

# Effects of Internet-Based Psychotherapy on Symptom Improvement, Quality of Life, and Mood in Cancer-Related Fatigue: A Meta-Analysis of Randomized Controlled Trials

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## Research Article

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# Abstract

## Background

Cancer-related fatigue (CRF) is a prevalent symptom among individuals with cancer, significantly impairing patients' quality of life (QoL), increasing the likelihood of treatment discontinuation, and contributing to poorer survival outcomes. Our aim was to investigate the efficacy of internet-based psychological interventions on alleviating fatigue symptoms, comorbid anxiety and depression, and improving QoL in patients with CRF.

## Methods

We conducted a meta-analysis of randomized controlled trials (RCTs) that required significant CRF as an eligibility criterion. The primary outcome was improvement in fatigue symptoms; secondary outcomes included QoL and mood-related measures. A random-effects model was used. Heterogeneity was quantified using  $I^2$ .

## Results

Nine RCTs were included. Internet-Based Psychotherapy significantly alleviated fatigue symptoms compared to control conditions (post-treatment between-group SMD [95% CI] = 0.54[0.16,0.92];  $I^2=84.8\%$ ). At follow-up, the between-group effect was no longer statistically significant (SMD = 0.46 [-0.07,0.98];  $I^2=81.0\%$ ). For secondary outcomes, we observed non-significant trends toward improved QoL (SMD = 0.48[-0.01, 0.98]), reduced anxiety (between-group SMD = 0.58 [0.00, 1.16]), and reduced depression (between-group SMD = 0.70[-0.16, 1.57]), though these estimates were based on few studies with wide confidence intervals.

## Conclusion

Internet-based psychological interventions reduce fatigue symptoms in patients with CRF immediately post-treatment, with effects that may not be statistically sustained at follow-up based on limited data. Improvements in QoL, anxiety, and depression remain inconclusive and require further high-quality RCTs.

## Introduction

Cancer-related fatigue (CRF) is a prevalent symptom among cancer patients <sup>1, 2</sup>. CRF is characterized by its persistence despite rest and may be accompanied by impaired emotional and cognitive function according to the guideline of National Comprehensive Cancer Network (NCCN) <sup>1, 3</sup>. Its contributing factors include the cancer itself, treatment side effects, neuroendocrine dysregulation, and psychological

stress. The prevalence of CRF ranges widely from 14% to 100%, with approximately 25% to 33% of survivors experiencing persistent fatigue for years after treatment completion<sup>1, 3, 4</sup>. CRF significantly impairs patients' quality of life (QoL) and increases the risk of treatment discontinuation, potentially leading to poor survival outcomes<sup>1, 3</sup>.

Current strategies for managing CRF encompass pharmacotherapy, exercise therapy, and psychosocial interventions<sup>1, 3</sup>. Among these, psychosocial interventions are particularly valuable, demonstrating positive effects on fatigue symptoms, QoL, and social functions<sup>5-7</sup>. Substantial evidence indicates that psychological interventions can effectively reduce CRF during and after treatment, resulting in a moderate positive effect that are often significantly superior to pharmacological options<sup>1, 8</sup>. However, traditional face-to-face psychological therapy faces clinical implementation barriers due to resource limitations, poor accessibility, and high costs<sup>9, 10</sup>. Internet-based psychological therapy offers a promising alternative to overcome spatiotemporal constraints and reduce economic burdens, thereby addressing limitations of traditional models<sup>2, 11</sup>. Current evidence suggests that telephone-based interventions provide a convenient way for cancer patients to self-manage symptoms, including depression, anxiety, emotional distress, and fatigue<sup>12</sup>. Nevertheless, in previous studies of internet-based psychological interventions, fatigue was frequently assessed as a secondary end point by single items or subscales of instruments designed to measure emotional distress, QoL, or general symptom burden<sup>13</sup>. Furthermore, fatigue was not an eligibility requirement for participants. Consequently, enrolled patients might not have experienced clinically significant fatigue levels, potentially limiting the observable intervention impact.

In order to provide more precise evidence regarding the efficacy of internet-based psychotherapy for patients with CRF, we conducted this meta-analysis, focusing exclusively on randomized controlled trials (RCTs) that explicitly required significant CRF as an eligibility criterion for participants. This study aims to explore the effects of internet-based psychological interventions on fatigue symptoms, anxiety and depression, and QoL in patients with CRF, thereby providing an evidence-based foundation for optimizing clinical management strategies.

## Methods

### Search strategy and study selection

This study was prospectively registered with PROSPERO (CRD420251048401). No restriction on country income level was applied, contrary to a previous protocol version; thus all available RCTs were considered. We systematically searched the PubMed, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases. The search was restricted to articles published in English from the inception until May, 2025. We used a combination of medical subject headings and free words to search, the detailed search strategy is provided in the **Supplementary Material**.

**Eligibility criteria were defined according to the Population, Intervention, Comparison, Outcomes, and Study Type (PICOS) framework:**

**P (Population):** Adult patients with cancer experiencing fatigue symptoms, irrespective of cancer type. Both patients undergoing active treatment and cancer survivors were included.

**I (Intervention):** Internet-based psychotherapy. We defined this as any structured psychological therapy (e.g., cognitive-behavioral therapy, mindfulness-based stress reduction, psychoeducation, self-management support) delivered primarily via web-based platforms, mobile applications, or other internet-mediated formats, with or without therapist guidance.

**C (Comparison):** Treatment as usual (TAU) or waitlist control.

**O (Outcomes):** Primary outcome: Improvement in fatigue symptoms measured by validated questionnaires (FACIT-F, BFI, CIS, CFS, FSI, PFS). Secondary outcomes: Quality of life (QoL) and mood-related measures (anxiety and depression) assessed by validated instruments. Anxiety and depression were not part of the primary search strategy but were extracted when reported in included studies.

**S (Study Type):** Randomized controlled trials (RCTs).

## Data extraction and risk of bias assessment

Data extraction and quality assessment were independently completed by two researchers (Shiyuan Liu and Hechao Zhao). Discrepancies were resolved through discussion and consultation with a third researcher (Shiyuan Liu and Ti Wang). The extracted data included the basic information (e.g., author, publication year, sample size, cancer types, intervention details) of the original studies. The mean values, standard deviations, and sample sizes for all outcomes of interest were extracted. Data for the primary outcome (fatigue) at post-treatment and follow-up time points (where available). The revised Cochrane Risk of Bias Assessment Tool for Randomized Trials (RoB2) was used to assess the risk of bias for each original study<sup>14</sup>, evaluating five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. We also performed sensitivity analyses excluding studies rated as high risk of bias to examine the robustness of pooled estimates.

## Statistical analysis

Meta-analyses were conducted using R software (version 4.5.0).. Statistical significance was set at  $P \leq 0.05$  (two-tailed). Continuous outcomes, measured using different scales, were pooled using standardized mean differences (SMD) with 95% confidence intervals (CI). SMD was calculated using Cohen's d (Hedges' g correction for small sample sizes applied when  $n < 20$ ). Binary outcomes (fatigue symptom improvement, yes/no) were pooled using risk ratios (RR) with 95% CI. A random-effects model was employed for all meta-analyses. Heterogeneity was quantified using the  $I^2$  statistic, with values  $>$

50% considered substantial heterogeneity. Between-group comparisons (intervention vs. control) were the primary analytic approach because all included studies were RCTs. Within-group pre-post comparisons are also reported for descriptive purposes but are interpreted with caution due to their susceptibility to bias (regression to the mean, natural history). Publication bias was assessed statistically using Egger's test when at least 10 studies were available; for outcomes with fewer studies, Egger's test results are reported but interpreted with caution (Cochrane Handbook). Subgroup analyses were performed based on cancer type (cancers specific to females vs. other cancers) as an exploratory analysis; no a priori hypotheses about differential efficacy were made. Sensitivity analyses were conducted to assess the robustness of the findings, primarily by comparing results using a random-effects model and by excluding high-risk-of-bias studies.

## Results

### Included studies and characteristics

The initial electronic database search identified 3,272 records. After screening, nine randomized controlled trials (RCTs) met the inclusion criteria<sup>15-23</sup>. These studies comprised nine experimental groups (n = 1,485 patients) and nine control groups (n = 1,221 patients). The mean participant age ranged from 50 to 60 years, with 23% to 100% female participants, and interventions ranged from 6 to 24 weeks. The reasons for excluding full-text articles are presented in the PRISMA flow diagram (**Figure. 1**). The key study characteristics are summarized in Table 1.

### Primary outcome: Fatigue

Between-group comparisons (intervention vs. control) were the primary analytic approach. Within-group pre-post comparisons are also reported for descriptive purposes.

#### Between-group effect post-treatment

Eight studies contributed data. Internet-based psychological interventions significantly reduced fatigue severity compared to control conditions (SMD [95% CI] = 0.54[0.16, 0.92];  $I^2=84.8\%$ ; Fig. 2c).

#### Between-group effect at follow-up

Four studies reported follow-up data. The effect was no longer statistically significant (SMD = 0.46[-0.07, 0.98];  $I^2=81\%$ ; Fig. 2d).

#### Within-group pre-post effect (for descriptive purposes)

Post-treatment SMD = 1.09[0.47, 1.72] ( $I^2=93\%$ ); Follow-up SMD = 0.98[-0.16, 2.11] ( $I^2=93.4\%$ ; Figs. 2a-2b). These large within-group effect sizes should not be directly compared to between-group estimates, as they do not account for spontaneous improvement or placebo effects.

#### Binary outcome

Patients receiving internet-based psychological interventions were more likely to achieve clinically significant fatigue improvement compared to controls (RR = 2.94 [2.09, 4.13]; Fig. 2e). The definition of "improvement" varied across studies; each original study used its own validated questionnaire and predefined cutoff for response.

### Sensitivity analysis

After excluding studies with a high risk of bias ( $n = 5$ ), the between-group effect size increased slightly (SMD = 0.86 [0.28, 1.43]) and was statistically significant.

### Subgroup analysis based on cancer type

Improvements in fatigue were observed in both female-related cancers (SMD = 0.82 [0.02, 1.62]) and other cancers (SMD = 0.36 [0.00, 0.72]) post-treatment (Fig. 3b). The difference between subgroups was not statistically significant ( $P$  for interaction = 0.30). High heterogeneity within the female-cancer subgroup ( $I^2=87.6\%$ ) may be due to small sample sizes and varying cancer types (breast, cervical, ovarian).

## Secondary outcomes

QoL: Meta-analysis of six studies indicated a trend towards improved QoL following internet-based psychotherapy. The pooled between-group effect showed a non-significant trend favoring intervention (SMD [95% CI] = 0.48 [-0.01, 0.98];  $I^2=87.5\%$ , **Figure. 4b**). Within-group pre-post (SMD [95% CI] = 1.60 [-0.35, 3.55];  $I^2=96.4\%$ , **Figure. 4a**). Given the wide confidence intervals and high heterogeneity, these results are inconclusive.

Anxiety and depression:

Anxiety (3 studies): Between-group SMD = 0.58 [0.00, 1.16] ( $I^2=86.1\%$ ; Fig. 4d). The lower bound of the CI included zero, indicating marginal statistical significance. Due to the small number of studies, this finding should be considered exploratory.

Depression (5 studies): Between-group SMD = 0.70 [-0.16, 1.57] ( $I^2=93.6\%$ ; Fig. 4f). The confidence interval crossed zero, indicating no statistically significant effect.

## Bias evaluation

Publication bias: The Egger test results of the primary outcome all suggested that no significant publication bias was found either after treatment (Self before and after comparison:  $t = 1.17$ ,  $df = 6$ ,  $P = 0.288$ ; Comparison with the control group:  $t = 1.82$ ,  $df = 6$ ,  $P = 0.119$ ) or at follow-up (Self before and after comparison:  $t = 0.86$ ,  $df = 1$ ,  $P = 0.550$ ; Comparison with the control group:  $t = 2.61$ ,  $df = 1$ ,  $P = 0.233$ ). However, Egger's test was performed despite limited study numbers ( $< 10$  for most outcomes), so

results are exploratory. For fatigue (post-treatment between-group,  $n = 8$ ):  $t = 1.82$ ,  $df = 6$ ,  $P = 0.119$  (no evidence of bias, but test has low power with  $< 10$  studies). For QoL (post-treatment between-group,  $n = 6$ ):  $t = 1.37$ ,  $df = 4$ ,  $P = 0.243$ . For anxiety and depression, the number of studies was too small ( $\leq 5$ ) for meaningful Egger's test; those results are not reported.

Evaluation of original research: Four studies had an uncertain risk of bias, and five studies had a high risk of bias (**Figure. 5**). The main source of bias of the study was the bias caused by the missing data. Dropout rates in the original studies ranged from 10% to 35%. Handling of missing data varied (last observation carried forward, multiple imputation, complete-case analysis). Most original studies used intention-to-treat (ITT) analyses, but ITT does not fully eliminate bias when dropout is high or non-random. As noted above, our sensitivity analysis—which excluded high-risk studies—showed a significant increase in fatigue effects, and the results remained statistically significant.

## Discussion

### Clinical implications

This study comprehensively evaluated the efficacy of internet-based psychotherapy on the primary outcome (fatigue symptoms), QoL, and mood-related outcomes among cancer patients with CRF. These findings support the effectiveness of online psychological treatment as a digital therapeutic approach for individuals with CRF.

The main finding is that these interventions significantly reduce fatigue compared to control conditions immediately post-treatment, with a small-to-moderate effect size ( $SMD = 0.54$ ). However, the effect at follow-up was not statistically significant, and evidence for secondary outcomes remains inconclusive due to limited study numbers and high heterogeneity.

Our findings are consistent with a previous meta-analysis by Seiler et al. (2017)<sup>24</sup>, which reported a comparable effect size for eHealth interventions in cancer survivors ( $r = 0.27$ , approximately  $SMD = 0.55$ ). However, our study extends this evidence by: requiring clinically significant CRF as an entry criterion; including patients undergoing active treatment; distinguishing between-group from within-group effects.

The lack of statistically significant sustained benefit ( $SMD = 0.46 [-0.07, 0.98]$ ) should be interpreted cautiously. Only four studies provided follow-up data (ranging from 3 to 6 months post-intervention), and the confidence interval includes the null. Thus, we cannot conclude that effects are “largely maintained.” Future trials with longer follow-up and lower attrition are needed.

The trends toward improved QoL, anxiety, and depression did not reach statistical significance. The wide confidence intervals and high heterogeneity indicate substantial uncertainty. Moreover, anxiety and depression were not part of our primary search strategy; they were extracted opportunistically from

included studies, which may introduce reporting bias. Therefore, these findings should be considered hypothesis-generating rather than conclusive.

In subgroup analyses, positive effects were observed for women with associated cancers as well as for those with other cancers. Although there was greater heterogeneity within subgroups of associated cancers among women, the improvement trend is notable.

High statistical heterogeneity was observed across most analyses. A wide variety of cancer types, such as breast cancer, ovarian cancer, cervical cancer, gastric cancer, chronic myeloid leukemia, and mixed-type cancers; differences in intervention content, such as cognitive behavioral therapy, mindfulness, psychoeducation, and self-management and different measurement instruments. Due to the limited number of studies ( $n = 9$ ), we could not perform meta-regression or subgroup analyses on most moderators. The subgroup analysis by cancer type was exploratory and showed no significant difference. High heterogeneity may reduce the precision and generalizability of pooled estimates; thus, results should be interpreted with caution.

Five of nine studies were rated as high risk of bias, primarily due to missing outcome data. In internet-based interventions, dropout is often non-random. While most original studies used ITT, the handling of missing data varied. We excluded sensitivity analyses conducted in studies with a high risk of bias; although these analyses increased the estimated effect size for fatigue, readers should exercise appropriate caution when interpreting the pooled estimates.

In terms of clinical application, our study identified the potential for internet psychotherapy to be an effective new clinical alternative treatment. Over the past decade, internet-based psychotherapy has become an important part of psychological treatment. Face-to-face psychotherapy plays a crucial role in the comprehensive approach to treating people with cancer<sup>2</sup>. However, the cost and accessibility of face-to-face treatment have hindered its widespread adoption<sup>10</sup>. Internet-based psychotherapy overcomes the limitations of time and space and can provide services to more patients, especially those who have difficulty accessing traditional face-to-face psychotherapy, due to limitations in region, transportation, and resources. Internet-Based Psychotherapy offers a scalable approach to managing CRF, particularly for patients with limited access to face-to-face therapy. They should be viewed as a complementary option rather than a replacement for traditional psychological support, especially for patients with complex psychiatric comorbidities or those who prefer human interaction. The interventions may be most suitable for patients during and after active treatment who have mild-to-moderate fatigue and basic digital literacy. Integration into survivorship care pathways could involve referral from oncology teams to evidence-based digital programs. Given the lack of robust follow-up effects, booster sessions or maintenance strategies might be needed.

Our findings are consistent with those of previous studies showing that internet-based psychotherapy improves psychosomatic outcomes<sup>13</sup>. We included a meta-analysis of outcomes after follow-up, but again, as in previous studies, evidence of long-term effects is lacking<sup>7</sup>. In addition, a meta-analysis of the

effectiveness of an online mindfulness intervention in cancer patients did not reveal differences in the improvement of fatigue symptoms in cancer patients<sup>25</sup>. This may be because psychological interventions for cancer patients with CRF focus more on improving fatigue. Therefore, more personalized psychological intervention programs may also be the key to better efficacy.

## **Study limitations**

It is necessary to recognize the limitations of this study. First, most pooled results in this study were heterogeneous. On the one hand, this may be due to the variety of cancer types included, and there are differences between different types of cancer, leading to heterogeneity. In addition, the studies were from many countries and regions, and different social and cultural backgrounds may also lead to heterogeneity. On the other hand, the measurement tools used differed from one study to another, and although we chose the SMD as the effect size, the differences among the measurement tools may also be a source of heterogeneity. Therefore, the results of this study should be interpreted with caution after the above heterogeneity is considered. Second, although this study analyzed follow-up time after treatment, there were few original studies with a follow-up, which may also introduce bias. Furthermore, due to the small number of studies, it was not possible to conduct a meaningful assessment of publication bias for most outcome measures. Additionally, anxiety and depression were not pre-specified secondary outcomes; therefore, the analysis of these measures was exploratory in nature.

## **Conclusions**

Our review summarizes and analyzes existing data on internet-based psychotherapy and CRF. Our findings highlight the potential therapeutic value of internet-based psychotherapy for patients with CRF, especially in improving fatigue symptoms. Future research could involve high-quality randomized controlled trials (RCTs) with larger sample sizes, standardized outcome measures, longer follow-up periods, and lower dropout rates. Researchers could also examine moderating factors such as the type of intervention, delivery method, cancer stage, and baseline fatigue severity.

## **Declarations**

## **Conflict of interest**

All the authors declare that they have no financial or non-financial competing interests.

## **Funding**

This work This job does not have any financial support.

## **Statement of ethics**

As this is a systematic review and meta-analysis of previously published studies, no ethical approval or participant consent was required

## Author Contribution

Shiyuan Liu, Ti Wang and Hechao Zhao participated in drafting and revising the manuscript for content, including medical writing, and in the study concept and design, data acquisition, analysis and interpretation of the data, and statistical analysis.

## Acknowledgments

None.

## Data availability

All the data generated during this study are included in this article. Further inquiries can be directed to the corresponding author.

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## Table

Table 1 is available in the Supplementary Files section.

## Figures

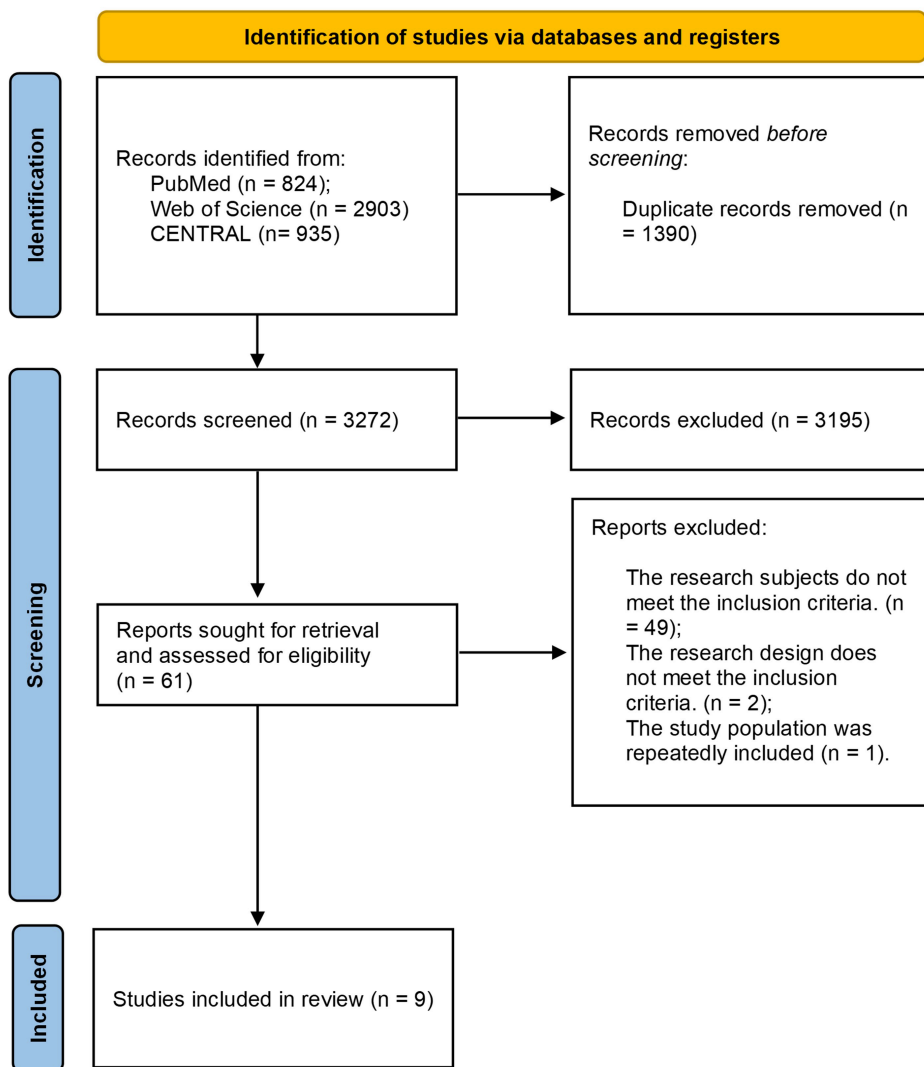


**Figure 1**

PRISMA flow diagram.

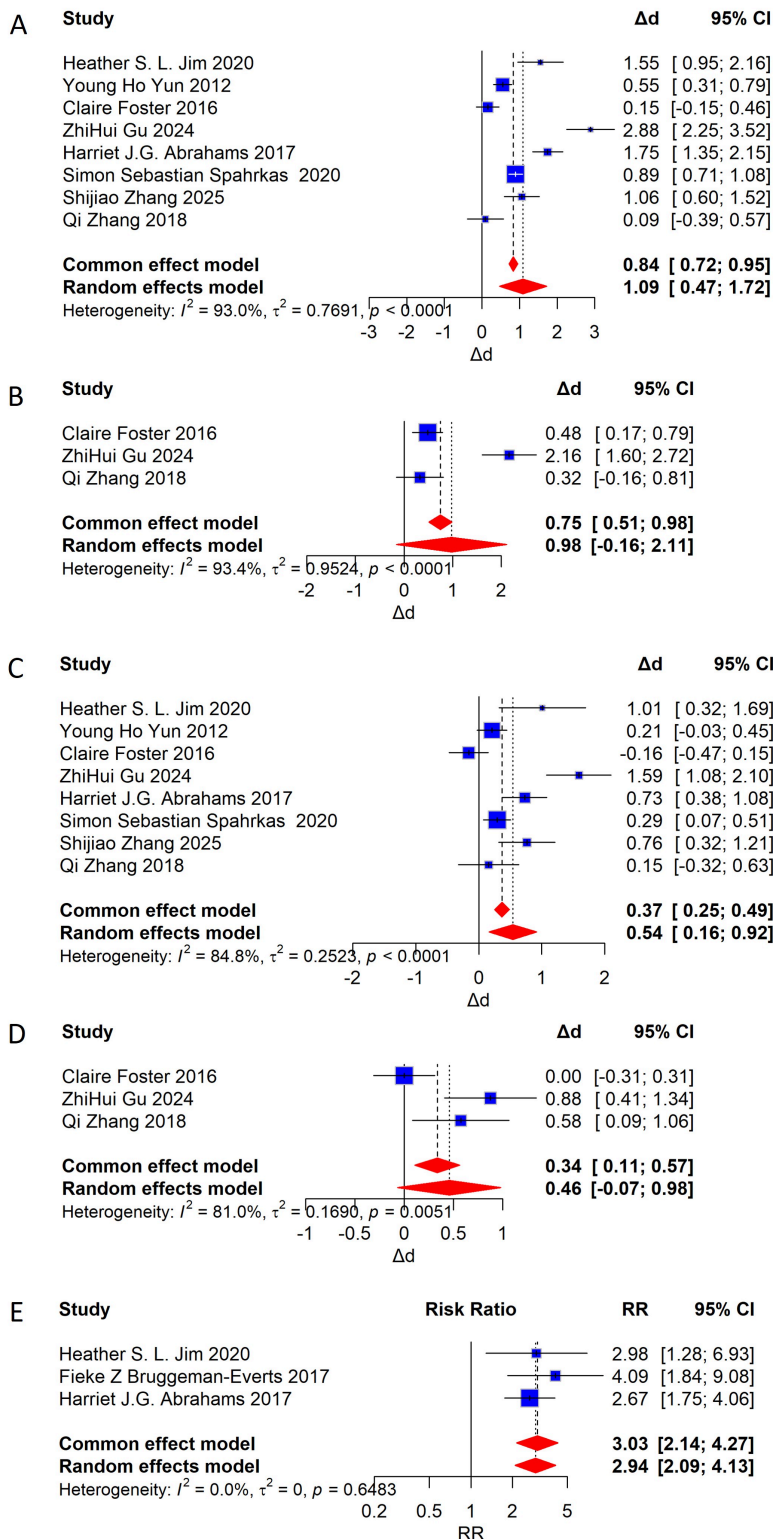


**Figure 2**

Results for the primary outcome (fatigue). (A) Within-group pre-post SMD after treatment; (B) Within-group pre-post SMD at follow-up; (C) Between-group SMD (intervention vs. control) after treatment; (D) Between-group SMD at follow-up; (E) Risk ratio for clinically significant fatigue improvement. SMD = standardized mean difference.

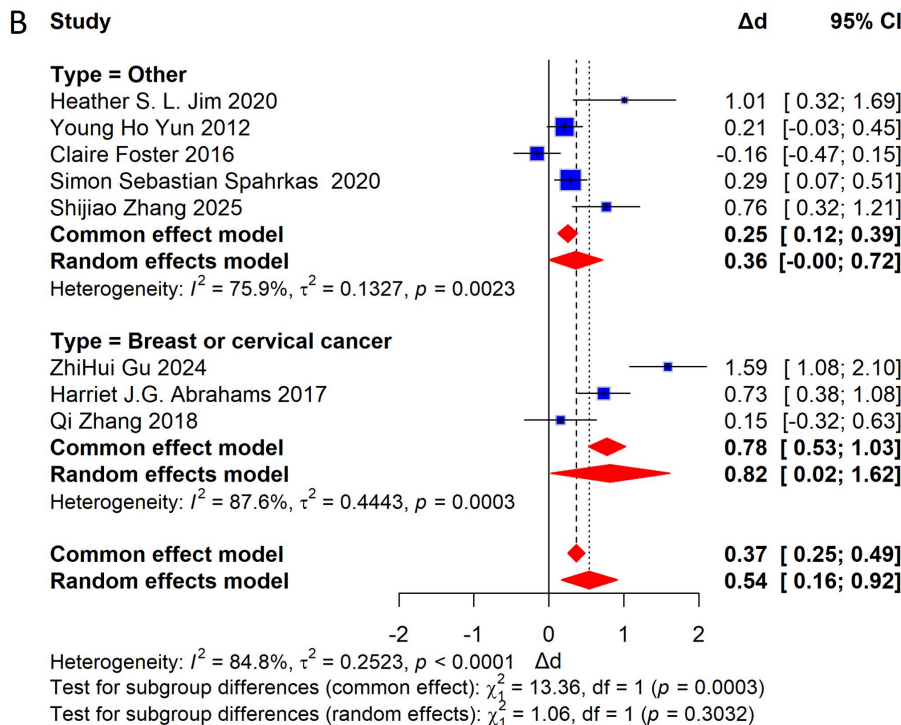
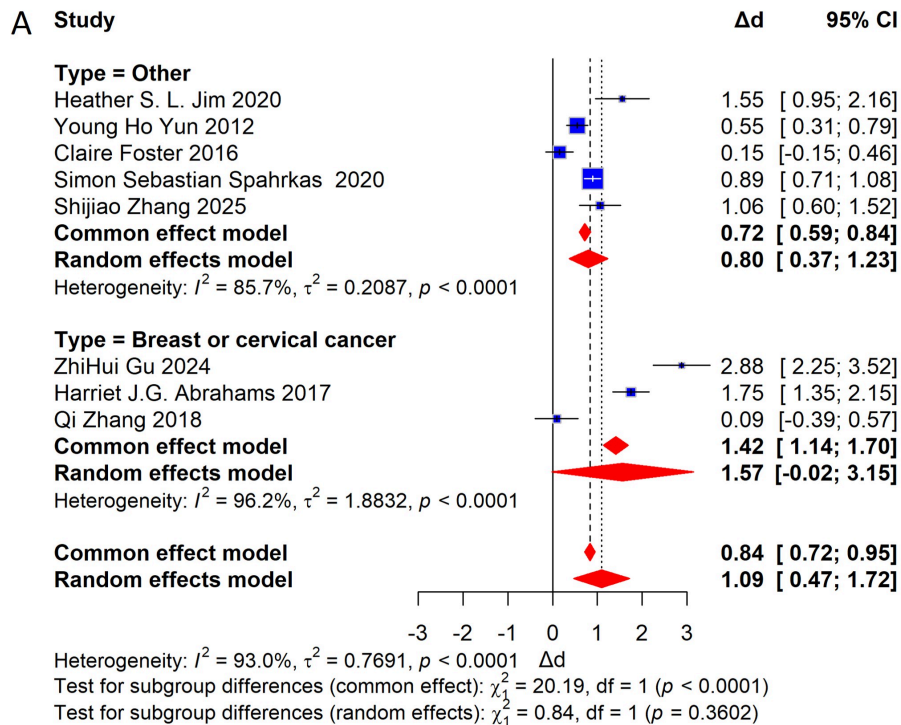


**Figure 3**

(A) Subgroup analysis for fatigue – Within-group comparisons (intervention vs. control) after treatment, stratified by cancer type (female-related cancers vs. other cancers);

(B) Subgroup analysis for fatigue – between-group comparisons (intervention vs. control) after treatment, stratified by cancer type (female-related cancers vs. other cancers);

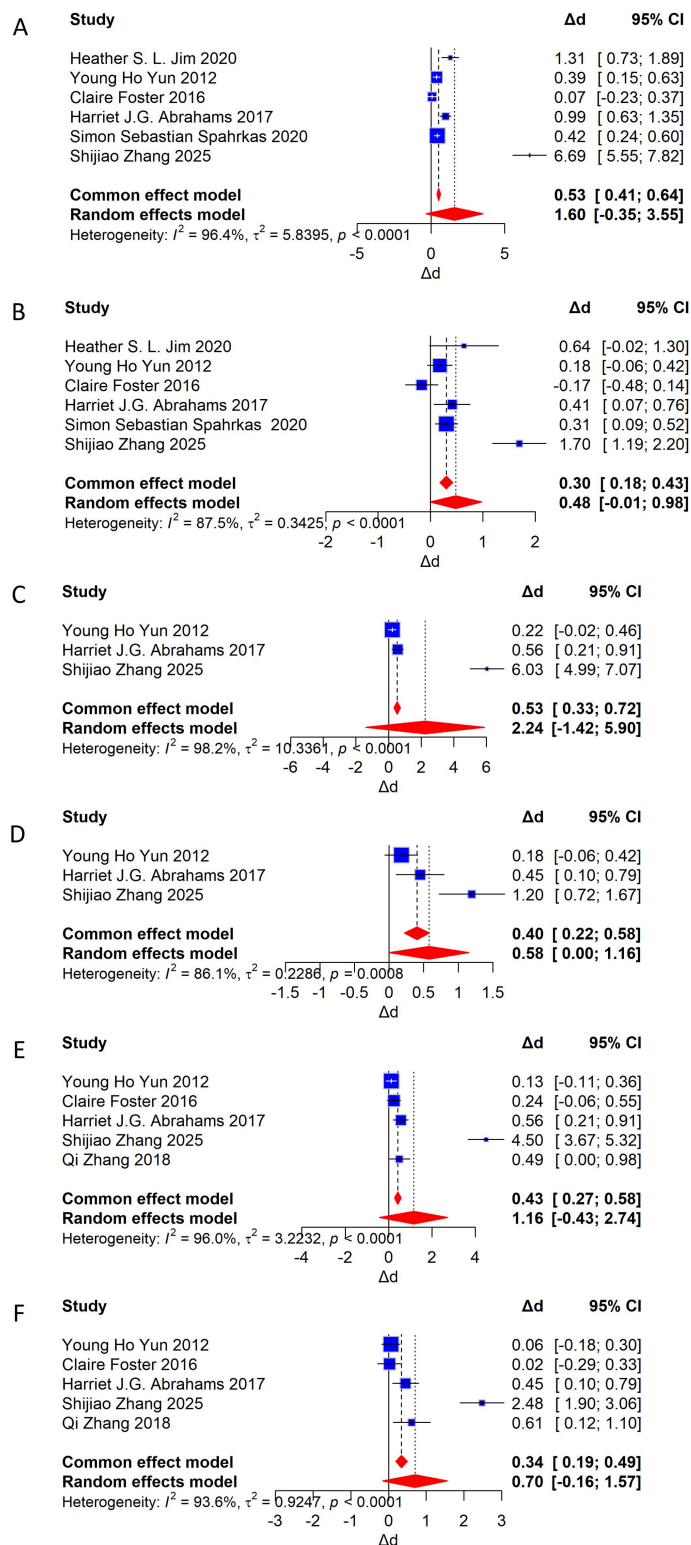


**Figure 4**

Results of secondary outcomes. A. Improvement in quality of life after treatment. B. The quality of life improved after treatment compared with the control group. C. Improvement of anxiety after treatment. D. Anxiety improved after treatment compared with the control group. E. Improvement of depression after treatment. F. Depression improvement after treatment compared with the control group.

| Study ID                      | Randomization process | Deviations from intended interventions | Missing outcome data | Measurement of the outcome | Selection of the reported result | Overall |               |
|-------------------------------|-----------------------|----------------------------------------|----------------------|----------------------------|----------------------------------|---------|---------------|
| Heather S. L. Jim 2020        | ?                     | ?                                      | ?                    | ?                          | +                                | !       | Low risk      |
| Young Ho Yun 2012             | +                     | ?                                      | ?                    | ?                          | ?                                | ?       | Some concerns |
| Fieke Z Bruggeman-Everts 2017 | ?                     | ?                                      | ?                    | ?                          | ?                                | ?       | High risk     |
| Claire Foster 2016            | +                     | ?                                      | ?                    | ?                          | +                                | ?       |               |
| ZhiHui Gu 2024                | +                     | ?                                      | ?                    | ?                          | +                                | !       |               |
| Harriët J.G. Abrahams 2017    | +                     | ?                                      | +                    | ?                          | +                                | !       |               |
| Simon Sebastian Spahrkäs 2020 | ?                     | ?                                      | ?                    | ?                          | +                                | ?       |               |
| Shijiao Zhang 2025            | +                     | ?                                      | ?                    | ?                          | +                                | ?       |               |
| Qi Zhang 2018                 | +                     | ?                                      | +                    | ?                          | ?                                | !       |               |

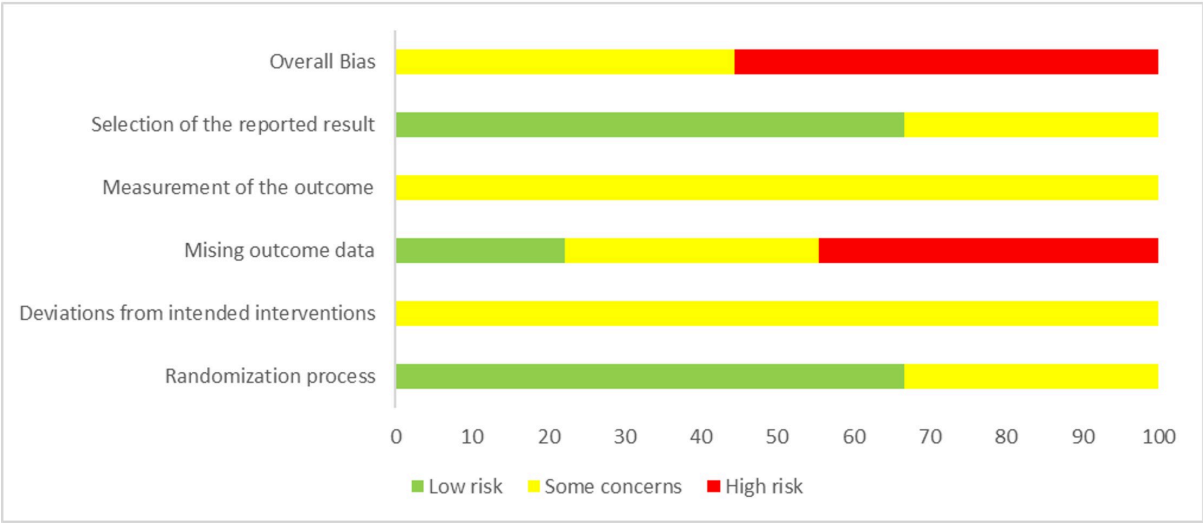


**Figure 5**

Evaluation of literature quality.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1.docx](#)