ernst M, Wagner C, Oeser A, et al. Resistance training for fatigue in people with cancer. *Cochrane Database Syst Rev.* 2024;11(11):CD015518. doi:10.1002/14651858.CD015518
49. Min J, Kim JY, Ryu J, et al. Early Implementation of Exercise to Facilitate Recovery After Breast Cancer Surgery: A Randomized Clinical Trial. *JAMA Surg.* 2024;159(8):872-80. doi:10.1001/jamasurg.2024.1633
50. Bruce J, Mazuquin B, Canaway A, et al. Exercise versus usual care after non-reconstructive breast cancer surgery (UK PROSPER): multicentre randomised controlled trial and economic evaluation. *BMJ.* 2021;375:e066542. doi:10.1136/bmj-2021-066542
51. Rafn BS, Christensen J, Larsen A, et al. Prospective Surveillance for Breast Cancer-Related Arm Lymphedema: A Systematic Review and Meta-Analysis. *J Clin Oncol.* 2022;40(9):1009-26. doi:10.1200/JCO.21.01681
52. de Boniface J, Filtenborg Tvedskov T, Rydén L, et al. Omitting Axillary Dissection in Breast Cancer with Sentinel-Node Metastases. *N Engl J Med.* 2024;390(13):1163-75. doi:10.1056/NEJMoa2313487
53. Reimer T, Stachs A, Veselinovic K, et al. Axillary Surgery in Breast Cancer - Primary Results of the INSEMA Trial. *N Engl J Med.* 2025;392(11):1051-64. doi:10.1056/NEJMoa2412063
54. ACTION Study Group. Health-related quality of life and psychological distress among cancer survivors in Southeast Asia: results from a longitudinal study in eight low- and middle-income countries. *BMC Med.* 2017;15(1):10. doi:10.1186/s12916-016-0768-2