Biomolecules and Biomedicine
ISSN: 2831-0896 (Print) | ISSN: 2831-090X (Online)
Journal Impact Factor® (2024): 2.2
CiteScore® (2024): 5.2
www.biomolbiomed.com | blog.bjbms.org

RESEARCH ARTICLE

Buhovac et al: Complementary therapies in breast cancer

Complementary therapies in early breast cancer: Oncologists' evidence-based decisions in a Southeast European vignette survey

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DOI: https://doi.org/10.17305/bb.2025.13413

ABSTRACT

Complementary therapies are increasingly integrated into the framework of integrative oncology. While numerous complementary therapies provide potential benefits, some may also carry risks, including interactions with conventional cancer treatments. The degree to which oncologists' real-world decisions regarding complementary therapies align with evidence-based guidelines remains uncertain. This study aimed to evaluate oncologists' evidence-based decisions on whether specific complementary therapies should be prohibited, permitted, or recommended for early breast cancer treatment. We conducted a cross-sectional online survey that included a randomized vignette experiment involving oncology specialists and residents from seven Southeast European countries. The primary outcome was the percentage of accurate classifications of 28 therapy-indication pairs in neoadjuvant and adjuvant settings, benchmarked against published evidence. Correctness was assessed using both a strict definition (one correct option) and an expanded definition (accepting "allow" or "recommend" when supported by evidence). A total of 136 respondents met the inclusion criteria and provided paired responses. Median accuracy was found to be 52% (95% CI 48-55) under the strict definition and 70% (95% CI 67-72) under the expanded definition, with no significant differences observed between neoadjuvant and adjuvant settings. Evidence-based therapies, such as physical exercise and cognitive behavioral therapy, were most frequently recommended, whereas most other therapies received endorsement from fewer than 25% of respondents. Overall, oncologists exhibited moderate alignment with evidence, demonstrating a tendency to permit rather than actively recommend complementary therapies, even when evidence indicated potential benefits and safety. These findings underscore the necessity for targeted educational interventions aimed at enhancing oncologists' understanding and ensuring the safe and informed integration of complementary therapies into clinical practice.

Keywords: Integrative medicine, integrative oncology, breast neoplasms, complementary therapies.

INTRODUCTION

Complementary therapies are medical products and practices used alongside and never instead of standard cancer care but not considered part of it. In this article we refer to complementary therapies as treatments with evidence of safety and some evidence supporting efficacy in specific indications. They can be categorized as nutritional (like diets, supplements, herbs and probiotics), psychological (such as meditation, hypnosis, music therapy and relaxation), physical (like acupuncture, massage and spinal manipulation) or combined approaches (including yoga and tai chi). Some treatments that start as complementary therapies can eventually become part of standard medical care if they are backed by sufficient high-quality evidence.

Integrative medicine combines conventional and complementary therapies in a way that respects patients' preferences and focuses on their mental, physical, and spiritual health (1). Interest in and use of complementary therapies among cancer patients have increased over the past couple of decades (2). According to a multicentre European survey across 14 countries, 35.9% of cancer patients reported using some form of complementary therapies with substantial variation between countries (3). In recent years, cancer patients have increasingly used complementary therapies for symptom management and supportive care rather than as an alternative to conventional treatment for cancer, reflecting a shift in patient preferences and attitudes (4). Given the growing evidence and guidelines (5,6), the substantial symptom burden, side effects of conventional treatments and strong patient interest, leading oncology institutions such as Memorial Sloan Kettering and MD Anderson have developed complementary therapies integrative oncology programmes, and educational and informational resources for both patients and healthcare providers (7). In 2002, the World Health Organization recommended that all countries develop national complementary therapies policies and procedures (8).

Due to the high prevalence of complementary therapy use and potential risks, oncologists should be well-informed about them and inquire about their use. According to some studies, more than 50% of cancer patients believe their physicians should be able to discuss these therapies and consider integrating them into cancer care (9). It is known that some types of complementary therapies may interact adversely with oncology treatments (10–12). In addition to interactions with cancer therapies, potential interactions with treatments for other comorbidities must be

considered - an issue that is often underestimated (13). On the other hand, there is evidence that complementary therapies may alleviate disease symptoms, reduce side effects of standard treatments, and improve the quality of life for cancer patients (14–18). There is also growing evidence supporting the importance of physical activity and nutrition in maintaining the health of cancer patients, and these factors have been associated with improved treatment outcomes (19–21).

Most studies reveal a gap between healthcare professionals' limited knowledge of complementary therapies and their interest in learning more (22). Negative or uncertain attitudes of physicians toward complementary therapies, as perceived by patients, may increase patient anxiety due to fears of treatment interactions (23). Physicians are frequently critical of complementary therapies due to the lack of scientific evidence for its efficacy (24). This lack of evidence contributes to their passive stance, and many do not routinely ask patients about their use of complementary therapies (25). This is especially important given the role of effective physician-patient communication in building trust. Better communication increases the likelihood that patients will follow medical recommendations and may help avoid harmful interactions between complementary and conventional therapies (26).

Recent advances in breast cancer treatment, both for early-stage and metastatic disease, have substantially improved survival outcomes and expanded therapeutic options (27–30). However, the introduction of novel systemic therapies also presents new challenges for clinicians, including managing treatment-related toxicities, maintaining quality of life, and navigating complex decision-making in everyday practice. These developments increase the need for oncologists to understand how integrative approaches can be safely incorporated into patient care. Monitoring and integrating evidence-based complementary interventions alongside evolving conventional treatments is therefore increasingly important to optimize both clinical outcomes and patient-centred care.

Globally, significant progress has been made in the integration of complementary therapies into healthcare systems. However, there are limited data on the use of such therapies among oncology physicians as well as patients in Southeast Europe. The objective of this study was to assess the accuracy of oncologists' decisions on whether particular complementary therapies should be prevented, allowed, or recommended in

early breast cancer (eBC), using a vignette-based approach grounded in published evidence.

MATERIALS AND METHODS

Study design

This cross-sectional online survey incorporated a randomized vignette experiment. We individually randomised respondents, using simple (unstratified) randomisation, to one of eight patient profiles defined by a 2×2×2 factorial combination of patient age (35 vs 75 years), education (primary vs university) and nodal status (N0 vs N1). The realised allocation across the eight profiles is shown in Supplementary Table S1. Each participant then evaluated 56 therapy-indication decisions (28 complementary therapy options, once in the neoadjuvant and once in the adjuvant setting) for the allocated patient profile. This analysis is part of a larger study on oncologists' use and perceptions of complementary and alternative medicine (CAM) in early breast cancer. The present analysis focuses specifically on oncologists' evidence-aligned decision-making regarding complementary therapies and not on alternative therapies at all. The study protocol was not preregistered on a public registry, but it was submitted as the proposal for the first author's doctoral thesis and is publicly available in the University of Mostar Faculty of Medicine repository.

Participants

Eligible participants were oncology specialists and residents who actively treated women with breast cancer (BC) at least once a month. Local collaborators from seven countries (Bosnia and Herzegovina, Bulgaria, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia) disseminated invitations and links to the survey. Although the LimeSurvey platform included Hungary and Romania as country options, only responses from the seven targeted Southeast European countries (Bosnia and Herzegovina, Bulgaria, Croatia, Montenegro, North Macedonia, Serbia, and Slovenia) were included in the analytic sample. The questionnaire was distributed electronically using LimeSurvey platform on a convenience sample. Participation was voluntary and responses were collected anonymously. To prevent duplicate entries, multiple responses from the same access code were disallowed. The survey was distributed via a single, open link, compatible with standard web browsers and devices, ensuring broad accessibility. Before data collection, we conducted an *a priori* power analysis

using PASS 2021 for a clustered design with country as the only random source of variation. We assumed an intraclass correlation coefficient (ICC) = 0.05, $\alpha = 0.05$ and 80% power to detect a standardised mean difference of Cohen's d = 0.50, which indicated a target of ~257 respondents. With the realised analytic sample of 136 respondents across seven countries, the design effect was ~2.4 (effective n ≈ 56), providing adequate power only for large, adjusted effects (roughly d ≈ 0.75; ≈ 10 percentage points under the strict and ≈ 7–8 percentage points under the expanded accuracy definitions).

Outcomes

The study used clinical vignettes in which a woman with early breast cancer receiving chemotherapy asked about using a specific complementary therapy for a defined indication. For each vignette, participants were asked whether they would prevent, allow, or recommend the use of the suggested complementary therapies across seven clinical domains: peripheral neuropathy, fatigue, nausea/vomiting, anaemia, mood disorders, sleep disturbances, and quality of life. Scoring keys were specified *a priori* based on evidence-based guidelines for integrative oncology – primarily Greenlee et al. (2017) and Witt and Cardoso (2016) – which appraise the efficacy and safety of complementary therapies modalities by indication (5,6). The prespecified scoring keys (Greenlee 2017; Witt and Cardoso 2016) were reviewed against 2023–2024 consensus updates for fatigue and anxiety/depression items (31–33). Concordance was confirmed and no re-analysis was required. Where those sources did not cover a given therapy-indication pair, evidence from contemporary peer-reviewed literature was used to guide the scoring (12,34–43). Therapies supported by moderate or strong evidence for the indication were keyed as recommend; therapies with limited or uncertain benefit but acceptable safety as allow; and therapies with evidence of harm, poor tolerability, or meaningful interaction risk as prevent. Participants were not shown evidence ratings.

The primary outcome was correctness of evidence-aligned decisions regarding complementary therapies across NA and ADJ settings, defined as the proportion of correctly classified therapy–indication pairs out of 28 in each setting (56 overall). We prespecified two related measures of correctness. The strict correctness rule was our primary definition and counted only the single evidence-concordant action as correct. The expanded correctness rule, treated as a prespecified secondary correctness

measure, reflected a broader construct in which responses that were directionally aligned with the evidence but not fully concordant with the strict rule were also counted as correct.

Secondary outcomes were: (i) item-level distributions of responses (prevent/allow/recommend) pooled across settings, and (ii) item-level endorsement rates (allow + recommend).

The outcome measures were developed through a literature review, expert discussion, and a pilot study among 12 oncologists and oncology residents and were revised for clarity. They were not validated on the independent sample, and their psychometric properties were not known in advance. The item set and coding scheme were not intended as a psychometric scale and were analysed as decision classifications, not latent scores.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of the University of Mostar, Faculty of Medicine (Approval No. 01-I-561/24). Participation was voluntary, and completion of the anonymous online survey was considered as provision of informed consent.

Statistical analysis

Before database lock, we finalised and documented the analytic structure, including the primary endpoint, covariates and planned sensitivity analyses in the doctoral project protocol. We followed this prespecified plan without post-hoc analytic modifications after inspecting the data. Among 136 participants included in the primary analysis (valid paired responses across neoadjuvant and adjuvant settings), three item-level responses were missing out of 7,616 possible (28 items × 2 settings × 136 participants; corresponding to an exact missingness of 0.039%.). To preserve paired comparisons, we applied a simple deterministic single-value imputation: when a respondent showed perfect internal consistency within a setting, we imputed the within-respondent modal response; otherwise, we imputed the cohort-level modal response for that item. For descriptive purposes in Table 3, denominators reflect the actual number of responses per item: up to 272 per item, with three items (Qi gong,

Comfrey, PC-SPES) having n = 271 due to one missing paired response each. Given the negligible missingness, multiple imputation was not warranted.

The primary outcome was participant-level accuracy across 56 therapy–indication decisions. Descriptively, we summarised medians and interquartile ranges (IQRs); 95% confidence intervals (CIs) for medians used the Bonett–Price method(44). By evidence category, accuracy was computed per participant restricted to items in that category and then summarised likewise. For Figure 2, 95% CIs for participant-level proportions were obtained using logit-transformed (score) binomial intervals, treating each participant as the unit of analysis.

As a sensitivity analysis, we reweighted each respondent's neoadjuvant responses by their self-reported annual percentage of neoadjuvant patients, while assigning unit weight to adjuvant responses (since all respondents routinely treat patients in the adjuvant setting). Practice-weighted accuracy was defined as (accADJ × 1 + accNA × propNA) / (1 + propNA) where accADJ is accuracy of decision in adjuvant (ADJ) setting, accNA accuracy of decision in neoadjuvant (NA) setting, propNA is the proportion of patients treated with neoadjuvant therapy by each participant.

In an additional sensitivity analysis, we weighted accuracy by the absolute number of patients treated in neoadjuvant setting to approximate real-world clinical impact. The annualised number of neoadjuvant patients (2 × number reported for six months) and the annual number of breast cancer patients (12 × monthly caseload) were used to derive neoadjuvant and adjuvant volumes, respectively. Impact-weighted accuracy per oncologist was defined as (accADJ × ADJvolume + accNA × NAvolume) / (ADJvolume + NAvolume) where ADJvolume and NAvolume are estimated number of patients treated annually in each setting. We also reported a population-level impact-weighted median across respondents using these volumes as analytic weights. Weighted and unweighted distributions were compared using the Wilcoxon signed-rank test to assess potential differences between practice-weighted and unweighted estimates.

Given differences between the country distribution in our sample and the underlying regional oncology workforce, we performed a post-stratification sensitivity analysis using country weights (population share / sample share). Weighted medians and IQRs were obtained using weighted quantiles; 95% CIs for medians were computed by

bootstrap (2,000 replicates). For clarity, non-parametric bootstrap 95% confidence intervals (2,000 replicates) were calculated and reported only for the country-weighted medians. Practice-weighted and impact-weighted medians were treated as descriptive robustness summaries and were presented without confidence intervals. They were compared with the corresponding unweighted medians using the Wilcoxon signed-rank test. Estimates of the size of the oncology workforce in each country were derived from a key-informant survey conducted in June 2015 among senior oncologists in Bosnia and Herzegovina, Bulgaria, Croatia, Montenegro, North Macedonia, Serbia and Slovenia, originally designed for earlier research on cancer control in the region (45). Where available, these estimates were cross-checked with senior representatives of pharmaceutical companies active in oncology in the respective countries to ensure that they reflected clinicians routinely involved in systemic anticancer therapy.

We modelled participant-level accuracy using beta regression with a logit link and Huber-White robust standard errors. Where boundary values (0 or 1) occurred, we applied the Smithson–Verkuilen transformation (46). Primary models included randomised vignette attributes (age, education, nodal status) and country fixed effects. "Full" models additionally included clinician characteristics (gender, professional status, speciality, years in oncology, institution type, number of breast-cancer patients treated monthly, frequency of patient contacts, number of patients treated with neoadjuvant therapy, and their share in the total number of patients). We report predictive margins (Acc) and average marginal effects (AME) with delta-method 95% CIs from margins. For categorical predictors, Acc is the predictive margin for each level and AME is the contrast versus the reference (Ref.). For continuous predictors, Acc is the predictive margin evaluated at the sample median and AME reflects the change per +10 units. We fitted all models using the strict correctness rule as the primary definition of correctness and then re-estimated them using the expanded correctness rule so that readers can see how far substantive conclusions depended on using a narrower versus a broader correctness construct. For the family of coefficients from the multivariable beta-regression models reported in Table 4, we controlled the false discovery rate using the Benjamini–Hochberg procedure with FDR set at < 5%.

Item-level differences between neoadjuvant and adjuvant settings (Supplementary Tables S4–S5) were analysed using paired McNemar tests, with Cohen's g as the standardised effect size. These analyses were not prespecified and were treated as exploratory. Accordingly, we report raw (unadjusted) p values without correction for multiple comparisons and interpret them descriptively only. We do not regard these exploratory p values as evidence of statistical significance or non-significance. In our questionnaire, all neoadjuvant (NA) items were presented as a block before all adjuvant (ADJ) items for every respondent. The order of NA and ADJ blocks was not randomised. All tests were two-sided. We conducted statistical analysis using StataCorp 2019 (Stata Statistical Software: Release 16, College Station, TX: StataCorp LLC).

RESULTS

Participant characteristics

Between 13 July 2024 and 3 May 2025, 278 individuals accessed the online questionnaire, and the final sample comprised 136 participants with valid paired responses (Figure 1). The last response was received on 3 May 2025, and the survey was officially closed on 13 May 2025 at 23:51 Central European Time, as reflected in the system timestamp on the printable questionnaire (Supplementary File 1). Participants were predominantly women, most were medical oncologists, and the majority practiced in university hospitals. The median age was 38 years [IQR 34–45], with a median of 10 years of oncology experience [IQR 5–15] (Table 1). Most reported daily contact with breast cancer patients. The median number of breast cancer patients examined monthly was 40 [IQR 20–88], and in the previous six months the median number treated with neoadjuvant chemotherapy was 20 [IQR 10–39]. Participants were recruited from seven Southeast European countries with unequal country contributions. Between-country comparisons were not planned, and the study was not powered for them. The distribution of respondents by country did not fully correspond to the regional oncologist population structure, with some countries overrepresented and others underrepresented in the sample (Supplementary Table 2).

Primary outcome

Across 56 therapy-indication decisions per participant, median accuracy was 52% (95% CI 48–55) under the strict definition of correctness and 70% (95% CI 67–72) under the expanded definition (Table 2). By evidence category, accuracy was 80% (95% CI 77–83) for therapies supported for use (allow or recommend), 50% (95% CI 39–61) for those supported for recommendation, 69% (95% CI 62–75) for those supported to be allowed but not recommended, and 60% (95% CI 54–65) for therapies where evidence advises against use.

Practice-weighted accuracy estimates, calculated as a sensitivity analysis, were virtually identical to the primary balanced analysis (Wilcoxon signed-rank test; strict definition: median 52% vs. 52%, unadjusted p = 0.669; expanded definition: median 68% vs. 70%, unadjusted p = 0.279). This indicates that accounting for variability in the proportion of neoadjuvant patients treated by each oncologist did not affect results.

Impact-weighted accuracy was likewise nearly identical to the balanced analysis (Wilcoxon signed-rank test; strict definition: median 51% vs. 52%, unadjusted p = 0.768; expanded definition: median 68% vs. 70%, unadjusted p = 0.281). At the population level, impact-weighted mean accuracy was 53% (strict) and 68% (expanded), closely paralleling balanced estimates. These findings confirm the robustness of the main results to different weighting schemes.

Country-weighted (post-stratified) sensitivity analysis, which reweighted respondents to match the national composition of the regional oncology workforce (weights in Supplementary Table 2), yielded medians of 54% (IQR 43-64; bootstrap 95% CI 49-58) for the strict and 68% (IQR 61-75; bootstrap 95% CI 64-72) for the expanded definition—values very similar to the unweighted estimates. Taken together, these sensitivity analyses confirm that the main findings are robust to alternative weighting schemes.

Secondary outcomes

Endorsement (allow + recommend) varied markedly across items (Figure 2; Table 3). Highest rates were for evidence-supported options: physical exercise for neuropathy and cognitive behavioural therapy for sleep (both ≈ 98%). In contrast, several therapies advised against were still frequently endorsed, including glutathione for neuropathy and green tea for anaemia (≈ 72% and ≈ 69%). Items supported only to be

allowed showed mixed uptake (e.g., ginseng for fatigue ≈ 58%, qi gong for sleep ≈ 46%, mistletoe for quality of life ≈ 26%) (Supplementary Table 3).

Neoadjuvant vs adjuvant settings contrasts were not a prespecified outcome and were analysed exploratorily. Overall, they showed no meaningful differences. The only items with nominally significant differences between settings were comfrey for quality of life (McNemar test; unadjusted p = 0.019; Cohen's g = –0.09 and acupressure for nausea/vomiting (McNemar test; unadjusted p = 0.035; Cohen's g = 0.05), with uniformly trivial effect sizes otherwise (Supplementary Tables S4 –S5).

In multivariable beta-regression models with country fixed effects adjusted simultaneously for all vignette and clinician covariates, accuracy differed by specialty and by frequency of contacts with breast cancer patients (Table 4). Compared with medical oncologists, clinical oncologists had lower accuracy under both definitions (strict AME −5.3 pp, 95% CI −10.4 to −0.2; p = 0.043; expanded AME −4.6 pp, −9.0 to −0.2; p = 0.040), but in both cases FDR was > 5%. Radiation oncologists showed larger deficits (strict −8.0 pp, −13.2 to −2.9; p = 0.002; FDR < 5%; expanded −10.3 pp, −15.1 to −5.5; p < 0.001; FDR < 5%). Seeing breast-cancer patients weekly or less often (vs daily) was associated with lower accuracy under the expanded definition (−4.5 pp, −8.1 to −0.9; p = 0.013; FDR < 5%). No other vignette attributes (age, education, nodal status) or clinician/institutional measures (gender, professional status, experience, institution type, number of breast cancer patients monthly, number or share of patients treated with neoadjuvant therapy) reached statistical significance with FDR < 5%.

DISCUSSION

Results of our study showed a moderate level of Southeast European oncologists' decisions alignment with the best available evidence of complementary therapies efficacy and safety in early breast cancer. Under the strict definition of correctness, participants correctly identified approximately half of complementary therapies-indication pairs in line with published evidence. However, when both "recommend" and "allow" were considered acceptable in situations where evidence supported either approach, the median accuracy increased to 70%. Among complementary therapies supported by clinical evidence, participants achieved a median of 80% accuracy, with higher recognition of therapies supported to be allowed compared to explicitly

recommended. This pattern may indicate a prevailing caution: oncologists are more ready to tolerate complementary therapies than to endorse them explicitly, even when robust evidence supports their benefits and safety. Sensitivity analysis confirmed the robustness of these findings, indicating that neither the individual clinical focus of the clinicians nor the number of patients they treated affected the observed accuracy.

Studies from Ireland and Jordan showed limited knowledge about complementary therapies among healthcare professionals (47,48). A multicentre study in Italy investigating physicians' attitudes toward complementary therapies found oncologists to be the best informed (49). A national survey in the United States found that two out of three oncologists reported insufficient knowledge to answer patients' questions about complementary therapies (50). In China, about one-third of oncologists had discussed complementary therapies with their patients and most did not initiate such conversations. Four out of five oncologists reported a lack of knowledge and most did not approve the use of complementary therapies by their patients (51). These studies consistently reported insufficient knowledge, limited training, and a lack of confidence to guide patients. Unlike previous studies which have largely depended on self-reported assessments of perceived knowledge, our study used a case-based, evidence-grounded approach to evaluate oncologists' ability to apply clinical guidelines in a realistic clinical decision-making scenario. This methodological distinction is important, as self-perception may not accurately reflect the ability to make evidence-concordant decisions in practice. The vignette-based method allows for a clearer insight into the gap between perceived competence and actual performance, which is crucial for developing targeted educational interventions. By using clinical vignettes and comparing responses to established guidelines and published safety data, our study provides a more objective assessment of decision accuracy. To our knowledge, this is the first study in Southeast Europe to evaluate oncologists' evidence-based understanding of complementary therapies in oncology using this type of structured and standardized scoring.

The results of our study indicate that the threshold for explicitly recommending complementary treatments, as opposed to merely allowing them, remains relatively high among oncology professionals. Even for treatments supported by moderate or strong evidence, many respondents chose to allow rather than recommend them. This suggests a cautious clinical approach, likely reflecting concerns about patient

expectations, therapeutic responsibility, or the strength of evidence. The minimal differences between neoadjuvant and adjuvant settings in terms of recommendation patterns imply that clinical context does not substantially influence oncologists' attitudes toward these treatments. However, the low overall recommendation rates for most treatments – especially those with limited or questionable efficacy – show the ongoing tension between openness to integrative approaches and adherence to evidence-based practice. These patterns emphasize the importance of continued professional education and clear communication about the evidence base for complementary interventions in oncology.

The present findings reveal notable inconsistencies in oncologists' ability to align their decisions regarding complementary therapies with published evidence. Although overall accuracy improved when a more inclusive definition of correctness was applied, a substantial proportion of responses remained incongruent with evidence-based guidance (5,6). Therapies supported by evidence to be allowed or recommended were generally identified with higher accuracy than those for which use is advised against. However, when disaggregated by response type, a more nuanced pattern emerged: therapies supported by evidence to recommendation were associated with the lowest accuracy, despite representing the strongest form of endorsement. In contrast, accuracy for therapies supported to be allowed (but not recommended) was higher, though not significantly different from that for therapies with evidence discouraging use. These findings suggest that participants may hesitate to actively recommend complementary therapies, even when robust evidence is available, possibly reflecting caution, perceived professional risk, or limited familiarity with the evidence base. Moreover, the expanded definition of correctness - accepting either allow or recommend when evidence supports any of them - may overestimate actual alignment, as it provides two acceptable options for therapies supported for use but only one for those discouraged. This asymmetry should be considered when interpreting comparative accuracy levels. Such patterns reflect previous studies indicating that oncologists are generally open to complementary therapies perceived as safe, even in the absence of strong efficacy data, but are less consistent in recognising those contraindicated due to harm, ineffectiveness, or interactions with conventional treatments (5,6). These gaps may indicate a tension between professional openness to patient-centred, integrative approaches and the demands of rigorous

evidence-based practice. From an educational standpoint, the findings highlight the need for targeted training in the evaluation and application of evidence relating to complementary therapies.

From our clinical experience, oncologists in Southeast Europe rarely initiate conversations about complementary therapies with patients, despite their relevance, because they feel insufficiently informed. Patients in this region more often ask about herbal medicines and dietary supplements, which may interact with oncology treatments and require careful consideration. Consequently, oncologists may find it easier to allow patients to pursue such therapies independently, thereby transferring responsibility to the patient. In contrast, mind-body interventions such as mindfulness, relaxation techniques, or yoga are less commonly requested and less frequently recommended, as they are not widely adopted in Southeast Europe compared to Western countries. However, given their low risk of harm or interactions, clinicians may be more comfortable allowing or recommending these interventions. This cautious approach is further compounded by the relatively underdeveloped state of integrative medicine in the region, highlighting the need for region-specific educational resources and confidence-building tools to support evidence-based integration of complementary interventions into routine care.

While vignette-based assessments provide a standardized measure of decision-making accuracy, they cannot fully capture the complexities of real-world encounters, including patient preferences, institutional constraints, or multidisciplinary input. These factors may modulate oncologists' recommendations, suggesting that observed patterns of caution may underestimate or overestimate actual clinical behaviour.

Another important challenge is the persistent lack of terminological clarity surrounding complementary, alternative, and integrative therapies. Although conceptually distinct, their definitions vary across professional societies, patient-facing organizations, and research publications. For example, complementary therapies are generally described as adjuncts to conventional oncology treatment, whereas alternative therapies are positioned as replacements for evidence-based care; integrative approaches refer to coordinated use of supportive modalities within conventional oncology. Despite these distinctions, the umbrella term complementary and alternative medicine (CAM) is often applied inconsistently, even in studies

focused solely on complementary use. From a clinician's perspective, this conceptual ambiguity complicates communication, contributes to variable interpretation of evidence, and can influence clinical decision-making. Addressing this lack of standardization is essential for improving both research comparability and real-world application of supportive therapies in oncology.

Limitations of the study

This study has several important limitations. First, we used a non-random, convenience sample with unknown representativeness for the targeted population and with a likely over-representation of clinicians who have a particular interest in complementary therapies. Second, the sample size was modest and fell short of the a priori target, which reduced statistical power and limited the precision and stability of subgroup-specific estimates. Third, the scoring system, although grounded in current evidence and guidelines, required some interpretation in cases where recommendations were not explicitly stated or where evidence was evolving. While this approach was carefully designed and pilot-tested, the classification of certain responses as correct or incorrect may still be debated. Fourth, the cross-sectional, vignette-based design assessed decision-making accuracy in hypothetical but standardised clinical contexts rather than in observed clinical practice. This may limit ecological validity and means that we cannot assess longitudinal changes in clinician knowledge or behaviour. Fifth, we did not include dedicated manipulation-check items (for example ratings of perceived prognosis or risk), so we cannot empirically verify how strongly respondents perceived the intended differences between patient profiles. We therefore interpret any apparent influence of patient attributes on decisions cautiously and keep our primary focus on correctness relative to trial evidence and guideline-based standards of care. Sixth, the study evaluates oncologists' decision-making accuracy but does not assess downstream patient outcomes such as survival, adherence or disease progression, so conclusions about clinical impact remain indirect. Seventh, in the post-stratification sensitivity analysis we used country weights (population share / sample share). Target population sizes in different countries were based on key-informant estimates from 2015 and may therefore have limited validity, reliability and precision. Our workforce estimates differ from figures reported in other surveys and more recent data sources (52,53). Eighth, in the questionnaire all NA items were presented before all ADJ items, so the

effect of clinical setting (neoadjuvant vs adjuvant) is intrinsically confounded with block order. We therefore cannot exclude the possibility that part of the observed NA–ADJ differences reflects order or fatigue effects rather than true setting-specific behaviour.

With increasing patient demand for integrative oncology, consistent and well-informed guidance from oncologists is essential. Decision aids, concise evidence summaries tailored to clinical settings, and the inclusion of complementary therapies in continuing medical education may help reduce variability and misalignment. Finally, although this study did not assess clinical outcomes, it raises important concerns regarding shared decision-making and the accuracy of information communicated to patients. Future research should examine whether discrepancies between clinician decisions and evidence contribute to overuse, underuse, or miscommunication regarding complementary therapies, and whether targeted interventions can improve the fidelity of evidence-based decisions in oncology.

CONCLUSION

This study offers insight into decision patterns regarding complementary therapies among surveyed oncologists in Southern Europe, but findings should be interpreted cautiously given non-probability sampling and limited representativeness. While moderate familiarity with evidence-based complementary therapies was observed, significant gaps and inconsistencies remain, particularly regarding the active recommendation of therapies with proven benefit. Bridging these gaps through targeted education and integration of clinical decision support tools is essential to ensure safe, evidence-based incorporation of complementary therapies into oncology care.

We recommend:

- Developing concise, evidence-based educational materials on complementary therapies for oncologists.
- Including complementary therapies guideline content in national oncology training programs across Southeast Europe.
- Providing institutional support mechanisms, such as complementary therapies counsellors to aid oncologists in navigating patient queries.

By addressing these gaps, we can promote safer and more integrated oncology practices, ultimately benefiting patient care and outcomes.

ACKNOWLEDGMENTS

The authors thank all oncologists who participated in the survey. As English is not the first language of any of the authors, a generative artificial intelligence (AI) tool (GPT-5 mini, OpenAI) was used only for language refinement to improve readability. No AI tools were used for data analysis, interpretation, or drawing scientific conclusions, and the authors are fully responsible for the content, accuracy and integrity of this study, its analysis and the manuscript.

Conflicts of interest: Authors declare no conflicts of interest.

Funding: Authors received no specific funding for this work.

Data availability: The questionnaire used in this study is provided as Supplementary File 1 (PDF). Other datasets supporting the conclusions of this article are included within the article and its supplementary materials or are available from the corresponding author upon reasonable request.

Submitted: October 22, 2025

Accepted: December 10, 2025

Published online: December 15, 2025

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TABLES AND FIGURES WITH LEGENDS

Table 1. Participants characteristics; unweighted data (*n* = 136)

	n (%)
Country	
Bosnia and Herzegovina	33 (24.3)
Bulgaria	10 (7.4)
Croatia	48 (35.3)
Montenegro	7 (5.1)
North Macedonia	11 (8.1)
Serbia	17 (12.5)
Slovenia	10 (7.4)
Age (years), median [IQR]	38 [34–45]
Gender	
men	39 (28.7)
women	97 (71.3)
Professional status	
residents	39 (28.7)
specialists	97 (71.3)
Specialization	
medical oncologist	84 (61.8)
clinical oncologist	40 (29.4)
radiation oncologist	12 (8.8)
Work experience in oncology (years), median [IQR]	10 [5–15]
Type of institution	

university hospital	89 (65.4)
general hospital	34 (25.0)
spec. oncology institution	13 (9.6)
Number of BC patients monthly, median [IQR]	40 [20–88]
Frequency of contacts with BC patients	
daily	98 (72.1)
weekly or less often	38 (27.9)
Number of BC patients treated with NA CHT during six months, median [IQR]	20 [10–39]
Percentage of patients with eBC treated NA annually, median [IQR]	30 [20–58]

Data are presented as a percentage of participants unless otherwise specified.
Abbreviations: IQR: Interquartile range; BC: Breast cancer; eBC: Early breast cancer; NA: Neoadjuvant; CHT: Chemotherapy.

Table 2. Accuracy of evidence-aligned decisions concerning complementary therapies, pooled from neoadjuvant and adjuvant settings (*n* = 136; m = 56 therapy-indication pairs per participant)

	Median [IQR]	(95% CI)	Min.	Max.
Strict definition of correctness	52 [43–63]	(48–55)	21	82
Expanded definition correctness	70 [61–76]	(67–72)	38	93
By evidence category				
Supported for use (allow or recommend) (m = 30)	80 [70–90]	(77–83)	3	100
Supported for recommendation (m = 14)	50 [14–82]	(39–61)	0	100
Supported to be allowed but not recommended (m = 16)	69 [50–88]	(62–75)	0	100
Evidence advising against use (to be prevented) (m = 26)	60 [37–77]	(54–65)	0	100

The strict rule recognizes only the single evidence-concordant action as correct, while the expanded rule permits or recommends actions based on supporting evidence. The variable m represents the number of therapy-indication pairs evaluated across both clinical settings. Seven indications were associated with four complementary therapies, resulting in 28 therapy-indication combinations assessed separately in adjuvant and neoadjuvant contexts, yielding a total of 56 evaluations. The categories "supported for recommendation" (m = 14) and "supported to be allowed" (m = 16) collectively form the category "supported for use" (m = 30). Abbreviations: m: Number of complementary therapies evaluated; IQR: Interquartile range; CI: Bonett–Price confidence interval for the median; Min.: Minimum; Max.: Maximum.

Table 3. Willingness to prevent, allow, or recommend complementary therapies in neoadjuvant and adjuvant settings

Indication	"Correct"	Pooled actual responses		
Treatment	response	prevent	allow	recommend
Prevention of peripheral neuropathy				
Physical exercise	allow	5 (1.8)	58 (21.3)	209 (76.8)
Compression therapy	allow	78 (28.7)	152 (55.9)	42 (15.4)
Glutathione	prevent	76 (27.9)	169 (62.1)	27 (9.9)
Acetyl-L-carnitine	prevent	118 (43.4)	134 (49.3)	20 (7.4)
Fatigue				
Yoga	recommend	16 (5.9)	112 (41.2)	144 (52.9)
Ginseng	allow	115 (42.3)	136 (50.0)	21 (7.7)
Guarana	prevent	178 (65.4)	87 (32.0)	7 (2.6)
Acetyl-L-carnitine	prevent	145 (53.3)	116 (42.6)	11 (4.0)
Nausea and vomiting				
Acupressure	recommend	57 (21.0)	157 (57.7)	58 (21.3)
Ginger	allow	48 (17.6)	166 (61.0)	58 (21.3)
Grapefruit	prevent	193 (71.0)	72 (26.5)	7 (2.6)
Glutamine	prevent	117 (43.0)	140 (51.5)	15 (5.5)
Anaemia				
Beet juice	allow	62 (22.8)	173 (63.6)	37 (13.6)
Colloidal silver	prevent	215 (79.0)	52 (19.1)	5 (1.8)
High-dose vitamin C	prevent	133 (48.9)	122 (44.9)	17 (6.2)

Green tea	prevent	83 (30.5)	178 (65.4)	11 (4.0)
Depression and other mood disorders				
Mindfulness	recommend	24 (8.8)	121 (44.5)	127 (46.7)
Yoga	recommend	13 (4.8)	132 (48.5)	127 (46.7)
Relaxation	recommend	6 (2.2)	78 (28.7)	188 (69.1)
St. John's Wort	prevent	183 (67.3)	81 (29.8)	8 (2.9)
Sleep disturbances				
CBT	recommend	6 (2.2)	99 (36.4)	167 (61.4)
Melatonin	allow	57 (21.0)	182 (66.9)	33 (12.1)
Qi gong	allow	146 (53.9)	108 (39.9)	17 (6.3)
Kava kava (lat. *Piper methysticum*)	prevent	180 (66.2)	86 (31.6)	6 (2.2)
Quality of life				
Meditation	recommend	11 (4.0)	119 (43.8)	142 (52.2)
Mistletoe	allow	202 (74.3)	66 (24.3)	4 (1.5)
Comfrey	prevent	178 (65.7)	89 (32.8)	4 (1.5)
PC-SPES mixture	prevent	193 (71.2)	75 (27.7)	3 (1.1)

Values represent the number (percentage) of responses, not the number of participants (denominator per item = 272; each participant provided responses for two vignette settings). Three items have $n = 271$ due to one missing paired response for each (Qi Gong, Comfrey, PC-SPES).

Data are presented as frequency (percentage) of responses rather than participants. The 'Correct Response' column identifies the evidence-based action corresponding to each therapy-indication pair, as outlined in published guidelines (Greenlee et al., 2017; Witt and Cardoso, 2016). Respondents were not provided with evidence ratings while

completing the survey; therefore, percentages may not total 100 due to rounding. Abbreviations: CBT: Cognitive behavioural therapy; PC-SPES: Prostate Cancer – Special Extract Series (herbal mixture).

Table 4. Accuracy and adjusted effects (AME, percentage points) of vignette attributes and clinician characteristics under strict and expanded accuracy definitions (*n* = 136)

		Strict definition				Expanded definition			
	n	Acc	AME	(95% CI)	*p*	Acc	AME	(95% CI)	*p*
Patient attributes form vignettes									
Age									
35 years	59	52.0	Ref.			69.3	0.0		
75 years	77	52.6	0.6	(-3.7 to 5.0)	0.776	68.2	-1.1	(-4.6 to 2.4)	0.541
Education									
primary school	72	53.2	Ref.		.	69.3	0.0		.
university	64	51.4	-1.8	(-5.8 to 2.1)	0.360	68.0	-1.3	(-4.3 to 1.7)	0.405
Lymph nodes									
negative	69	53.6	Ref.		.	70.2	0.0		.
positive	67	51.1	-2.5	(-6.8 to 1.8)	0.251	67.1	-3.0	(-6.6 to 0.5)	0.093
Clinicians' (respondents) characteristics									
Gender									

men	39	50.1	Ref.		.	66.9	0.0		.
women	97	53.3	3.2	(-1.5 to 7.9)	0.186	69.4	2.6	(-1.1 to 6.2)	0.167
Professional status									
residents	39	52.1	Ref.		.	67.3	0.0		.
specialists	97	52.5	0.3	(-5.3 to 6.0)	0.905	69.2	1.9	(-2.7 to 6.4)	0.420
Specialization									
medical oncologist	84	54.6	Ref.		.	70.9	0.0		.
clinical oncologist	40	49.3	-5.3	(-10.4 to -0.2)	0.043	66.3	-4.6	(-9.0 to -0.2)	0.040
radiation oncologist	12	46.6	-8.0	(-13.2 to -2.9)	0.002 *	60.6	-10.3	(-15.1 to -5.5)	0.000 *
Work experience in oncology	136	52.6	-1.5	(-4.8 to 1.8)	0.379	68.8	-0.7	(-3.7 to 2.3)	0.658
Type of institution									
university hospital	89	53.3	Ref.		.	69.4	0.0		.
general hospital	34	50.9	-2.5	(-8.3 to 3.3)	0.400	67.1	-2.3	(-7.2 to 2.6)	0.360
spec. oncology institution	13	49.7	-3.7	(-12.0 to 4.7)	0.389	68.2	-1.2	(-6.8 to 4.5)	0.691
Number of BC patients monthly	136	52.8	-0.1	(-0.3 to 0.1)	0.361	69.2	-0.1	(-0.3 to 0.1)	0.164
Frequency of contacts with BC patients									
daily	98	53.5	Ref.		.	69.9	0.0		.
weekly or less often	38	49.4	-4.2	(-8.7 to 0.4)	0.071	65.4	-4.5	(-8.1 to 0.9)	0.013 *
Number of BC patients	136	51.9	0.1	(-0.0 to 0.3)	0.146	68.5	0.1	(-0.1 to 0.2)	0.358

treated with NA CHT during six months									
Percentage of patients with eBC treated NA annually	136	52.7	-0.4	(-1.4 to 0.7)	0.518	69.1	-0.5	(-1.4 to 0.4)	0.248

Note: * FDR < 5%. The accuracy (Acc.) values presented are predictive margins derived from a beta-regression model utilizing a logit link, incorporating country fixed effects, robust standard errors, and the Smithson–Verkuilen transformation where applicable. For categorical predictors, Acc. denotes the predictive margin for each level; for continuous predictors, it reflects the predictive margin with the predictor set to its sample median, while averaging all covariates over their observed distribution. Average marginal effects (AME) are expressed in percentage points: for categorical predictors, they indicate the difference compared to the reference level (Ref.); for continuous predictors, they represent the change associated with an increase of 10 units in the predictor (a negative AME suggests lower accuracy relative to the reference).

Abbreviations: n: Number of respondents in each row; Acc.: Predicted accuracy (%); AME: Average marginal effect (percentage points); 95% CI: 95% confidence interval; p: p value; Ref.: Reference category; BC: Breast cancer; eBC: Early breast cancer; NA: Neoadjuvant; CHT: Chemotherapy.

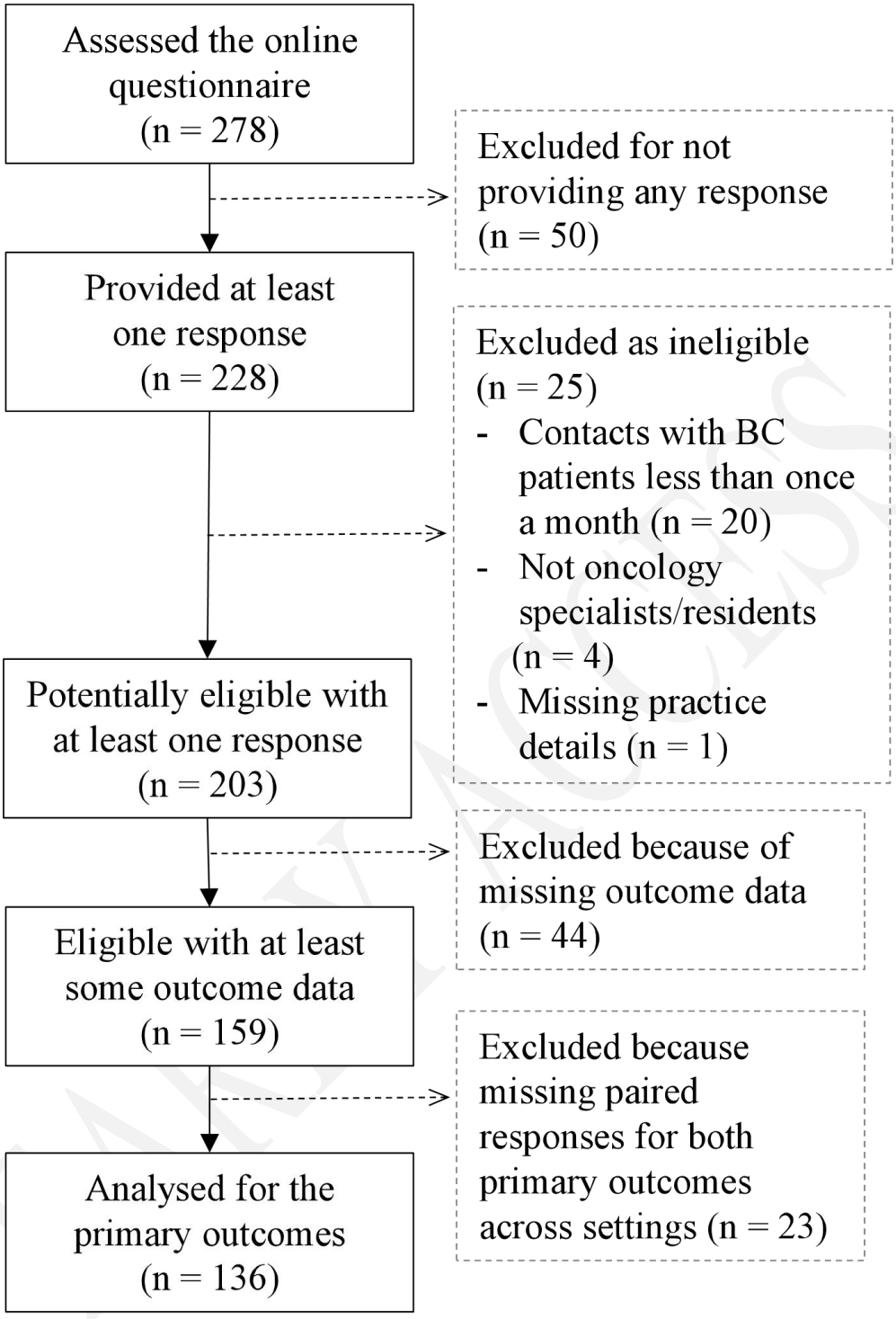

Figure 1. Study sample and participant flow. Flow of participants from initial survey access to inclusion in the final analysis (*n* = 136 valid paired responses).

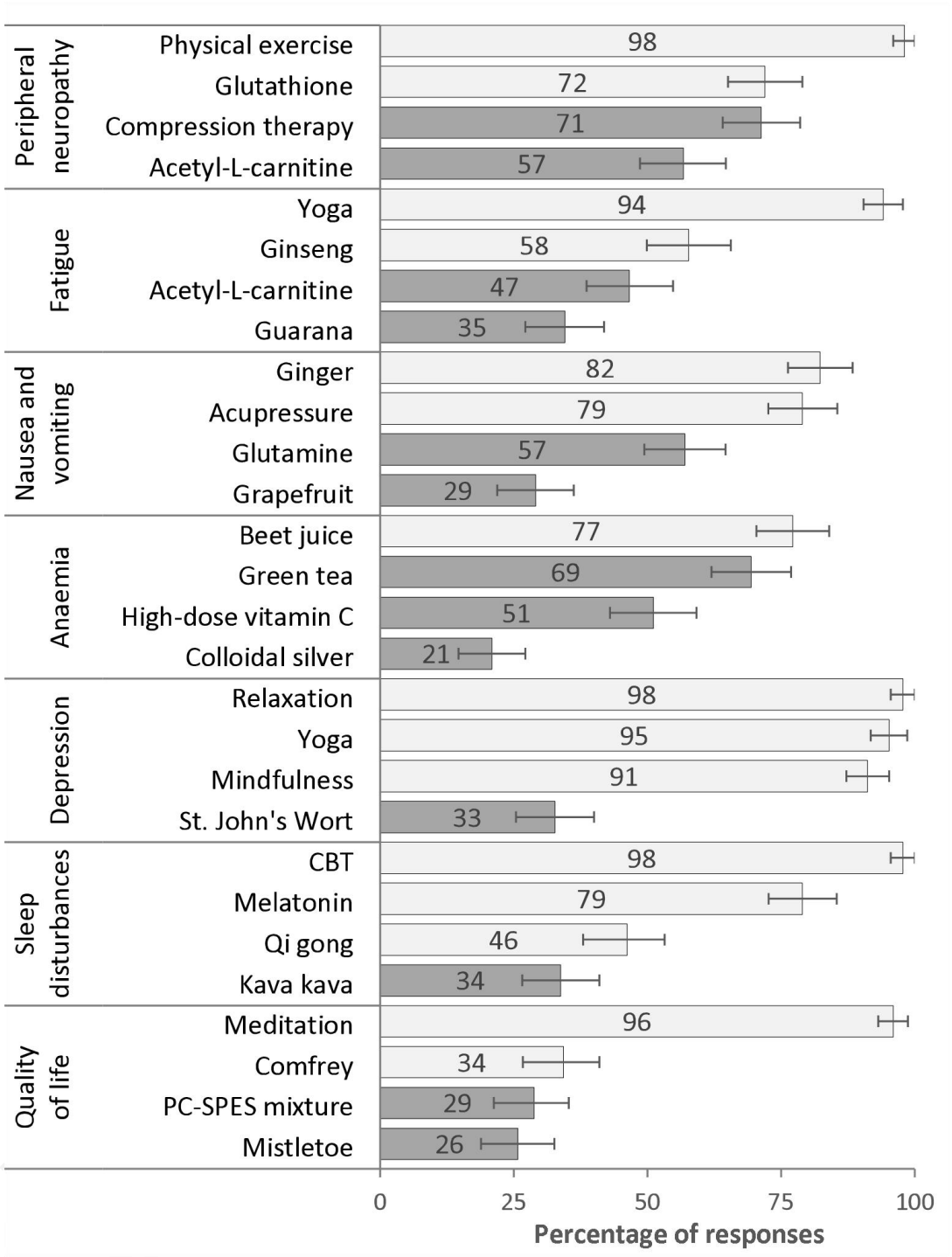

Figure 2. Endorsement of complementary therapies in neoadjuvant and adjuvant settings. The bars represent the percentage of responses categorized by endorsement for each indication. Error bars illustrate the 95% confidence intervals for participant-level proportions, calculated using logit-transformed binomial intervals (n = 136; each participant contributed two vignette responses; unweighted data). Dark bars indicate therapies for which existing evidence recommends against use ("prevent"), reflecting responses that are not aligned with the evidence.

SUPPLEMENTAL DATA

Supplemental data are available at the following link:

https://www.bjbms.org/ojs/index.php/bjbms/article/view/13413/4081