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Changes in health-related quality of life among endometrial cancer survivors: a prospective cohort study

Luiza Vianna Conteville
Programa de Pós-Graduação em Oncologia (PPGO-INCA)
Juliane Alves Silva
Instituto Nacional de Câncer (INCA)
Lidiane Araujo Cezário
Instituto Nacional de Câncer (INCA)
Priscila Helena Marietto Figueira
Instituto Nacional de Câncer (INCA)
Fernando Lopes Tavares Lima
Instituto Nacional de Câncer (INCA)
Wenderson Santana Souza
Universidade Estadual de Feira de Santana, Feira de Santana
Giovanna Adrielly Santos Oliveira
Universidade Federal de Pernambuco
Yasmin Jassanan Resende Martins
Universidade Federal de Minas Gerais
Maria Fernanda Agostinho Pinheiro
Universidade Federal Rural do Rio de Janeiro
Dafiny Vitoriano Carvalho
Universidade do Estado do Rio de Janeiro
Késia Pacanhã Malafaia Miranda
Universidade Estácio de Sá
Gabriela Villaça Chaves
gchaves@inca.gov.br

Instituto Nacional de Câncer (INCA)

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Abstract

Objective

To analyze longitudinal changes in health-related quality of life (HRQoL) among women with endometrial cancer (EC) and assess the clinical relevance of these changes over follow-up.

Methods

This prospective observational cohort study included women aged over 20 years diagnosed with endometrioid EC who had received no prior treatment and underwent curative-intent surgery. HRQoL was assessed using the EORTC QLQ-C30 (version 3.0). The Minimal Important Difference (MID) approach was used to classify changes as small or moderate, but clinically meaningful, improvements or deteriorations. Longitudinal changes in HRQoL were further evaluated using linear mixed-effects models adjusted for time, age, body mass index (BMI), and adjuvant treatment (chemotherapy and/or radiotherapy).

Results

Most HRQoL domains remained stable or showed changes of small to moderate magnitude over time. Higher BMI was associated with poorer physical functioning and role functioning, greater insomnia and pain, and lower dyspnea scores. Older age was associated with poorer physical functioning and higher insomnia scores. Adjuvant treatment was not significantly associated with HRQoL outcomes.

Conclusion

These findings suggest an adaptive process during cancer survivorship, characterized by improvements in emotional and social functioning despite the persistence of some symptoms. Higher BMI appeared to have a greater impact on HRQoL than adjuvant treatment. Follow-up care for EC survivors should therefore be individualized and aligned with each woman's specific needs.

INTRODUCTION

Endometrial cancer (EC) is the most common gynecological malignancy in high-income countries, and its incidence has been increasing in several regions worldwide, a trend mainly associated with population aging and the rising prevalence of obesity [1]. In Brazil, EC is the sixth most incident cancer among women [2].

Women treated for endometrial cancer often experience physical and psychosocial sequelae resulting from both the disease and its treatment, including hormonal changes, fatigue, pain, urinary and bowel dysfunction, as well as impaired mental health, all of which may negatively affect quality of life [3, 4].

Health-related quality of life (HRQoL) has become an important outcome in oncology, particularly for malignancies with favorable prognosis. Previous studies suggest that EC survivors may experience reduced quality of life, especially those diagnosed at more advanced stages (III and IV) [5]. Banning et al. [6] observed poorer physical, social, and functional performance among women with advanced-stage EC compared with those diagnosed at an early stage. Conversely, Warring et al. [7], in a study of women with predominantly early-stage EC (stage IA) prior to treatment, found lower sexual interest and greater fatigue compared with the reference population. They also reported that obesity was associated with worse global health status, physical functioning, fatigue, and other HRQoL domains.

Despite evidence highlighting the relevance of HRQoL in endometrial cancer, the available literature remains limited. Most existing studies have focused on women with early-stage disease and have used cross-sectional designs, limiting the understanding of temporal changes in HRQoL. In addition, given that HRQoL is influenced by socioeconomic and cultural factors, data from the Brazilian population are essential to contextualize the impact of the disease and its treatment and to support care strategies tailored to the local context. Therefore, the present study aimed to analyze the temporal evolution of HRQoL in endometrial cancer survivors and to assess the clinical relevance of these changes throughout follow-up.

METHODS

Study design

This was a prospective observational cohort study conducted at a High-Complexity Oncology Care Center in Rio de Janeiro, Brazil, between November 2016 and December 2019.

Study population

Eligible participants were women aged > 20 years diagnosed with endometrioid endometrial cancer who had not received any previous treatment and for whom surgery was indicated with curative intent. Women who received neoadjuvant radiotherapy and/or chemotherapy were excluded. Eligibility criteria is presented in Fig. 1.

Data collection

Data collection was performed before surgery (T0), at 6 months (T1), 1 year (T2), 2 years (T3), and 3 years (T4) after surgery. All participants provided written informed consent. The study was approved by the Research Ethics Committee of the Instituto Nacional de Câncer (INCA) under protocol number 1,563,774, approved on May 29, 2016.

Variables and data sources

Clinical and sociodemographic data were collected from electronic and paper medical records. Sociodemographic variables included age at diagnosis (in complete years), educational level (categorized according to completed years of formal education), marital status (categorized as with partner or without partner), monthly household income, and self-reported skin color (categorized as White or non-White).

Clinical variables included tumor stage, according to the classification of the International Federation of Gynecology and Obstetrics [8], and the type of adjuvant treatment received (external pelvic radiotherapy, systemic chemotherapy, and/or vaginal brachytherapy).

Weight was measured using a calibrated digital scale (platform model, Filizola), and height was measured with a stadiometer attached to the scale. BMI was calculated using the formula weight (kg)/height² (m^2) and classified according to World Health Organization criteria [9] as underweight (< 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obesity (≥ 30.0 kg/m^2).

HRQoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30, version 3.0), a multidimensional questionnaire widely used worldwide to assess HRQoL in individuals with cancer and validated for Portuguese [10]. The instrument consists of 30 items evaluating multiple domains, including physical, emotional, social, and cognitive functioning, as well as symptoms such as pain, fatigue, gastrointestinal disturbances, nausea and vomiting, and the financial impact of treatment. It also includes self-reported assessment of overall health and quality of life during the week preceding evaluation.

Responses to items 1–28 are based on a four-point Likert scale: 1 = “not at all,” 2 = “a little,” 3 = “quite a bit,” and 4 = “very much,” referring to the week prior to assessment. Items 29 and 30, which compose the global health status/quality of life scale, use a seven-point numerical scale ranging from 1 (“very poor”) to 7 (“excellent”).

Scores were calculated according to the EORTC scoring manual guidelines [11], applying linear transformation to convert raw scores into standardized scales ranging from 0 to 100. For all functional scales and for the global health status/quality of life scale, higher scores indicate better functioning and HRQoL. For symptom scales, higher scores indicate greater symptom burden and, therefore, worse HRQoL.

The questionnaire was administered by a team of interviewers previously trained to ensure standardized application of the instrument at all assessment time points (T0, T1, T2, T3, and T4). Interviews were conducted in person during follow-up visits or, when this was not feasible, by telephone after prior scheduling with the participant. The mode of administration (in-person or telephone) was recorded for each assessment. The average time required to complete the questionnaire was approximately 10–15 minutes.

To assess the clinical relevance of changes in HRQoL over follow-up, the concept of Minimal Important Difference (MID) was adopted, defined as the smallest change in score capable of reflecting a clinically meaningful difference perceived by the patient. Score changes were calculated relative to baseline (T0) at each follow-up time point (T1, T2, T3, and T4). Changes were categorized according to the magnitude of the difference, with an MID greater than 5 points considered a small but clinically meaningful improvement or deterioration, and changes greater than 10 points considered moderate [12].

Statistical analysis

Continuous variables were described using means and standard deviations, whereas categorical variables were presented as absolute frequencies (n) and percentages (%). HRQoL domains were summarized as means and standard deviations at each follow-up time point.

Linear Mixed-Effects Models (LME) were used to evaluate the longitudinal trajectories of HRQoL domains. This approach was chosen because it accounts for the intra-individual correlation inherent to repeated measures by incorporating subject-specific random intercepts. In addition, LME models allow the handling of missing data under the Missing At Random (MAR) assumption, enabling the inclusion of patients with incomplete follow-up data.

All models were adjusted for the following covariates: time, age (years), BMI (kg/m^2), and adjuvant treatment with chemotherapy and/or radiotherapy (yes/no). Analyses were performed using R software (version 4.0.3) with the lme4 package. Statistical significance was set at 5% for all analyses.

RESULTS

The sociodemographic and clinical characteristics of participants at baseline are presented in Table 1. The study population consisted predominantly of women younger than 65 years, without a partner, and with low income. Regarding clinical characteristics, most participants were diagnosed at early stages (I–II), slightly more than half received adjuvant treatment with chemotherapy and/or radiotherapy, and nearly 90% were overweight or obese.

Table 1
Sociodemographic, clinical, and physical activity characteristics of the study population during the 3-year follow-up.

Variables	n	%
	241	**100**
Age group (years)[a]		
< 64	196	81.3
≥ 65	45	18.7
Skin color[b]		
White	109	53.4
Non-white	95	46.6
Marital status[c]		
Without partner	137	58.1
With partner	99	41.9
Years of education[d]		
0 a 9	140	58.3
10 a 12	80	33.3
≥ 13	20	8.3
Income range in minimum wages[e]		
Class B	4	1.7
Class C	27	11.5
Class D	85	36.3
Class E	118	50.4
Body Mass Index (BMI)[f]		
Underweight	1	0.4
Normal weight	24	10.0
Overweight	53	22.2
Obesity	161	67.4
Stage		
I-II	216	89.6
III-IV	25	10.4
Type of treatment perfomed		
Surgery	112	46.5
Surgery + adjuvante treatment	129	53.5

[a]Age group at T0; [b]n=204, missing: 37; [c]n=236, missing: 5; [d]n=240, missing: 1; [e]n=234, missing: 7; Class B: 5 to 15 minimum wages; Class C: 3 to 5 minimum wages; Class D: 1 to 3 minimum wages; Class E: <1 minimum wages; [f]Body Mass Index (BMI) at T0.

Table 2 presents the mean HRQoL domain scores, while Figs. 2 and 3 illustrate changes in HRQoL over time based on MIDs for each domain. Most functional domains remained stable throughout follow-up. Emotional functioning showed a small but clinically meaningful improvement, whereas role functioning showed a small improvement at T1 and T3, a decline below the threshold for clinical significance at T2, and a moderately clinically important improvement at T4. Physical and cognitive functioning remained stable over time. Social functioning improved progressively, reaching a moderately clinically important improvement from T3 onward (Fig. 2).

Table 2
Mean of quality of life domains in endometrial cancerer survivors over the study period

Domains	T0[a]	T1[b]	T2[c]	T3[d]	T4[e]
Global health status	66.91	72.87	70.58	73.24	71.96
Score summary	78.37	80.36	80.63	81.70	81.84
Physical functioning	77.17	75.73	75.45	77.74	76.30
Role functioning	75.07	81.09	79.11	83.98	85.74
Cognitive functioning	77.15	76.16	77.20	77.41	78.71
Emotional functioning	58.56	67.72	67.37	67.82	65.84
Social functioning	82.22	87.66	91.56	93.61	93.45
Fatigue	25.37	24.06	24.32	23.39	24.60
Appetite loss	8.89	7.85	7.38	7.69	4.92
Insomnia	38.13	31.91	32.92	35.64	32.66
Pain	10.14	9.42	9.28	11.67	11.56
Nausea and vomit	32.50	29.15	31.84	28.15	31.79
Dyspnea	11.95	13.15	9.78	8.15	9.44
Constipation	17.78	17.49	18.41	14.26	13.87
Diarrhea	6.67	10.61	8.96	9.63	7.32
Financial difficulties	29.45	28.10	22.88	18.71	15.99

[a]n=240; [b]n=223; [c]n=201; [d]n=180; [e]n=173.

For the symptom domains (Fig. 3), insomnia showed a small but clinically meaningful improvement only at T1 and T2, whereas no significant changes relative to baseline were observed at T3 and T4. Fatigue, appetite loss, pain, dyspnea, nausea and vomiting, diarrhea, and constipation showed no clinically meaningful changes over follow-up, with MID values remaining stable throughout the study period. In contrast, financial difficulties showed a small but clinically meaningful improvement from T2 onward, with progressive improvement over time, reaching a moderate clinically meaningful improvement at T4. Global health status showed fluctuations over time, reaching a small improvement at T1 and T3 while remaining stable at the other assessment points. In contrast, the summary score remained stable throughout follow-up (Fig. 2).

The fixed-effects estimates from the mixed-effects models for the HRQoL domains are presented in Table 3. Time was positively associated with summary score ($p = 0.02$), role functioning ($p < 0.01$), emotional functioning ($p = 0.03$), and social functioning ($p < 0.01$), indicating improvement in these domains over follow-up. Among symptom domains, financial difficulties significantly decreased over time ($p < 0.01$), whereas no significant changes were observed in the other symptom domains. No statistically significant association was observed for global health status ($p = 0.17$), although the coefficient suggested improvement over time.

Higher BMI was negatively associated with physical functioning ($p < 0.01$) and role functioning ($p = 0.007$), indicating worse functioning among women with higher BMI values. In addition, higher BMI values were associated with higher insomnia ($p < 0.01$) and pain scores ($p < 0.01$), indicating greater symptom burden, and with lower dyspnea scores ($p = 0.015$). Increasing age was associated with poorer physical functioning ($p = 0.01$) and higher insomnia scores ($p = 0.03$). Variables related to treatment (chemotherapy and radiotherapy) were not significantly associated with the HRQoL outcomes analyzed.

Table 3
Fixed-effects estimates from mixed-effects models for the EORTC QLQ-C30 domains

Fixed-effect estimates														
Domains	Time			Body Mass Index (BMI)			Chemotherapy			Radiotherapy			Age	
	Estimated coefficient	SE[a]	t	Estimated coefficient	SE[a]	t	Estimated coefficient	SE[a]	t	Estimated coefficient	SE[a]	t	Estimated coefficient	SE[a]
Global health status	0.59	0.43	1.36	-0.16	0.14	-1.09	-1.49	2.96	-0.50	-0.10	2.47	-0.04	0.11	0.17
Score summary	0.65*	0.28	2.26	-0.20	0.11	-1.79	-1.31	2.45	-0.53	1.19	2.05	0.57	-0.06	0.14
Functional scales														
Physical functioning	0.12	0.40	0.30	-0.81*	0.14	-5.63	-1.11	2.98	-0.37	2.56	2.49	1.02	-0.44*	0.17
Role functioning	2.75*	0.66	4.15	-0.51*	0.18	-2.70	-1.50	3.72	-0.40	1.27	3.09	0.41	-0.26	0.21
Emotional functioning	1.24*	0.59	2.10	-0.29	0.20	-1.44	-4.55	4.13	-1.10	2.08	3.44	0.60	0.35	0.24
Cognitive functioning	0.08	0.52	0.15	-0.09	0.20	-0.46	-5.61	4.20	-1.33	-0.52	3.52	-0.14	0.01	0.24
Social functioning	2.83*	0.51	5.44	0.03	0.15	0.21	2.30	3.05	0.75	1.72	2.53	0.67	-0.07	0.17
Symptom scales/items														
Fatigue	0.19	0.55	0.34	0.25	0.18	1.33	1.25	3.86	0.32	-1.24	3.22	-0.38	-0.22	0.22
Appetite loss	-0.50	0.36	-1.39	0.06	0.10	0.58	0.77	2.06	0.37	-1.11	1.71	-0.64	-0.01	0.12
Insomnia	-1.15	0.69	-1.66	0.90*	0.22	3.97	-0.42	4.60	-0.09	0.93	3.84	0.24	0.59*	0.26
Pain	0.55	0.53	1.02	0.67*	0.15	4.28	1.88	3.10	0.60	-4.13	2.58	-1.60	0.18	0.18
Nausea and vomiting	0.01	0.83	0.01	0.28	0.26	1.06	-2.78	5.38	-0.51	1.42	4.48	0.31	-0.02	0.31
Dyspnea	-0.50	0.58	-0.86	-0.38*	0.15	-2.43	2.88	3.11	0.92	-3.67	2.58	-1.42	-0.05	0.18
Constipation	-1.10	0.64	-1.71	-0.04	0.21	-0.22	5.76	4.30	1.33	-3.97	3.59	-1.10	0.33	0.25
Diarrhea	0.44	0.58	0.75	0.06	0.13	0.46	-3.04	2.66	-1.14	0.28	2.20	1.13	-0.16	0.15
Financial difficulties	-2.96*	0.75	-3.92	-0.14	0.25	-0.57	7.07	5.05	1.40	-6.30	4.21	-1.49	0.13	0.29

[a]Standard Error; *p-value < 0.05

DISCUSSION

To date, longitudinal studies evaluating temporal changes in HRQoL among endometrial cancer survivors using the EORTC QLQ-C30 are scarce, and the application of MID to interpret these changes remains limited. In our population, we observed clinically meaningful small improvements in emotional functioning, role functioning, insomnia, and global health status. In turn, social functioning and financial difficulties showed moderate improvement over the follow-up period. In the longitudinal mixed-effects analysis, follow-up time was associated with improvement in summary score, role functioning, emotional functioning, and social functioning, as well as with a significant reduction in financial difficulties. Among the clinical variables, BMI was the variable most consistently associated with HRQoL, being related to worse physical functioning, poorer role functioning, greater insomnia and pain intensity, and lower dyspnea intensity. Age, in turn, was associated with worse physical functioning and greater insomnia severity. In contrast, chemotherapy and radiotherapy were not associated with the evaluated outcomes.

Most functional domains remained stable over time according to both MID and longitudinal mixed-effects analyses, which is consistent with the findings of Zandbergen et al. [5] in a prospective study evaluating HRQoL among gynecologic cancer survivors during the first two years after treatment. In women with endometrial cancer, the authors observed significant improvements in HRQoL across most domains during the first six months after treatment, while cognitive functioning remained stable. However, after this initial recovery period, most domains stabilized, with relative declines observed only in physical functioning and role functioning after 12 months.

The mixed-effects model showed significant improvements over time in social and emotional functioning, which may reflect an adaptive process during cancer survivorship. These findings are consistent with the longitudinal study by Ferrandina et al. [13], who reported reduced anxiety and progressive

recovery of psychosocial well-being after treatment among women with endometrial cancer. This pattern may be explained by the gradual adjustment to the physical and emotional consequences of cancer, as well as by the progressive resumption of social activities and daily roles disrupted during treatment.

In addition to the physical and emotional burden imposed by cancer diagnosis and treatment, patients may also experience substantial economic impact, a phenomenon commonly referred to as financial toxicity. This concept encompasses direct and indirect costs related to cancer care, including expenses with medications, transportation, food, caregiving, unemployment, and concerns about future financial stability [14, 15]. The moderate clinically meaningful improvement observed in financial difficulties according to the MID analysis may reflect the gradual reduction in healthcare-related demands after treatment completion, as well as patients' progressive adaptation to the economic consequences of cancer, although this aspect remains poorly investigated among endometrial cancer survivors. Moreover, better socioeconomic conditions may be associated with improved emotional functioning, particularly during the early follow-up period [5], possibly by facilitating coping strategies, enabling return to work or other income-generating activities for both patients and caregivers, and improving access to social and financial support, thereby reducing the burden of financial toxicity.

In our study, no significant associations were observed between adjuvant treatments (chemotherapy or radiotherapy) and HRQoL outcomes, which contrasts with some previous findings. Warring et al. [7], in a study of women with endometrial cancer prior to surgical treatment, reported poorer overall quality of life among those receiving radiotherapy and worse physical functioning among those treated with chemotherapy. Similarly, Dobrzycka et al. [16] observed poorer emotional functioning in patients who underwent adjuvant radiotherapy. In contrast, Zandbergen et al. [5] reported progressive improvements in emotional and cognitive functioning among endometrial cancer survivors treated with radiotherapy, whereas these domains remained stable among women who did not receive radiotherapy. These inconsistent findings may reflect differences in study populations, treatment characteristics, timing of HRQoL assessment, and duration of follow-up.

Several studies have investigated the relationship between excess body weight and poorer HRQoL, consistently reporting associations between higher BMI and impaired physical functioning [7, 17]. Our findings are in line with this evidence, as higher BMI was associated with worse physical functioning and role functioning over time. Fader et al. [18], using the FACT-G and the SF-36 summary measures, also reported negative correlations between higher BMI and functional capacity, general health, and other HRQoL domains. Additionally, older age in their study was associated with lower physical functioning scores, corroborating our findings. Similarly, Kamga et al. [19], using the SF-12 in gynecologic cancer survivors, observed poorer physical quality of life among women with overweight and comorbidities. Although different HRQoL instruments were used, these findings support the consistency of the association between excess body weight and poorer physical functioning across populations. Notably, Warring et al. [7] reported worse dyspnea among women with higher BMI, which contrasts with our findings of lower dyspnea scores in women with higher BMI.

This study has important strengths. To our knowledge, it is the first Brazilian study with a prospective design and a three-year follow-up to longitudinally assess quality of life among endometrial cancer survivors. In addition, a validated instrument was used to evaluate quality of life, and the analysis combined different methodological approaches, including the assessment of the MID, a measure that has been scarcely explored in the literature for this population, and mixed-effects models, allowing for a more comprehensive evaluation of this outcome.

However, some limitations should be considered. The study was conducted at a single center, which may limit the generalizability of the findings. Additionally, the predominance of patients with early-stage disease and excess weight, although consistent with the epidemiology of endometrial cancer, may restrict the extrapolation of the results to populations with different clinical characteristics. Finally, the loss to follow-up observed during the study period may have reduced the statistical power to detect changes over time.

CONCLUSION

In conclusion, over the follow-up period, MID analysis showed fluctuations in global health status, whereas the summary score remained stable, with clinically meaningful improvements observed in emotional functioning, social functioning, role functioning, and financial difficulties. In addition, older age and higher BMI were associated with poorer physical functioning, highlighting subgroups that may require closer monitoring during survivorship care.

These findings underscore the importance of systematic quality-of-life assessment during post-treatment follow-up of endometrial cancer survivors, as unmet physical, emotional, social, and financial needs may persist long after treatment completion. Survivorship care should therefore integrate multidisciplinary strategies, including dietary counseling, physical activity promotion, psychological care, and social and financial assistance. Individualized follow-up planning based on each woman's specific needs may help preserve functional capacity, promote overall health, and improve long-term quality of life among endometrial cancer survivors.

Declarations

Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

This study was approved by the Research Ethics Committee of the National Cancer Institute under protocol number 1,563,774 on May 29, 2016.

Clinical trial number

not applicable

Consent to participate

Informed consent was obtained from all individual participants included in the study.

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Author Contribution

G.V.C contributed to the conception and design of the study. Material preparation, data collection, and analysis were performed by L.C.V, L.A.C, J.A.S and G.V.C. All authors contributed to the writing of the manuscript, read, and approved the final version.

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Figures

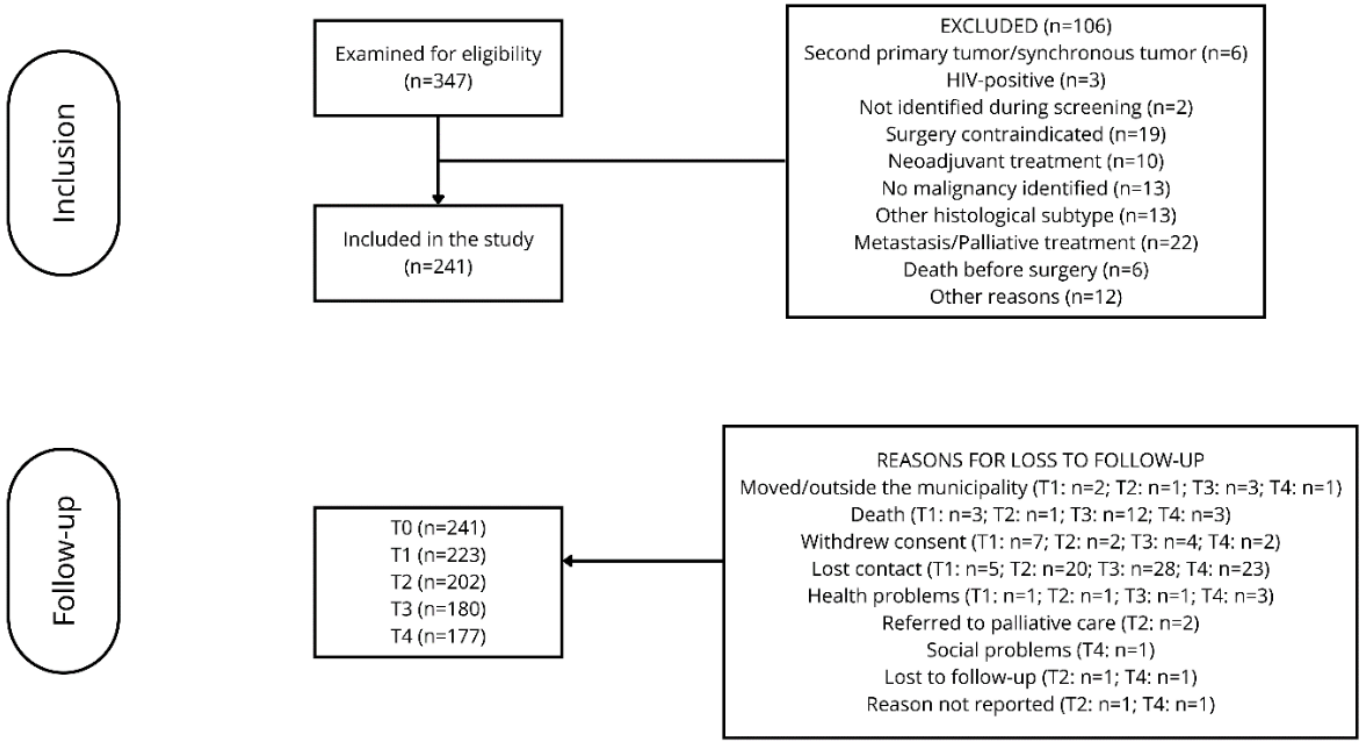


Figure 1

Eligibility criteria

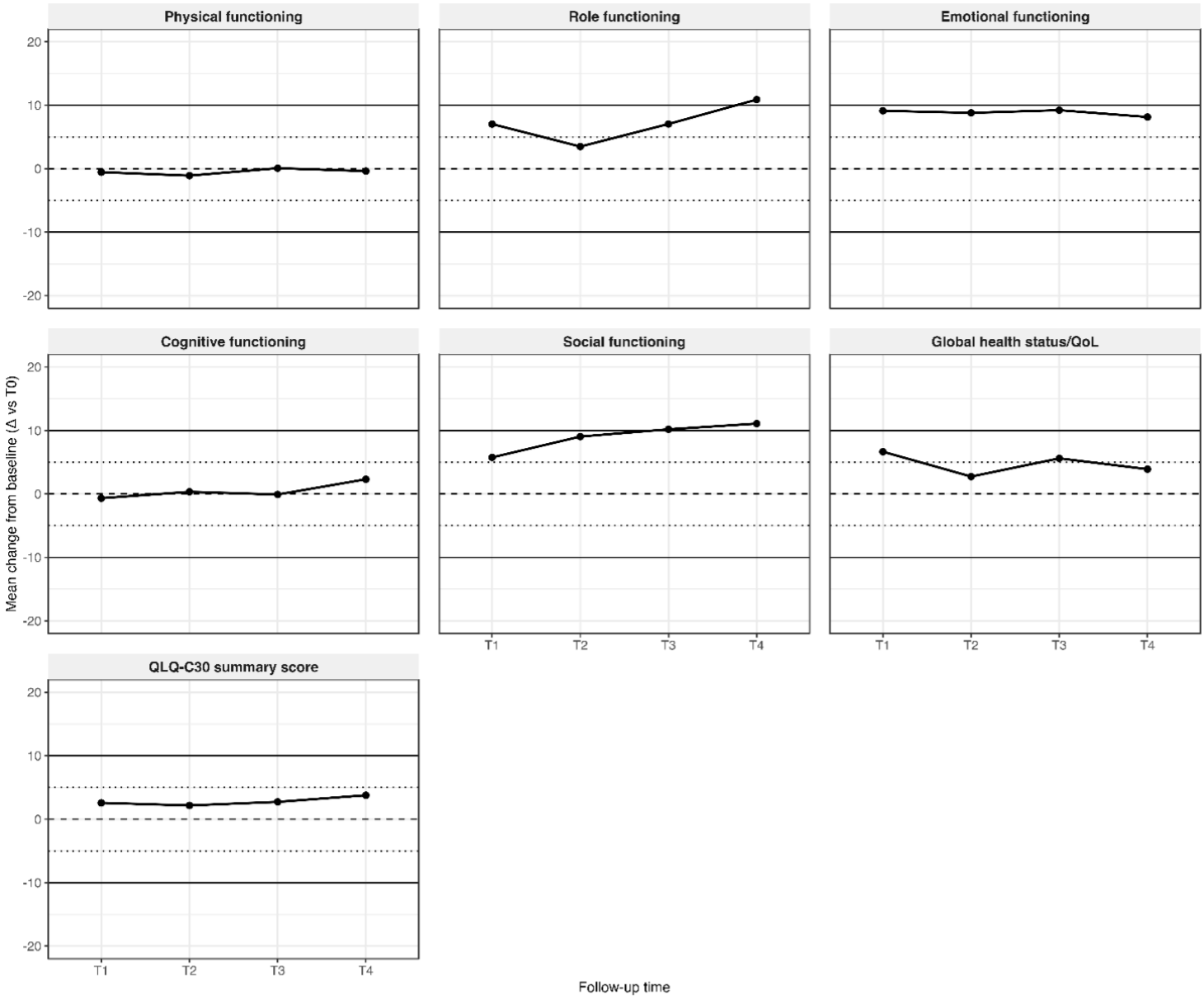


Figure 2

Changes in health-related quality of life over time based on the minimal important difference (MID) for each domain.

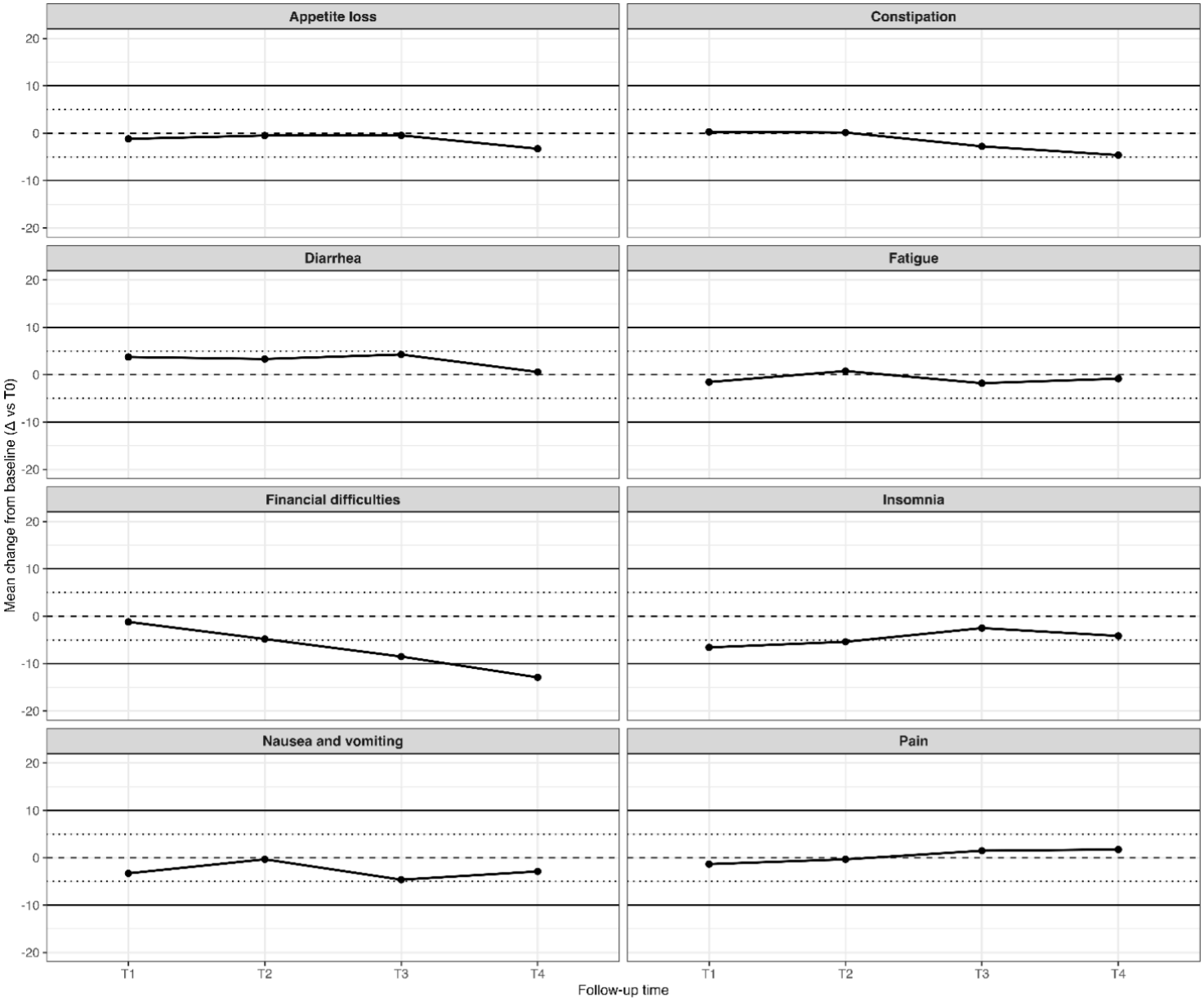


Figure 3

Changes in health-related quality of life over time based on the minimal important difference (MID) for each symptom domain.