

EVALUATION OF SYMPTOM PREVALENCE AND PSYCHO-ONCOLOGICAL INTERVENTION EFFICACY IN CANCER PATIENTS

Ph.D. Thesis

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Budapest

2026

***“An Individual Doesn't Get Cancer,
a Family Does”***

Terry Tempest Williams

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1. LIST OF ABBREVIATIONS

CI – confidence intervals

HR – hazard ratio

OS – overall survival

PC – pancreatic cancer

PI – psychological intervention

QoL – quality of life

RFS – recurrence-free survival

SMD – standardized mean difference

2. STUDENT PROFILE

2.1. Vision and mission statement, specific goals

My vision is to shape cancer care by ensuring that every patient - as well as their families - receives psychological support, improving their quality of life, compliance and resilience throughout the treatment journey.



My mission is to integrate personalized, evidence-based psychological care into standard oncology practice, providing continuous support to patients from diagnosis through all stages of treatment, regardless of the disease outcome.

My specific goal is to contribute to the translation of psycho-oncological research into routine clinical practice by providing clear evidence on the effectiveness of psychological interventions. Through this work, I aim to support the wider recognition and implementation of evidence-based psychological care as an essential component of oncology treatment.

2.2. Scientometrics

Number of all publications:	3
Cumulative IF:	10,5
Avg. IF/publication:	3,5
Ranking (SCImago):	Q1
Number of publications related to the subject of the thesis:	2
Cumulative IF:	6,7
Avg. IF/publication:	3,5
Ranking (SCImago):	Q1
Number of citations on Google Scholar:	58
Number of citations on MTMT (independent):	40
H-index:	2

The detailed bibliography of the student can be found on pages 66-67.

2.3. Future plans

Beyond traditional hospital settings, a major focus of my work will be the development and testing of online therapy formats. Expanding online interventions is essential to

provide care for patients living in small towns where clinical psychologists are unavailable, and to offer a realistic alternative for those who are physically too ill to travel to a clinic. Furthermore, specialized online platforms can help overcome the psychological barriers of stigma, allowing patients to seek and receive support from the privacy of their homes.

3. SUMMARY OF THE THESIS

Psychological symptoms represent a major but often underrecognized component of cancer care. Despite advances in oncological treatment, the emotional and psychological needs of patients remain secondary. The present thesis aims to provide a comprehensive synthesis of evidence on the efficacy of psychological interventions in patients with a broader cancer population and on the prevalence of psychological symptoms in pancreatic cancer (PC) in an understudied patient group.

To improve clinical understanding and support the integration of psychological care into oncology, we conducted two meta-analyses. The first study assessed the effects of different psychological interventions on quality of life (QoL), and survival across various cancer types. The second examined the prevalence and of psychological symptoms among patients with PC. In the meta-analysis of psychological interventions, we found that these interventions significantly improved patients' QoL, especially in early-stage cancer, but not survival compared to control groups. Our results further demonstrated that psychological symptoms are highly prevalent among patients with PC, with depression and anxiety being the most frequent in the examined population.

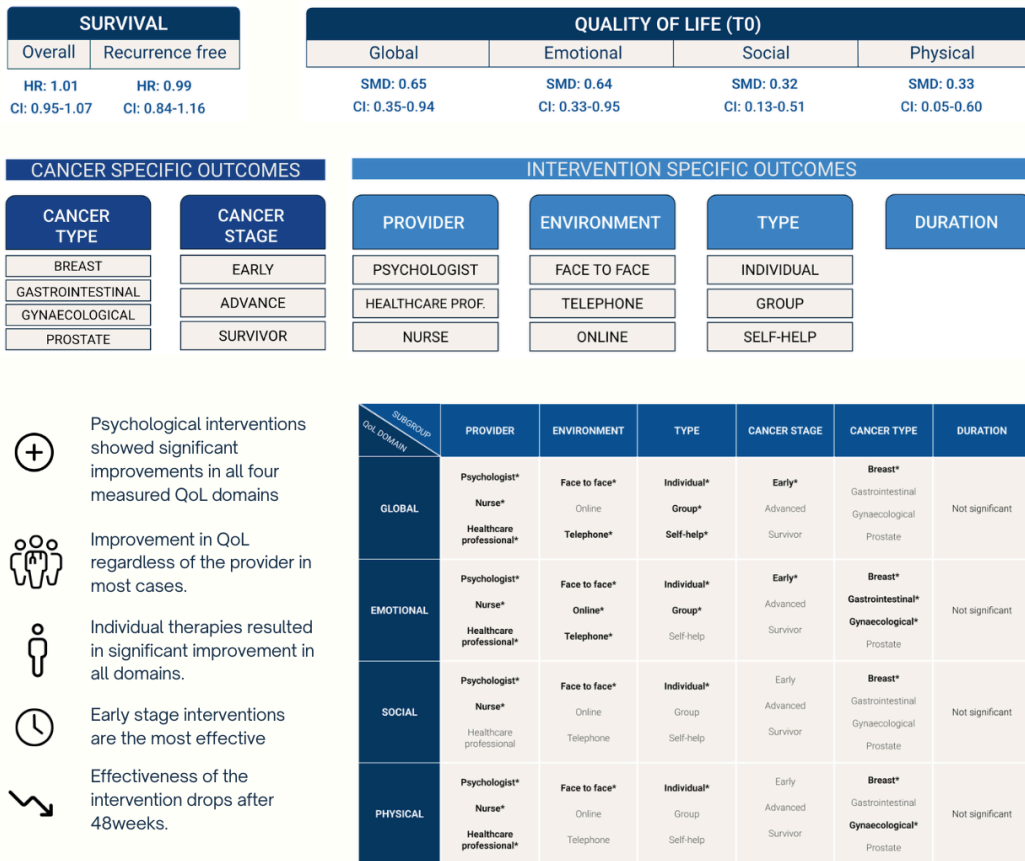
In conclusion, our findings underline the high psychological burden experienced by cancer patients, particularly those with PC, and demonstrate the overall efficacy of psychological interventions in improving quality of life. By identifying both the magnitude of the problem and evidence-based means of addressing it, this thesis supports the integration of systematic psychological assessment and intervention into routine oncological care.

4. GRAPHICAL ABSTRACT

Systematic Insights into Psycho-Oncology: Prevalence and Intervention Efficacy for Psychological Symptoms in Cancer Patients.



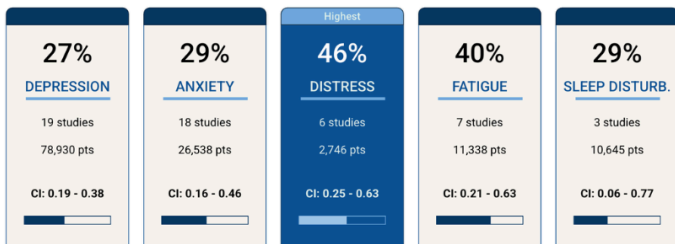
I. Psychological intervention improves quality of life in patients with early-stage cancer: a systematic review and meta-analysis of randomized clinical trials



The significant differences between the intervention and the control groups are marked in bold *

II. One out of four patients with pancreatic cancer experience psychological symptoms: A systematic review and meta-analysis

Prevalence of psychological symptoms among pancreatic cancer patients



The examined symptoms developed in more than a quarter of the studied population



The timing of diagnosis does not have an impact on the development of these psychological symptoms in a relevant amount, allowing plenty of time for interventions.

5. INTRODUCTION

5.1. Overview of the topic

5.1.1. *What is the topic?*

My research focuses on two core subjects: first, evaluating the efficacy of psychological interventions (PIs) on survival outcomes and on different domains of QoL in cancer patients; and second, determining the prevalence of psychological symptoms among patients with PC, in an understudied patient population.

5.1.2. *What is the problem to solve?*

Cancer remains a major global health challenge. According to GLOBOCAN 2022, an estimated 20.0 million new cancer cases and 9.7 million cancer deaths occurred worldwide, making cancer one of the leading causes of morbidity and mortality worldwide.(1) PC accounted for 510,992 new cases and 467,409 deaths, ranking as the 6th leading cause of cancer-related death.(1) More recent estimates from the United States indicate that PC is projected to be the third leading cause of cancer-related death in 2026.(2) Cancer is not only a life-threatening physical illness but also a psychologically demanding condition.(3, 4) PC is an aggressive malignancy that is frequently diagnosed at an advanced stage and commonly accompanied by early cachexia and nutritional deterioration, creating a considerable physical and psychological burden from the outset of the disease.(5, 6) Given the growing number of individuals affected by cancer worldwide, understanding not only the physical but also the psychological consequences of the disease has become more important. Within this wide oncological population, PC represents a particularly vulnerable subgroup due to its exceptionally high mortality and rapid disease progression. The effectiveness of psychological interventions to significantly improve QoL or prolong survival remains unclear.(7) There has been no prior consensus on the degree of psychological symptom burden in this understudied group. To address these questions, we aimed to analyse all available data on this topic and conduct two comprehensive meta-analyses.

5.1.3. What is the importance of the topic?

The importance of this topic lies in the significant, yet often overlooked, role that psychological symptoms play in cancer care. A large proportion of patients with cancer develop symptoms of depression, anxiety, or other forms of psychological distress during the disease trajectory.(8-10) These symptoms can negatively affect treatment adherence, patient cooperation, communication with healthcare providers, and overall engagement in care, ultimately impacting clinical outcomes.(11-13) Although psychology still developing as a science, growing evidence suggests that the field of psychology can make a meaningful contribution medicine. Therefore, greater openness toward psychology from medical professionals and the integration of these findings into standard clinical practice would color and widen the approach to patient care.

The present work aims to contribute to this effort by evaluating the actual efficacy of psychological interventions and providing precise estimates of the prevalence of psychological symptoms among patients with PC. Ultimately, this thesis provides practical, usable, and important data that can directly support the development of evidence-based interventions for everyday oncology care.

5.1.4. What would be the impact of our research results?

The impact of the combined research results from both studies is significant in shaping future cancer care practices. Our findings may serve as a basis for the inclusion of psychological support as a standard part of cancer care, particularly for those with aggressive cancers like PC and their families. This can lead to better-targeted interventions and more holistic patient care. Our research could inspire policy changes that include mental health care for cancer patients, particularly those with more challenging diagnosis, and drive further research into effective psychological treatments.

6. OBJECTIVES

6.1. Study I. – Psychological Intervention Improves Quality of Life, but Not Survival in Patients with Early-Stage Cancer: a Systematic Review and Meta-analysis of Randomized Clinical Trials

Survival used to be almost the only goal of cancer treatment; however, QoL is increasingly recognized as an important outcome factor for oncological treatments and has been linked to the prediction of survival. (14, 15) The effectiveness of psychological interventions (PI) for improving QoL and the effect on survival in malignant diseases is yet controversial.(7, 16, 17) Our aim was to investigate the effect of PI on survival and QoL in patients with different cancer.

6.2. Study II. – One out of Four Patients with Pancreatic Cancer Experience Psychological Symptoms: a Systematic Review and Meta-analysis

The death rate from PC is one of the highest of all cancers, with increasing incidence every year over the past decades in both sexes.(2) In comparison to other types of cancer, our understanding of the psychological burden of such a deadly disease is still limited. Recognizing and addressing the psychological aspects of PC are crucial for comprehensive patient care. We, therefore, aimed to quantify the psychological burden of patients with PC.

7. METHODS

7.1. Study I. - Psychological Intervention Improves Quality of Life, but Not Survival in Patients with Early-Stage Cancer: a Systematic Review and Meta-analysis of Randomized Clinical Trials

7.1.1. Methodology and Protocol

We followed the recommendations of the Cochrane Collaboration(18) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 reporting guidelines(19) for both studies. The review protocols were registered in the International Prospective Register of Systematic Reviews (registration number CRD42021282327), and no deviations from the original protocols occurred.

7.1.2. Eligibility Criteria

Our inclusion criteria were limited to peer-reviewed, full-text randomized controlled trials (RCTs). We enrolled studies evaluating patients with any cancer diagnosis who underwent psychological interventions, provided that the publication reported quantitative data on QoL or survival outcomes (OS or RFS).

7.1.3. Information Sources and Search Strategy

We formulated our clinical question and defined the search strategy using the PICO-S (population, intervention, comparison, outcome, study type) framework. The systematic search was performed in three databases: MEDLINE (via PubMed), Cochrane Library (CENTRAL), and EMBASE from inception until 18th October 2021, with the restrictions to include adult patients. The search was updated on 1st of February 2024.

7.1.4. Study Selection and Data Extraction

We extracted the first author, year of publication, country, number of centers, and the demographic characteristics of the patients from each study. We also collected data on the interventions, including type, duration, provider, and environment. For the outcomes, we recorded OS, RFS, QoL tools, measurement times, and the reported questionnaire scores.

7.1.5. Risk of Bias and Quality of Evidence Assessment

Two authors (ASB and NV) performed the risk of bias assessment independently using the Cochrane risk-of-bias tool for randomized trials Version 2 (RoB 2).(20) Disagreements were resolved by a third party (BF).

7.1.6. Data Synthesis and Analysis

To account for anticipated between-study heterogeneity, a random-effects model was used to pool effect sizes. For the survival data, pooled hazard ratios (HR) with 95% confidence intervals (CI) were calculated using an inverse variance weighting method, heterogeneity was estimated using a restricted maximum-likelihood estimator, with the Q profile method for the CI.(21) Regarding QoL outcomes, standardizing was necessary due to the diverse instruments and questionnaires utilized across the included studies. Therefore, the standardized mean difference (SMD) with a 95% CI was used to evaluate the treatment effect between the intervention and the control groups. We used Hedges' g to calculate SMDs.(22) The magnitude of the SMD was interpreted based on established thresholds: 0.2-0.5 - small effects, 0.5-0.8 - medium effects, and values > 0.8 - large effects. As the included studies presented QoL results at different follow-up time points, to make a prediction, we created a longitudinal model for predicting QoL at 0, 12, 24, and 48 weeks post-intervention, using the time and the square of time as predictors of change in time. Forest plots show the results at these specific time points (T0=week 0, T12=week 12 T24=week 24, T48=week 48). A separate longitudinal prediction-model was applied for different QoL domains and subcategories. Inverse variance weighting was used to calculate the pooled SMD in the longitudinal meta-analysis.

Publication bias and small study effects were assessed using funnel plots. All statistical analyses were made with R (v4.2.1)(23) using the following packages: metafor (v3.4.0)(24) and clubSandwich (v0.5.8) for model calculations, publication bias and influential assessment, meta (v5.5.0)(25) for forest plots, ggplot2 (v3.3.6)(26) for additional prediction plots. We report the results as point estimates of the effect size (lower - upper limit of 95% CI) format.

7.2. Study II. - One out of Four Patients with Pancreatic Cancer Experience Psychological Symptoms: a Systematic Review and Meta-analysis

7.2.1. Methodology and Protocol

We followed the recommendations of the Cochrane Collaboration(18) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 reporting guidelines(19) for both studies. The review protocols were registered in the International Prospective Register of Systematic Reviews (registration number CRD42022288805), and no deviations from the original protocols occurred.

7.2.2. Eligibility Criteria

We applied the CoCoPop (Condition, Context, Population) framework to define our clinical question. We accepted full-text articles reporting any psychological symptoms in pancreatic ductal adenocarcinoma in the adult population. We accepted any 'psychological symptoms' if the diagnosis based on a standardized diagnostic criteria or clinical questionnaires. For the subgroup analysis by severity (mild, moderate, severe), we used the original categories from the articles. We excluded studies where patients had psychiatric diseases before the cancer diagnosis. Case reports and case series were excluded, but all other article types were accepted. We did not use any limits for publication date or language.

7.2.3. Information Sources and Search Strategy

The search was conducted in MEDLINE, EMBASE, and Cochrane Library on May 22, 2022, and updated on March 3, 2025.

7.2.4. Study Selection and Data Extraction

We used reference manager software (EndNote X9, Clarivate Analytics, Philadelphia, PA, USA) to identify and delete duplicate records. Two reviewers (DAS and CP) separately screened the titles, abstracts, and then the full texts in pairs based on prespecified criteria. Disagreements were solved with the help of a third reviewer (SAB). We then calculated Cohen's kappa coefficients to evaluate inter-rater agreements.

Two authors (DAS and SAB) extracted all relevant data from the included papers into a Microsoft Excel spreadsheet (Microsoft Office 365, Redmond, WA, USA).

Publication details (first author, year, country of origin, and number of clinical centers), demographic data of the sample, specific measurement instruments, assessment timelines (categorized into time groups), and the reported prevalence of any psychological symptoms. We defined prevalence as the percentage of PC patients experiencing a given psychological symptom at any specific point of assessment.

7.2.5. Risk of Bias and Quality of Evidence Assessment

Two reviewers (DAS and SAB) independently evaluated the methodological quality of the included studies using the Joanna Briggs Institute (JBI) Prevalence Critical Appraisal Tool.(27) When the two reviewers disagreed on a risk of bias score, they resolved it by consulting a third reviewer (CP). The JBI tool consists of nine items that look at different study characteristics, such as design, duration, participant retention, and how the results are reported. For each item, a 'yes' means good methodological quality, while 'no' means poor quality, and 'unclear' is used for ambiguous answers. We calculated a quality score for each study by giving 1 point for 'yes' and 0 points for 'no' or 'unclear'. We then turned these total scores into percentages. Based on the JBI checklist, we grouped the studies into three risk of bias categories: high risk of bias (20–50% 'yes' scores), moderate risk of bias (50–80% 'yes' scores), and low risk of bias (80–100% 'yes' scores).

7.2.6. Data Synthesis and Analysis

We proceeded under the assumption of considerable between-study heterogeneity in all instances, consequently employing a random-effects model for pooling effect sizes using a frequentist method. The designated measure for effect size was the proportion (prevalence) of symptoms, presented with a 95% CI. To accurately calculate this proportion, we systematically extracted the total patient numbers and the count of those exhibiting the event of interest from every included study. The results derived from the meta-analysis were visually summarized in forest plots. Furthermore, prediction intervals (representing the anticipated range of effects in future studies) were reported when applicable—specifically, where the sample of included studies was adequately sized (greater than five) and the observed effects were not excessively heterogeneous. Between-study heterogeneity was described by the between-study variance (τ^2) and Higgins and Thompson's I^2 statistics.(28) Results were reported in the format of effect

size or statistics and [95% CI]. Small study publication bias was assessed by visual inspection of funnel plots and calculating modified Egger's test p-values. However, we kept in mind that the test had limited diagnostic assessment below ~10 studies. Potential outlier publications were detected using different influence measures and plots following the recommendation by Harrer et al.(29) All statistical analyses were calculated by R software (23)(v4.3.3) using the meta(25) (v7.0.0) package for basic meta-analysis calculations and plots and the dmetar[(30) (v0.1.0) package for additional influential analysis calculations and plots.

8. RESULTS

8.1. Study I: - Psychological Intervention Improves Quality of Life, but Not Survival in Patients with Early-Stage Cancer: a Systematic Review and Meta-analysis of Randomized Clinical Trials

8.1.1. Study Search and Selection

A total of 11,374 articles were screened for eligibility after removing duplicates and excluding irrelevant records based on title and abstract. An additional 312 papers were excluded for missing outcome parameters or ineligible study criteria (including inappropriate control groups, incorrect outcome measures, and cohorts with pre-existing psychological illnesses), leaving 129 articles for analysis. The updated search screened 1,431 deduplicated records; 28 full-text articles were assessed, adding 14 studies to the final sample. The complete study selection workflow is shown in the PRISMA flowchart (Figure 1), and due to its length, the baseline characteristics of the included studies are detailed in the original publication.⁽³¹⁾ The outcomes of our analysis of the subgroups are summarized in Figure 2.

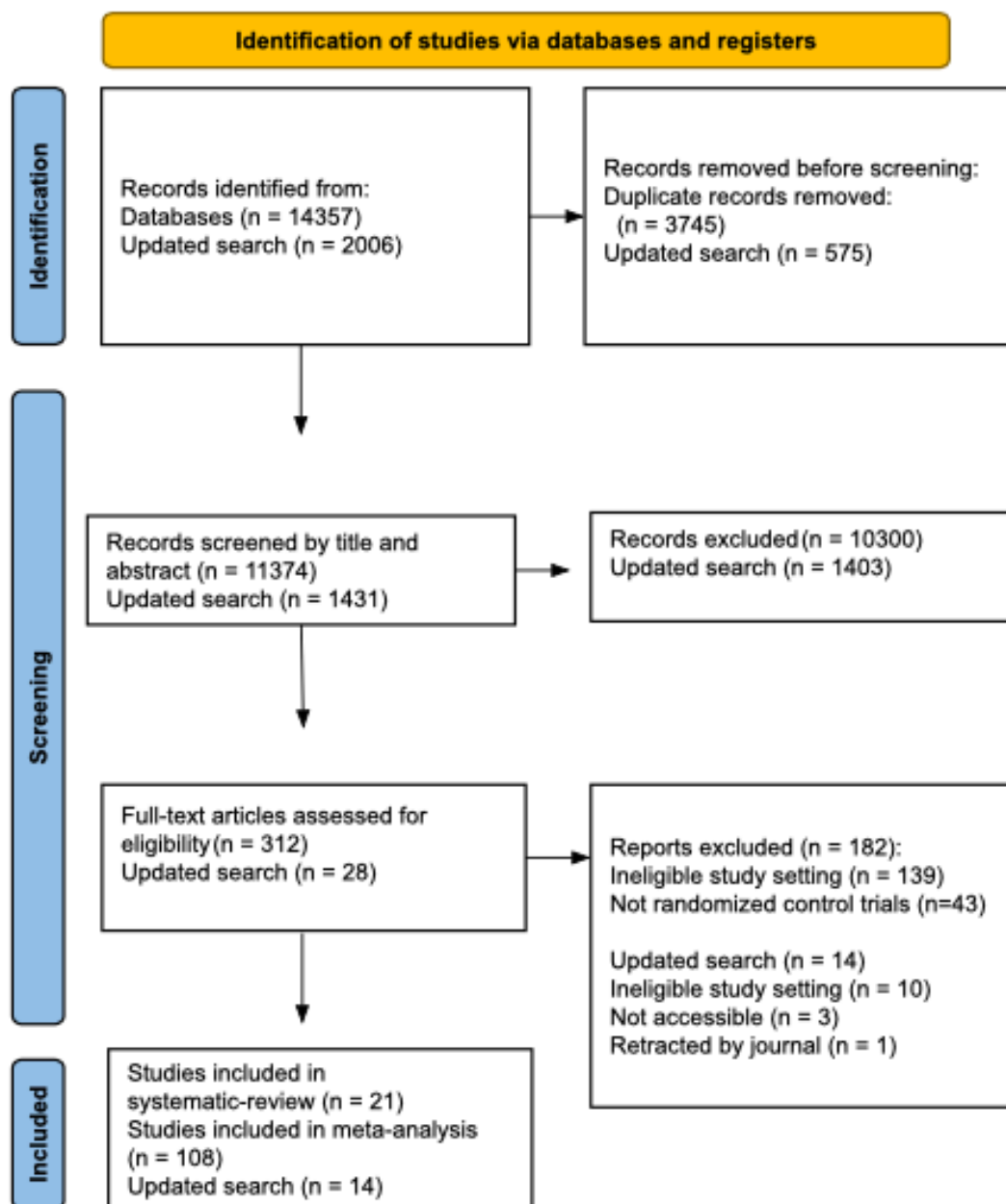


Figure 1. PRISMA 2020 flowchart representing the study selection process for Study I.(31)

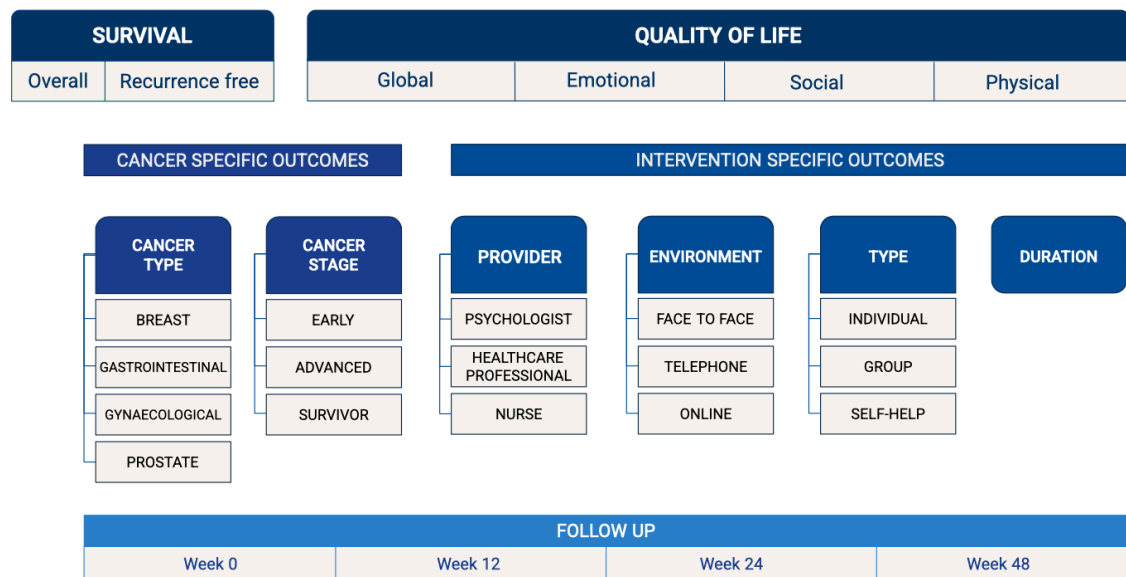


Figure 2. The figure shows the structure of our analysis and the investigated outcomes (survival and quality of life), based on subgroups, and subcategories.(31)

8.1.2. Survival Outcomes

Fourteen studies evaluated OS, representing a total pool of 2,683 patients, while five studies monitored RFS across 900 patients. The meta-analysis demonstrated that overall survival did not differ significantly between patients receiving psychological interventions and those undergoing standard care (HR=0.97; 95% CI=0.87–1.08). Similarly, no significant difference was observed between the groups regarding RFS (HR=0.99; 95% CI=0.84–1.16).as illustrated in Figure 3.

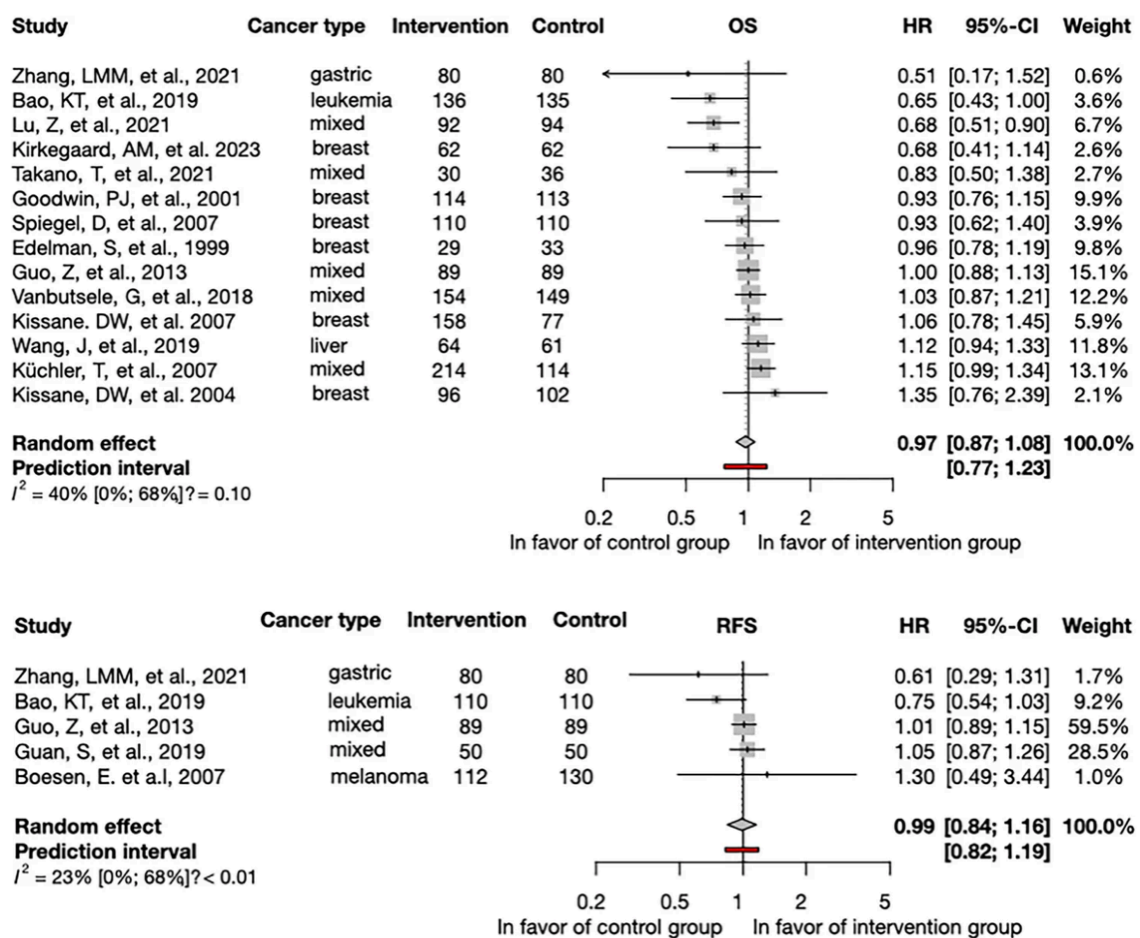


Figure 3. Forest plot of the effects of psychological interventions on overall survival (OS) and recurrence-free survival (RFS). Individual and pooled hazard ratios (HR) and corresponding 95% confidence intervals (CI) are shown across various cancer types.(31)

8.1.3. Quality of Life Outcomes

The longitudinal model-based predictions indicated that psychological interventions showed a significant positive effect across all evaluated QoL domains immediately after the intervention period (T0). Medium effect sizes were detected for the global domain (SMD=0.65; 95% CI=0.35–0.94) and the emotional domain (SMD=0.64; 95% CI=0.33–0.95). Small but statistically significant effect sizes were found for the social domain (SMD=0.32; 95% CI=0.13–0.51) and the physical domain (SMD=0.33; 95% CI=0.05–0.60) (Figure 4).

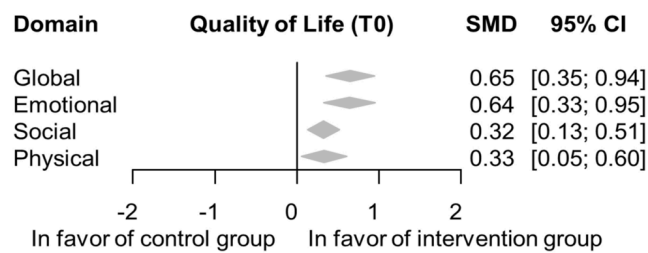


Figure 4. Forest plot of the pooled results shows that psychological interventions significantly improve quality of life in all domains compared to the control group. Standardized mean differences (SMD), confidence intervals (CI).(31)

Subgroup Analysis of Global QoL

Provider: Significant improvements in global QoL were observed across all provider categories, including interventions led by psychologists (SMD=0.46; CI=0.14–0.77; $p=0.006$), non-specified healthcare professionals (SMD=0.77; CI=0.38–1.16; $p=0.0004$), and nurses (SMD=0.74; CI=0.25–1.23; $p=0.005$).

Environment: Delivery format significantly influenced outcomes. While face-to-face sessions (SMD=0.56; CI=0.22–0.91; $p=0.003$) and online delivery (SMD=0.58; CI=0.08–1.07; $p=0.029$) led to significant global QoL gains, telephone-based protocols did not produce a significant change (SMD=0.26; CI=–0.63 to 1.15; $p=0.418$).

Intervention Type: Significant benefits were maintained across individual treatments (SMD=0.68; CI=0.37–0.99; $p<0.001$), group therapies (SMD=0.61; CI=0.27–0.95; $p=0.0009$), and guided self-help regimens (SMD=0.59; CI=0.10–1.08; $p=0.026$).

Cancer-related outcomes: Stratification by cancer stage showed significant global QoL improvements only for patients in the early stages of the disease (SMD=0.66;

CI=0.14–1.17; $p=0.017$). When analysed by malignancy type, a significant positive effect was exclusively detected within the breast cancer population (SMD=0.53; CI=0.18–0.87; $p=0.004$) (Figure 5.)

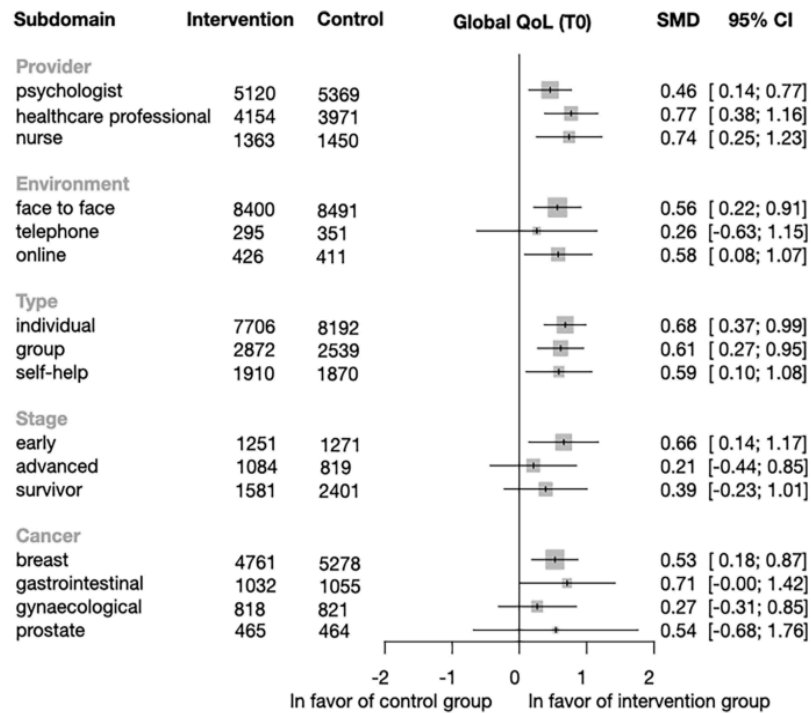


Figure 5. Forest plot showing the results of subgroup analysis of the global QoL by provider, environment, type, and cancer stage. Standardized mean differences (SMD), confidence intervals (CI).(31)

Subgroup Analysis of Emotional QoL

Provider: Emotional well-being improved significantly regardless of who delivered the therapy, showing positive effects for psychologists (SMD=0.61; CI=0.25–0.97; $p=0.0018$), healthcare professionals (SMD=0.69; CI=0.37–1.02; $p=0.0002$), and nurses (SMD=0.86; CI=0.45–1.28; $p=0.0002$).

Environment: All delivery settings showed significant emotional QoL improvements, including face-to-face formats (SMD=0.77; CI=0.35–1.19; $p=0.001$), online programs (SMD=0.94; CI=0.57–1.30; $p=0.0004$), and interventions via telephone / telemedicine (SMD=0.65; CI=0.24–1.06; $p=0.005$).

Intervention Type: Significant effects were seen in individual interventions (SMD=0.60; CI=0.26–0.95; $p=0.001$) and group therapies (SMD=0.73; CI=0.29–1.16; $p=0.0025$).

Guided self-help programs did not lead to a statistically significant difference (SMD=0.68; CI=-0.78 to 2.14; p=0.212).

Cancer-related outcomes: Significant positive changes in emotional QoL were found only in early-stage patients (SMD=1.03; CI=0.24–1.83; p=0.016). By cancer type, significant improvements occurred in breast cancer (SMD=0.77; p=0.0006), gastrointestinal cancer (SMD=1.34; CI=0.54–2.14; p=0.014), and gynecological cancer (SMD=0.62; CI=0.13–1.11; p=0.02). The prostate cancer group did not show a significant change (SMD=0.56; CI=-0.04 to 1.16; p=0.062). (Figure 6.)

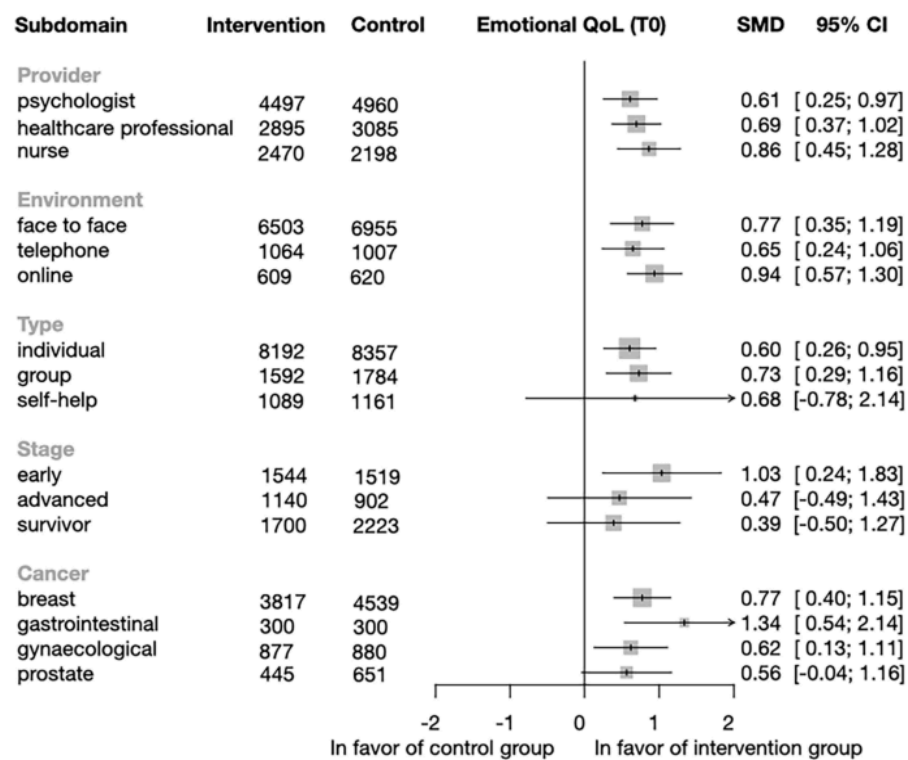


Figure 6. Forest plot showing the results of subgroup analysis of the emotional QoL by provider, environment, type, and cancer stage. Standardized mean differences (SMD), confidence intervals (CI).(31)

Subgroup Analysis of Social QoL

Provider: Social QoL gains achieved statistical significance when delivered by psychologists (SMD=0.32; CI=0.06–0.58; p=0.019) or nurses (SMD=0.43; CI=0.19–0.68; p=0.001). Interventions by other healthcare professionals did not achieve significance (SMD=0.22; CI=-0.04 to 0.48).

Environment and type: Face-to-face sessions represented the only environment that significantly improved social outcomes (SMD=0.32; CI=0.10–0.54; p=0.006). Similarly, individual therapy was the only format type that led to a significant positive change (SMD=0.35; CI=0.15–0.55; p=0.001).

Cancer-related outcomes: Social QoL did not improve significantly when stratified by cancer stage (early, advanced, or survivor). Breast cancer was the only malignancy type to show a significant baseline difference (SMD=0.26; CI=0.04–0.48; p=0.021).

(Figure 7).

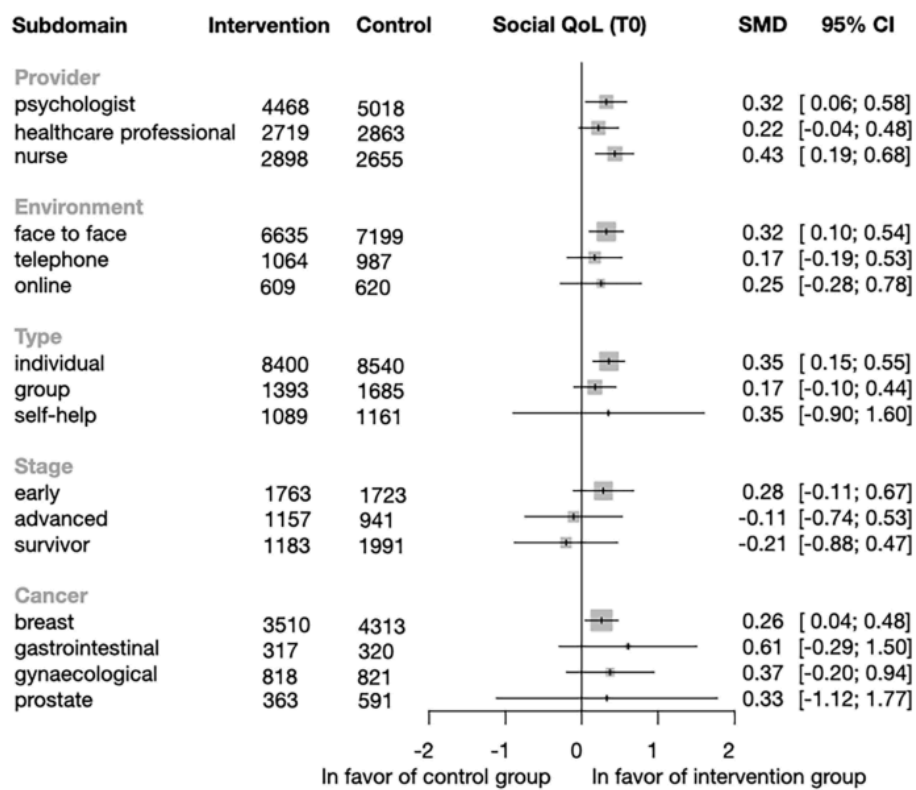


Figure 7. Forest plot showing the results of subgroup analysis of the social QoL by provider, environment, type, and cancer stage. Standardized mean differences (SMD), confidence intervals (CI).(31)

Subgroup Analysis of Physical QoL

Provider: Interventions significantly improved physical QoL scores across all provider roles, including psychologists (SMD=0.66; CI=0.32–0.99; p<0.001), healthcare

professionals (SMD=0.73; CI=0.42–1.04; $p<0.001$), and nurses (SMD=0.58; CI=0.33–0.82; $p<0.001$).

Environment and type: Statistically significant benefits were limited to face-to-face delivery formats (SMD=0.32; CI=0.0019–0.64; $p=0.049$) and individual therapy type settings (SMD=0.31; CI=0.05–0.57; $p=0.022$).

Cancer-related outcomes: Significant positive changes in emotional QoL were found only in early-stage patients (SMD=0.30; CI=0.00–0.60; $p=0.048$). However, significant enhancements were observed in breast cancer (SMD=0.55; CI=0.20–0.89; $p=0.003$) and gynecological cancer cohorts (SMD=0.50; CI=0.03–0.98; $p=0.042$). (Figure 8.)

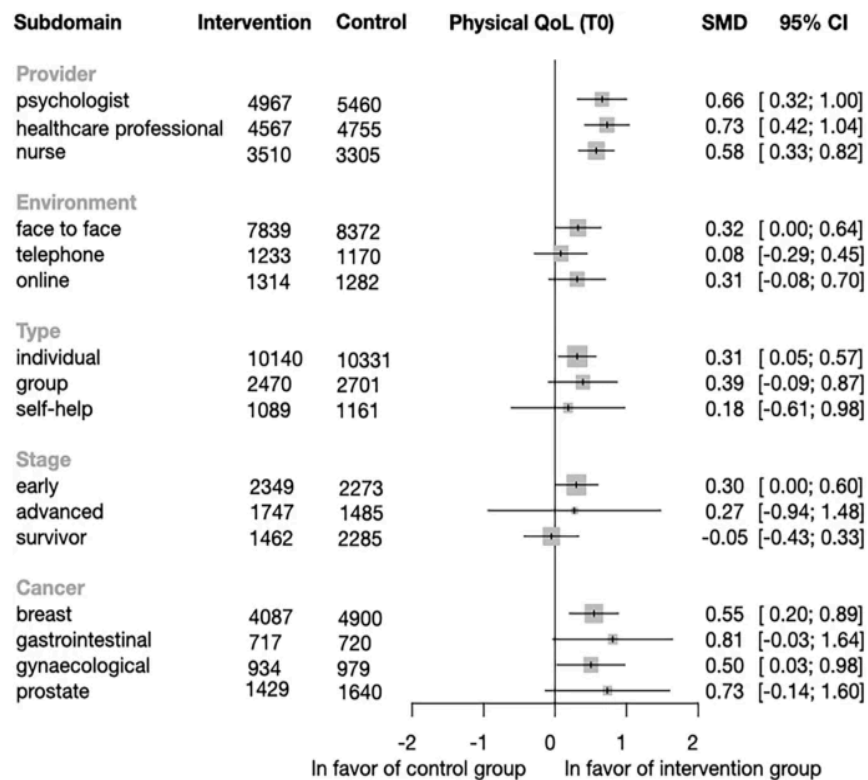


Figure 8. Forest plot showing the results of subgroup analysis of the physical QoL by provider, environment, type, and cancer stage. Standardized mean differences (SMD), confidence intervals (CI).(31)

Impact of the Interventions over Time in the Four Domains of QoL

Immediately after intervention (T0), significant positive effects were observed across all four subdomains of QoL. During the follow-up period, the point estimates consistently

remained in favor of the intervention group. In the Physical domain, this significant benefit was maintained throughout the entire observed follow-up period, up to week 48 (SMD = 0.38, 95% CI [0.09; 0.67]). For the Global, Emotional, and Social domains, the point estimates stayed positive. However, by week 48, the 95% CIs for these three subdomains widened substantially and crossed the zero line, indicating a loss of statistical significance at the final follow-up time. (Figure 9.)

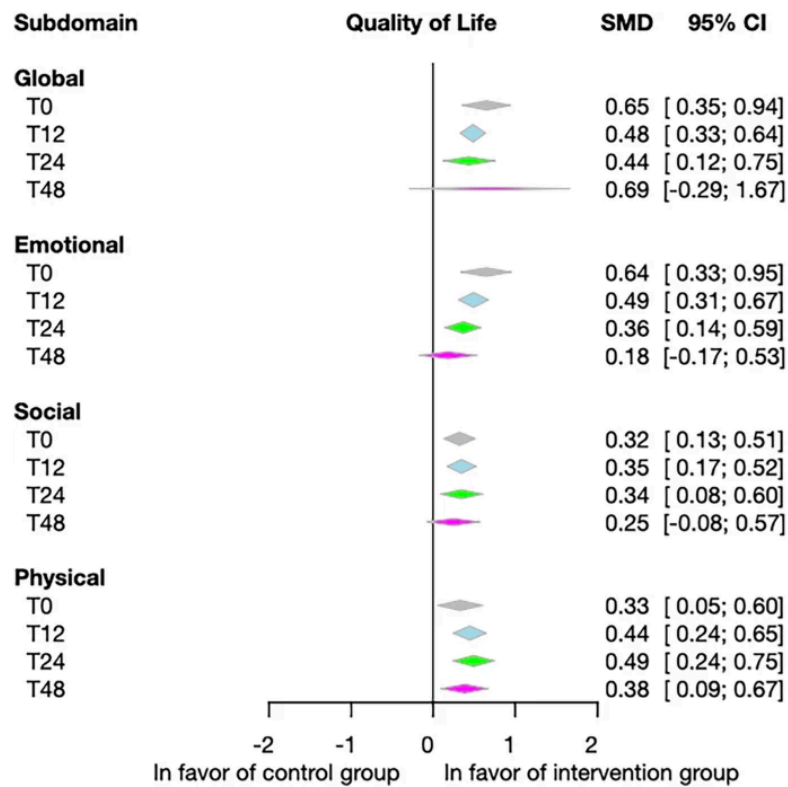


Figure 9. Summary forest plot representing the intervention outcomes at different follow-up times. Timepoints include immediately post-intervention (T0) and at weeks 12 (T12), 24 (T24), and 48 (T48). Standardized mean differences (SMD), confidence intervals (CI).(31)

Duration of Intervention

Finally, the total net duration of the intervention (measured in net minutes per patient) did not significantly modify the effect sizes in any QoL domain. Change per minute was non-significant for global (SMD=0.06; CI=-0.01 to 0.12; p=0.05), emotional

(SMD=0.80; CI=-0.28 to 1.33; p=0.006), social (SMD=0.29; CI=-0.10 to 0.64; p=0.146), and physical domains (SMD=0.23; CI=-0.09 to 0.56; p=0.159).

Qualitative Analysis

A total of thirteen studies(32-40) evaluated global QoL, with nine of them showing better outcomes in the PI group than in the control group. For emotional QoL, five out of seven studies(32-34, 41, 42) noted clear improvements following the PI. Regarding physical QoL, two out of three studies(39, 40) reported higher scores in physical domains for the PI group. For social QoL, three out of five studies(32, 34, 41) found superior scores among individuals receiving the PI compared to controls. These specific studies were excluded from the meta-analysis due to missing data.

8.1.4. Risk of Bias Assessment

Regarding both survival outcomes and QoL, the majority of the analyzed papers were classified as having "some concerns" for overall bias, which was primarily driven by limitations within the randomization process. The detailed results of the risk of bias assessment are presented in the original publications.(31)

8.1.5. Quality of Evidence

Regarding the survival data, potential publication bias from smaller trials was observed for the OS; however, the influence of these small studies did not alter the primary conclusions to any meaningful degree. For the RFS, a definitive evaluation of publication bias among small studies was restricted due to the very limited number of available papers. Further information can be found in the original publications.(43) Statistical heterogeneity was quantified as moderate for OS ($I^2=40\%$, [0%,68%]) and low for RFS ($I^2=23\%$, [0%,68%]).

For the QoL outcomes, visual inspections of the funnel plots could not completely rule out the presence of potential publication bias. However, rather than pointing to a systemic reporting bias across the literature, the distribution suggests the presence of a few outlier publications. Further information can be found in the original publications.(31)

8.2. Study II: - One out of Four Patients with Pancreatic Cancer Experience Psychological Symptoms: a Systematic Review and Meta-analysis

8.2.1. Study Search and Selection

After removing duplicates, we screened titles and abstracts, which left 313 papers for a detailed eligibility check. During the full-text selection phase, we excluded 194 articles. Ultimately, we included 28 papers in the meta-analysis and 31 papers in the systematic review section. The complete selection process is shown in the PRISMA flowchart Figure 10. The baseline characteristics of the included studies are detailed in Table 1.

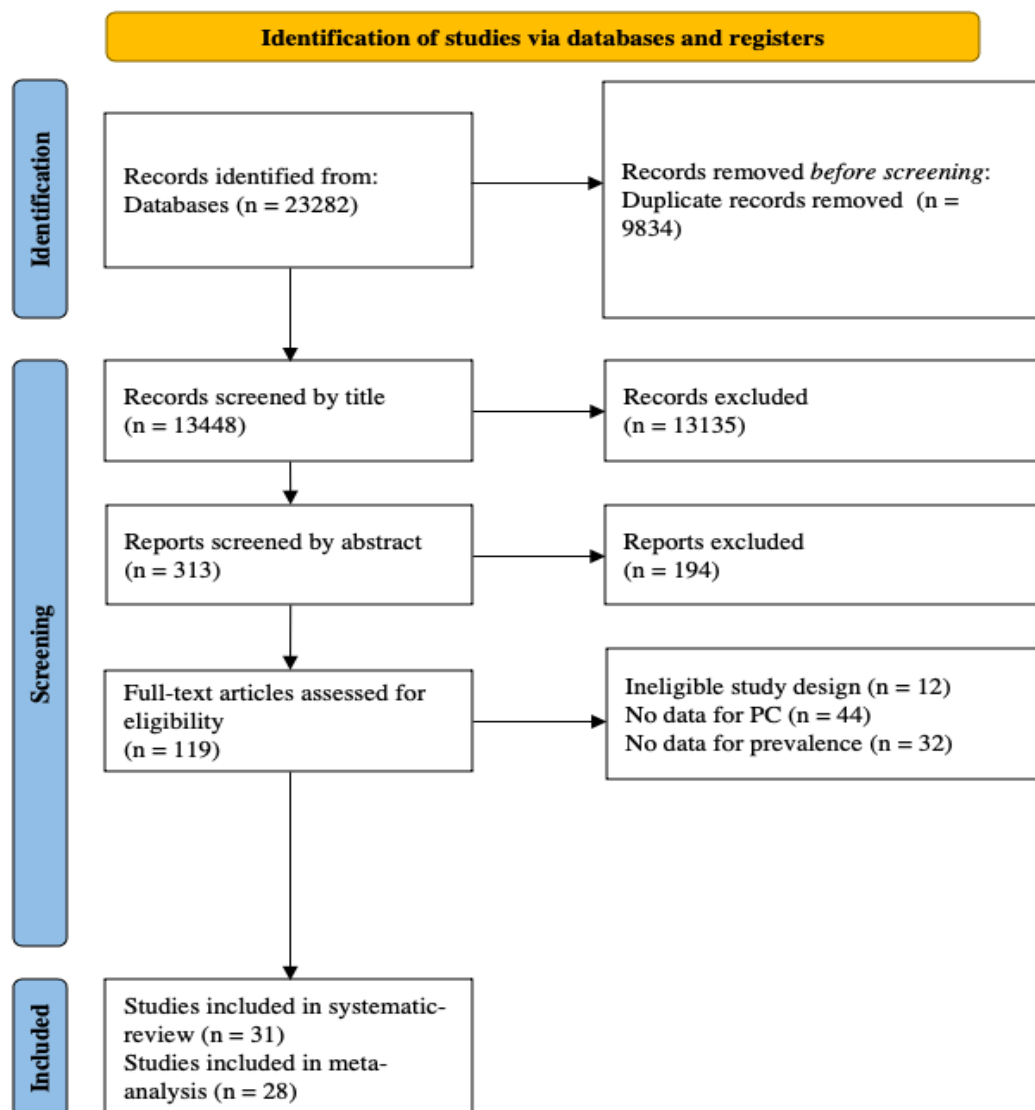


Figure 10. PRISMA 2020 flowchart representing the study selection process for Study II.(43)

First Author	Year of publication	Country	Mean (Age)	SD (Age)	Sex(% female)	Population size	Outcome	Measurement tool	Time group
Akizuki, et al.(44)	2016	Japan	61.7	9.8	38.2	110	depression anxiety	DSM-III-R (SCID)	short
Batra, et al.(45)	2021	Canada	NA	NA	47.8	94	depression anxiety	ESASr	long
Boyd, et al.(46)	2012	USA	65.0	NA	45.5	22	depression anxiety	PHQ9 PSWQ	long
Brintzenhofe, et al.(47)	2009	USA	NA	NA	NA	185	depression anxiety	BDI HADS	NA
Carlson, et al.(48)	2004	USA	NA	NA	NA	112	distress	BSI-18	short
Carlson, et al.(49)	2019	USA	NA	NA	NA	148	distress	NCCN DT	short
Carruba, et al.(50)	2022	Italy	NA	NA	NA	11	depression anxiety	HADS	NA
Clark, et al.(51)	2010	USA	60.4	10.8	45.1	304	depression anxiety distress fatigue	BSI-18 Problem Checklist	short
Cui, et al.(52)	2023	China	63.36	9.94	45.0	114 134	anxiety fatigue	EQ-5D VAS	NA

First Author	Year of publication	Country	Mean (Age)	SD (Age)	Sex(%) female	Population size	Outcome	Measurement tool	Time group
Dai, et al.(53)	2019	Canada	65.0	10.0	45.0	2043	distress	ESAS	short
Del Piccolo, et al.(54)	2021	Italy	NA	NA	NA	400	depression anxiety	PHQ-9 STAI	short
Fras, et al.(55)	1967	USA	NA	NA	NA	50 35	depression fatigue Anxiety	MMPI	short
Godby, et al.(56)	2020	USA	70.0	7.2	43.7	88	depression	PROMIS®	short
Harris, et al.(57)	2021	USA	NA	NA	NA	10378	depression anxiety	NA	long
Hartung, et al.(58)	2017	Germany	NA	NA	NA	82	depression	PHQ-9	short
Hohmann, et al.(59)	2022	Germany	NA	NA	64,0	11	distress	HSI	NA
Janda, et al.(60)	2017	Australia	66.6	9.6	48.0	136	depression anxiety	FACT_G HADS	long
Kim, et al.(61)	2023	Canada	NA	NA	38.0	36	depression	PHQ-9	short
Lelond, et al.(62)	2021	Canada	NA	NA	47.2	123	fatigue anxiety	NA	short

First Author	Year of publication	Country	Mean (Age)	SD (Age)	Sex(%) female	Population size	Outcome	Measurement tool	Time group
Mehnert, et al.(63)	2014	Germany	57.6	11.1	51.5	52	anxiety	CIDI	short
Pezzili, et al.(64)	2017	Italy	70.1	11.5	63.6	22	depression	BDI	short
Salm, et al.(65)	2021	Germany	NA	NA	NA	80	depression anxiety	Database	NA
Schmidt, et al.(66)	2020	Germany	NA	NA	NA	33	fatigue	EORTC QLQ-FA12	NA
Seoud, et al.(67)	2020	USA	NA	NA	NA	10 220 62450 10 220	fatigue depression anxiety	ICD	long
Subramaniam, et al.(68)	2024	USA	68	12.3	49.9	4029	depression anxiety	From database	short
Vehling, et al.(69)	2022	Germany	58.6	10.98	49.5	50	depression anxiety	CIDI	long
Yeo, et al.(70)	2023	USA	69.4	34.9	46	403	depression distress fatigue	DT	NA
Zhang, et al.(71)	2022	China	NA	NA	46	100	anxiety	SAS	NA

Table 1. *Basic characteristics of the included studies in the meta-analysis. BDI-Beck Depression Inventory; BSI-Brief Symptom Inventory; CIDI-Composite International Diagnostic Interview; DT- Distress Thermometer EORTC QLQ-FA12 -European Organization for Research and Treatment of Cancer Fatigue; ESAS-Edmonton Symptom Assessment System; ESASr-Edmonton Symptom Assessment System Revised; EQ-5D VAS- EuroQol-5D- visual analogue scale; FACIT-G-Functional Assessment of Cancer Therapy - General; HADS-Hospital Anxiety and Depression Scale; HIS-Hornheider Screening Instrument; ICD-International Classification of Diseases; MMPI-Minnesota Multiphasic Personality Inventory; NCCN (DT)-National Comprehensive Cancer Network's Distress Thermometer; PHQ-9-Personal Health Questionnaire; PO-Bado-Basic Documentation for Psycho-Oncology; PROMIS®-Patient-Reported Outcomes Measurement Information System; PSWQ-Penn State Worry Questionnaire; SAS-Self-rating Anxiety Scale; SCID-DSM-III-R-Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders; STAI-State Trait Anxiety Inventory. Time group: 'short'-within six months from the diagnosis of cancer; 'long'-beyond six months from the cancer diagnosis. NA-not applicable*

8.2.2. Outcomes

Prevalence of Depression

For the depression analysis, 19 studies were included with a total sample size of 78,930 patients. The pooled proportion for this symptom was 27% (95% CI: 0.18–0.39), with a very high heterogeneity ($I^2=98.2\%$, [97.8%–98.5%]). (Figure 11.)

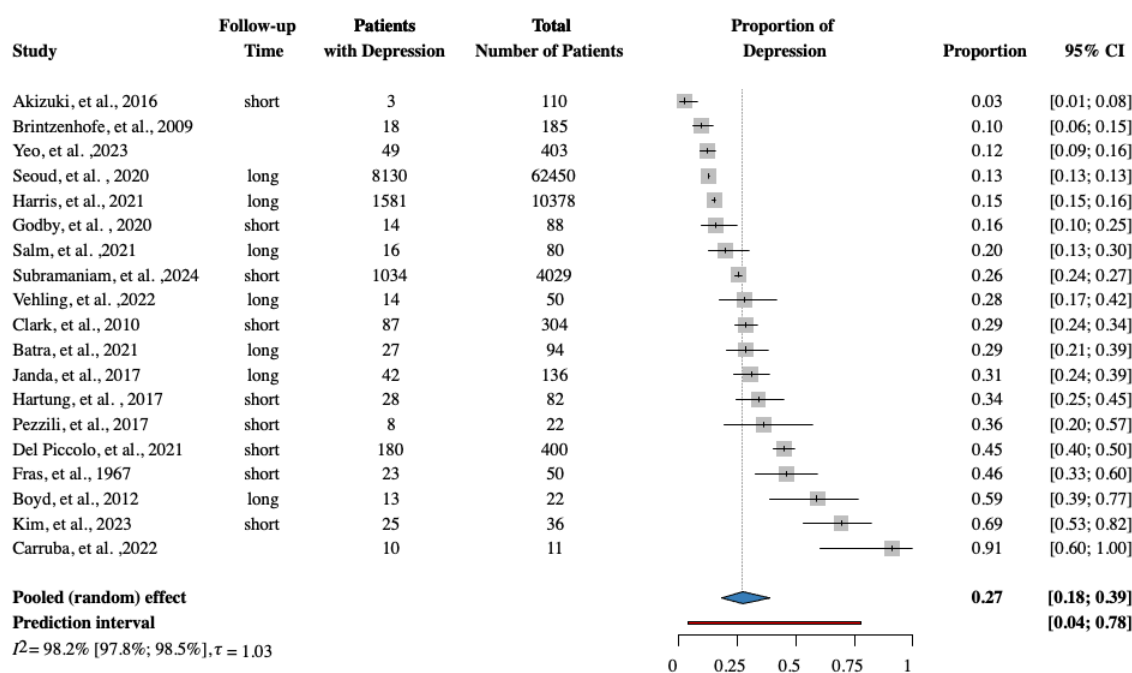


Figure 11. The forest plot shows the prevalence of depression following a pancreatic cancer diagnosis ‘Short’-within six months of cancer diagnosis; ‘long’-beyond six months from cancer diagnosis. Confidence intervals (CI).(43)

Based on the available data from the original articles, the severity subset analysis showed the following proportions: the prevalence of mild depression was 0.26 (95% CI: 0.16–0.38); moderate depression was 0.28 (95% CI: 0.11–0.55); and severe depression was the lowest, at 0.16 (95% CI: 0.11–0.22). (Figure 12.)

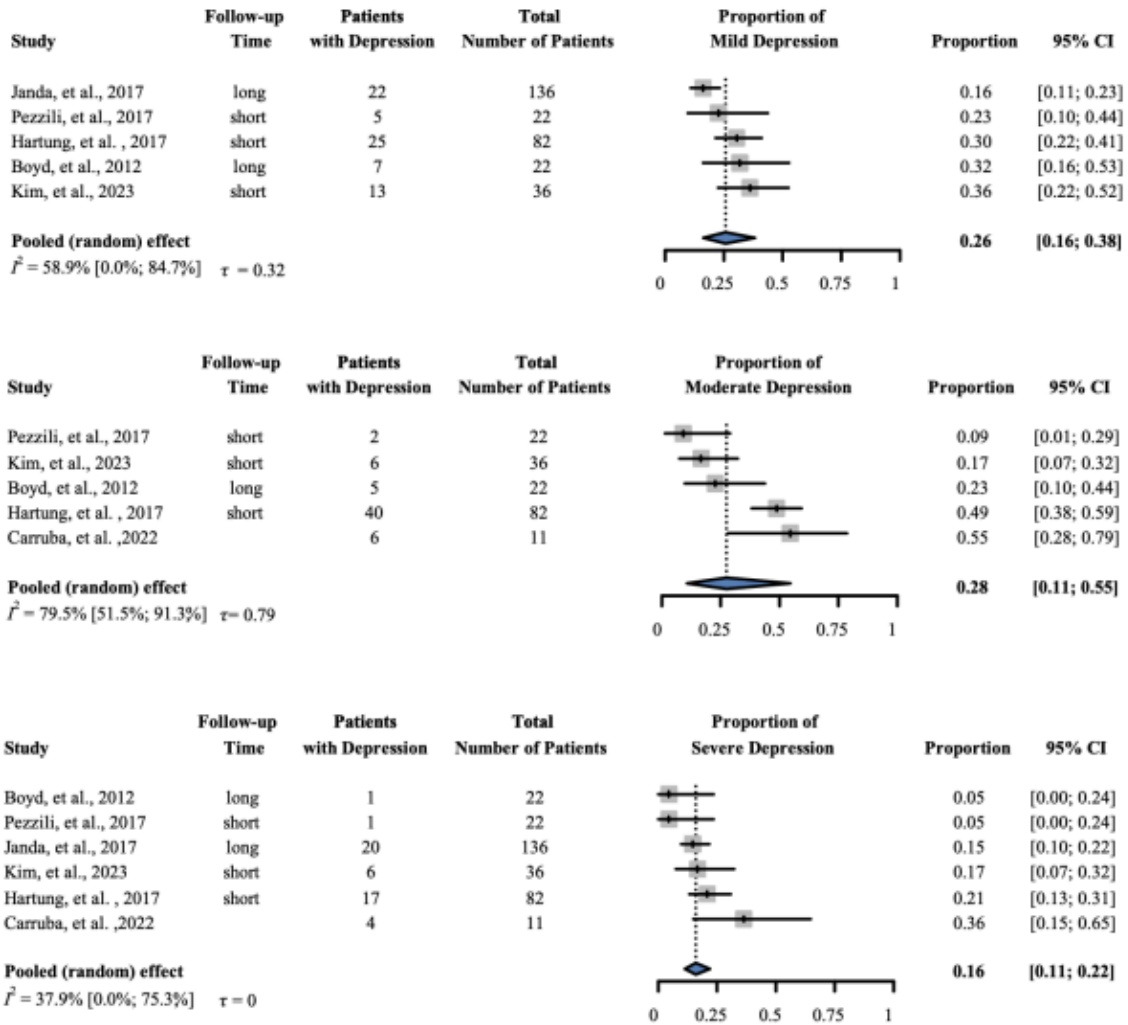


Figure 12. The forest plot shows the prevalence of depression in a subgroup analysis based on severity (mild, moderate, severe) following a pancreatic cancer diagnosis. ‘Short’-within six months of cancer diagnosis; ‘long’-beyond six months from cancer diagnosis. Confidence intervals (CI).(43)

Prevalence of Anxiety

For the anxiety analysis, 18 studies were included with a total sample size of 26,538 patients. The pooled proportion of patients experiencing symptoms was 0.29 (95% CI: 0.16–0.46), with a very high heterogeneity $I^2 = 99.4\%$ [99.4%-99.5%]. (Figure 13.)

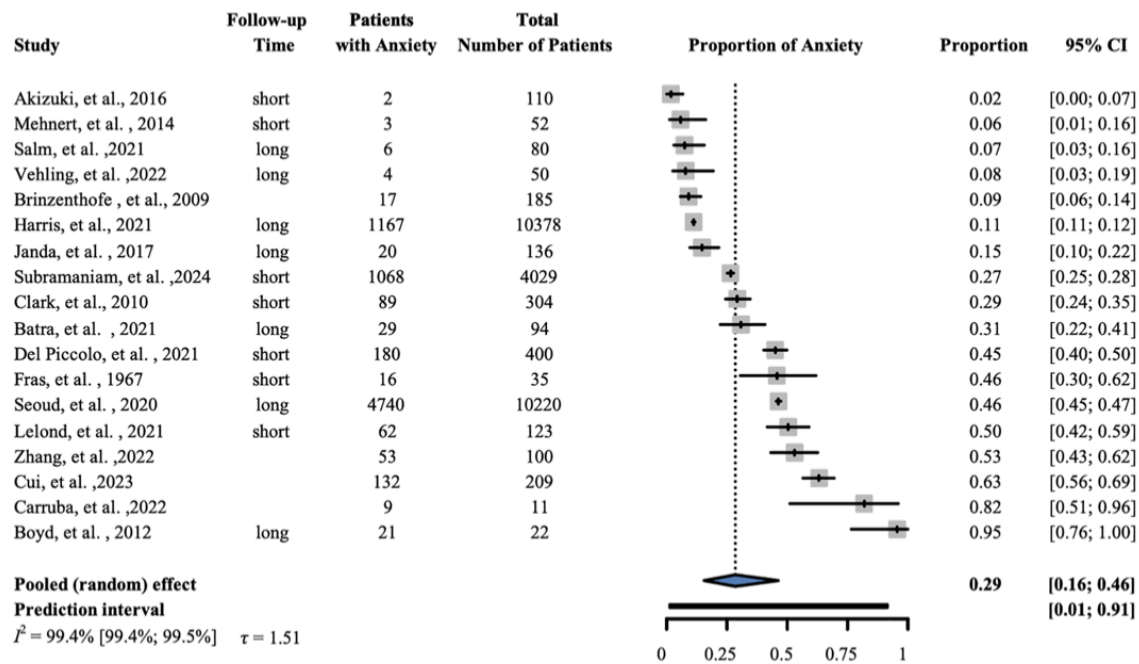


Figure 13. The forest plot shows the prevalence of anxiety following a diagnosis of pancreatic cancer. 'Short'-within six months of cancer diagnosis; 'long'-beyond six months from cancer diagnosis. Confidence intervals (CI).(43)

Prevalence of Distress

Data of 2,746 patients from six studies were analyzed for distress. Our results showed that the proportion of distress was 0.43 (95% CI: 0.25-0.63); $I^2 = 96.6\%$ [94.5%-97.8%]. (Figure 14.)

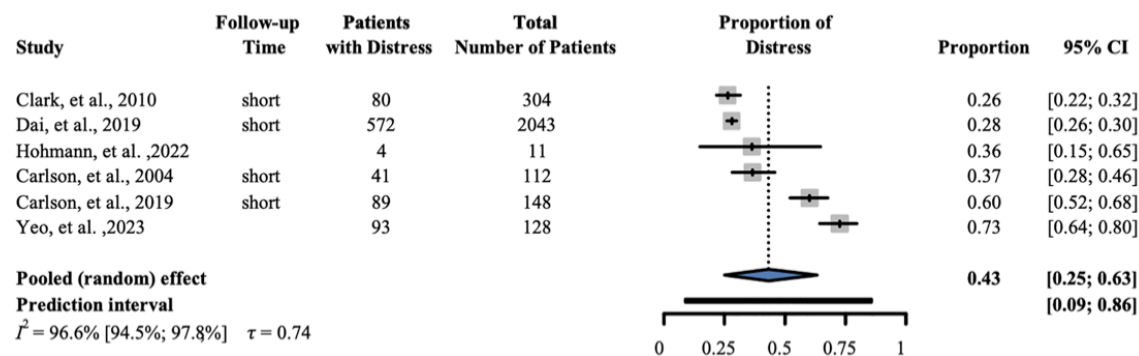


Figure 14. The forest plot shows the prevalence of distress following a diagnosis of pancreatic cancer. 'Short'-within six months of cancer diagnosis; 'long'-beyond six months from cancer diagnosis. Confidence intervals (CI).(43)

Prevalence of Fatigue

For the fatigue analysis, 7 studies were involved with a total sample size of 11,338 patients. The results showed that the pooled proportion was 0.40 (95% CI: 0.21–0.63), with a very high heterogeneity ($I^2 = 97.3\%$, [95.9%–98.2%]). (Figure 15.)

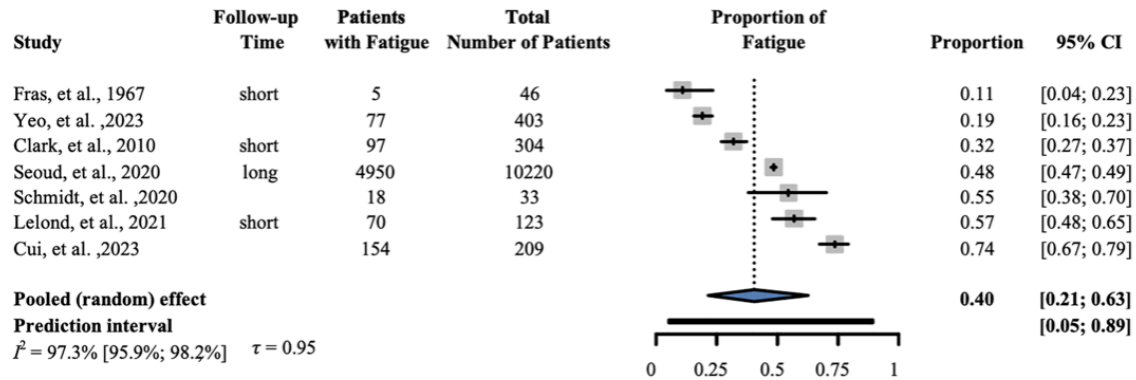


Figure 15. The forest plot shows the prevalence of fatigue following a diagnosis of pancreatic cancer. ‘Short’-within six months of cancer diagnosis; ‘long’-beyond six months from cancer diagnosis. Confidence intervals (CI).(43)

Prevalence of Sleep disturbances

For the sleep disturbances analysis, 3 studies were involved with a total sample size of 10,645 patients. The results showed that the pooled proportion was 0.31 (95% CI: 0.06–0.77), with a very high heterogeneity ($I^2 = 98.1\%$, [96.5%–99.0%]). (Figure 16.)

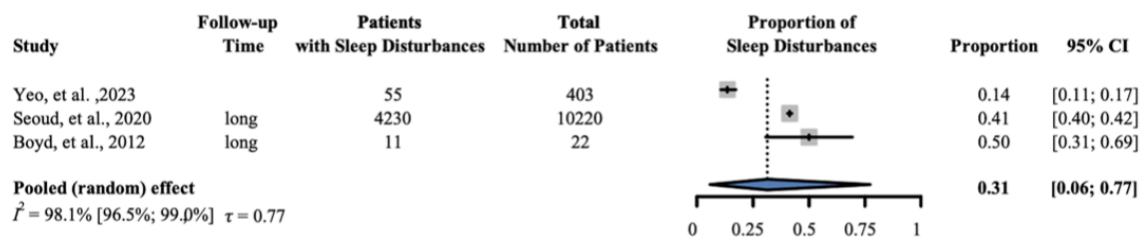


Figure 16. The forest plot shows the prevalence of sleep disturbances following a diagnosis of pancreatic cancer. ‘Short’-within six months of cancer diagnosis; ‘long’-beyond six months from cancer diagnosis. Confidence intervals (CI).(43)

8.2.3. *Risk of Bias Assessment*

According to the JBI tool, 75.0% (n = 21) of the 28 included studies were rated as low risk of bias, 21.4% (n = 6) as moderate risk, and 3.6% (n = 1) as high risk. The detailed scores and specific appraisal outcomes for each study are provided in Table 2.

JBI Checklist No.	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score	Weight
First Author											
Akizuki, et al. 2016	Y	Y	N	Y	Y	Y	Y	Y	Y	8	88.8
Batra, et al. 2021	N	Y	N	N	Y	Y	Y	N	Y	5	55.5
Boyd et al. 2012	N	Y	N	Y	Y	Y	Y	Y	Y	7	77.7

JBIChecklist No. ----- ----- --	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score	Weight
First Author											
Brintzenhofe, et al. 2009	Y	Y	Y	Y	U	Y	Y	Y	Y	8	88.8
Carlson, et al. 2004	Y	Y	Y	Y	Y	Y	Y	N	Y	8	88.8
Carruba, et al. 2022	Y	U	Y	Y	Y	Y	Y	Y	Y	8	88.8
Carlson,	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	100

JBIChecklist No. ----- --	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score	Weight
First Author											
et al. 2019											
Clark, et al. 2010	Y	Y	N	Y	Y	Y	Y	Y	Y	8	88.8
Cui, et al. 2023	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	100
Dai, et al. 2019	N	Y	Y	Y	Y	Y	Y	Y	Y	8	88.8
Del	N	Y	N	Y	N	Y	Y	Y	Y	6	66.6

JBIChecklist No. ----- --	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score	Weight
First Author											
Piccolo, et al. 2021											
Dengso, et al. 2020	Y	Y	Y	Y	Y	U	U	Y	Y	7	77.2
Fras, et al. 1967	Y	N	N	N	N	Y	Y	Y	Y	2	22.2
Godby, et al. 2020	Y	Y	Y	Y	N	Y	Y	Y	Y	8	88.8

JBIChecklist No. ----- --	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score	Weight
First Author											
Harris, et al. 2021	Y	Y	Y	Y	Y	U	U	Y	Y	7	77.7
Hartung, et al. 2017	Y	Y	N	Y	Y	Y	Y	Y	Y	8	88.8
Hohmann, et al. 2022	Y	Y	N	Y	Y	Y	Y	Y	Y	8	88.8
Janda, et al. 2017	Y	Y	N	Y	Y	Y	Y	Y	Y	8	88.8

JBIChecklist No. ----- ----- --	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score	Weight
First Author											
Kim, et al. 2023	Y	Y	N	Y	Y	Y	Y	Y	Y	8	88.8
Lelond, et al. 2021	Y	Y	N	Y	N	Y	Y	U	Y	6	66.6
Mehnert, et al. 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	100
Pezzili, et al. 2017	N	Y	N	Y	N	Y	Y	Y	Y	6	66.6

JBIChecklist No. ----- ----- --	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score	Weight
First Author											
Salm, et al. 2021	Y	Y	Y	N	Y	Y	Y	Y	Y	8	88.8
Schmidt, et al. 2020	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	100
Seoud, et al. 2020	Y	Y	Y	Y	Y	Y	U	Y	Y	8	88.8
Subramaniam, et al.	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	100

JBIChecklist No. ----- --	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Score	Weight
First Author											
2024											
Vehling, et al. 2022	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	100
Yeo, et al. 2023	Y	Y	Y	Y	Y	Y	Y	Y	Y	9	100
Zhang, et al. 2022	Y	Y	Y	Y	Y	U	Y	Y	Y	7	88,8

Table 2. *The Joanna Briggs Assessment of the methodological quality. N-no; Y=yes, U-unclear. The JBI appraisal checklist consists of 9 items and each item is assessed by scoring (yes = 1), (no = 0), and (unclear = 0). Weight: high risk of bias = 20–50% items scored yes; moderate risk of bias = 50–80% items scored yes; and low risk of bias = 80–100% items scored yes.*

8.2.4. Publication bias and Heterogeneity

Regarding publication bias, funnel plot analyses accompanied by p-values were provided exclusively for depression and anxiety, as a funnel plot assessment was not performed when the number of studies fell below ten. For depression, Egger's test resulted in a p-value of 0.0413, indicating potential publication bias. Conversely, the Egger's test p-value for anxiety was 0.7877, indicating no potential publication bias. To assess heterogeneity and stability, a leave-one-out analysis was conducted, which revealed that potentially influential studies had no relevant impact on the final pooled result. Further information can be found in the original publications.(43)

9. DISCUSSION

9.1. Summary of Findings, International Comparisons (including all studies)

The main objective of this doctoral thesis was to map the psychological dimensions of oncological care from two distinct but connected perspectives: first, by analyzing how targeted psychological interventions affect survival and QoL in cancer patients, and second, by quantifying the exact prevalence of psychological symptoms in a special and under-studied patient population, those with PC.

Our first analysis demonstrated that while psychological interventions do not prolong overall survival (HR=0.97; 95% CI=0.87–1.08) or recurrence-free survival (RFS: HR=0.99; 95% CI = 0.84–1.16), they provide significant improvements across all measured QoL domains immediately after the intervention (T0). Compared to control groups, individuals in the experimental groups achieved better global (SMD=0.65), emotional (SMD=0.64), social (SMD=0.32), and physical (SMD=0.33) QoL.

These findings are crucial because the long-term psychological difficulties in cancer care are broad, spanning from anxiety and helplessness to physical fatigue and cognitive impairments.(72) These challenges are even more common in advanced stages(73), making QoL an even more important focus in oncological care.(15) Research by Firkins et al.(74) underscores that QoL can remain compromised for anywhere from 2 to 26 years following a diagnosis, which highlights the essential need for continuous long-term psychological support.

When evaluating who provides the care, where it happens, and how it is delivered, our subgroup analyses revealed that the therapeutic relationship itself matters. Global and emotional QoL improved significantly regardless of whether the intervention was led by a psychologist (SMD=0.66), a healthcare professional (SMD=0.99), or a nurse (SMD=0.93). Thorough research design and training heavily boost provider confidence, making the provider's specific profession or personality less crucial.(75) The lower score for psychologists may reflect the persistent social stigma and anxiety associated with psychologist; individuals often feel defensive or threatened when referred to a psychologist, whereas they more readily accept coping support from nurses and familiar healthcare staff as a routine, non-threatening part of their medical care.(76, 77) It is worth noting also that most of the included studies utilized non-psychotherapy

approaches, though the core clinical guidance of a licensed psychologist remains essential to ease the burden on both individuals and the healthcare team.

In terms of the setting, face-to-face sessions were the most effective, showing that personal interaction is a key factor. Online formats were only effective for global and emotional domains. While online platforms offer a valid alternative for individuals too ill to travel, literature reviews show they cannot fully match the consistent quality of face-to-face therapy(78). More research is needed to make online options more effective for less mobile individuals.

Looking at the format, individual therapies brought improvements across all domains, proving especially valuable in physical and social areas. Group-based therapies were effective only for global and emotional areas. People often prefer individual sessions due to specific worries(79); seeing fellow participants in worse conditions can be frightening, and mixed groups make it hard to tailor care. Guided self-help showed success only in the global domain, but data was too limited to draw firm conclusions.

Surprisingly, the total duration of the intervention (net minutes per person) did not significantly alter QoL outcomes. This matches previous findings that session count and length do not necessarily drive therapeutic gains.(80) This is a valuable finding for funding and planning, suggesting we could create short, intensive programs a few times a year to offer cost-effective and time-saving care.

Regarding disease stage, the point estimates were higher for early-stage individuals. Some researchers suggest that psychological support mostly helps in early-stage cancer, as the rapid natural progression of advanced disease might overshadow the impact of psychological factors.(16) Our results support this idea, suggesting that support is most effective when started early rather than in the late palliative phase.

Psychological interventions alone cannot alter hard biological endpoints in advanced stages. In the late phase, individuals face entirely different psychological challenges, where the focus shifts toward processing grief and preparing for the end of life. While early-stage individuals saw higher improvements, we found no impact on survival-phase groups. These individuals may experience post-traumatic growth, which these interventions might not deeply affect. Research shows that the positive changes from surviving cancer can last up to four years before scores begin to drop.(81) Even with limited data, monitoring needs through all stages should be a standard practice.

Regarding cancer types, individuals with breast cancer benefited the most from psychological interventions, while the prostate cancer group saw no improvement. This raises the question of whether gender influences the decision to seek help. Literature confirms that gender predicts attitudes toward seeking professional care, though culture and education play major roles as well.(82, 83) Figure 17. shows the sum of the subgroup analysis of QoL domains.

SUBGROUP QoL DOMAIN	PROVIDER	ENVIRONMENT	TYPE	CANCER STAGE	CANCER TYPE	DURATION
GLOBAL	Psychologist*	Face to face*	Individual*	Early*	Breast*	Not significant
	Nurse*	Online*	Group*	Advanced	Gastrointestinal	
	Healthcare professional*	Telephone	Self-help*	Survivor	Gynaecological Prostate	
EMOTIONAL	Psychologist*	Face to face*	Individual*	Early*	Breast*	Not significant
	Nurse*	Online*	Group*	Advanced	Gastrointestinal*	
	Healthcare professional*	Telephone*	Self-help	Survivor	Gynaecological* Prostate	
SOCIAL	Psychologist*	Face to face*	Individual*	Early	Breast*	Not significant
	Nurse*	Online	Group	Advanced	Gastrointestinal	
	Healthcare professional	Telephone	Self-help	Survivor	Gynaecological Prostate	
PHYSICAL	Psychologist*	Face to face*	Individual*	Early*	Breast*	Not significant
	Nurse*	Online	Group	Advanced	Gastrointestinal	
	Healthcare professional*	Telephone	Self-help	Survivor	Gynaecological* Prostate	

Figure 17. The figure shows the cumulative findings of subgroup analysis of all measured QoL domains. We indicated the significant differences between the intervention and the control groups in **bold ***.

Our second analysis focused specifically on PC, a disease where individuals face a remarkably poor prognosis and rapid physical decline, making psychological endpoints even more critical.(46, 62) Our findings showed that more than a quarter of this population suffers from severe psychological symptoms: 27% experience depression, 29% anxiety, 43% distress, 40% fatigue, and 31% sleep disturbances. In the wider international context, mood disturbances routinely affect 30% to 50% of these individuals.(84)

Our subgroup analysis regarding depression severity showed lower prevalence in the severe group, which most likely reflects rapid physical deterioration; these individuals often require heavy sedation or medication in intensive care units, making standard psychological testing impossible. Anxiety is also common even before surgical interventions or preoperative counseling.(51, 84, 85) When compared to adults facing other malignancies, individuals with PC consistently report higher levels of anxiety, depression, and a significantly lower psychological QoL.(86)

Furthermore, sleep issues and fatigue are pervasive. Treatments for PC often cause a severe loss of skeletal muscle mass, which directly worsens both physical fatigue and psychological distress.(87) International data confirms that fatigue, anxiety, and depression are deeply interconnected.(88, 89)

We also observed that the time since diagnosis (short-term vs. long-term) did not relevantly alter the prevalence of these symptoms. This means that these psychological burdens persist throughout the entire disease course, leaving a wide and necessary window for therapeutic intervention.

9.2. Strengths (including all studies)

A major strength of this doctoral thesis is its objectivity, which we achieved by using rigorous meta-analytical methods. For the intervention analysis, we were able to provide the highest level of clinical evidence by including only randomized controlled trials with a high number of pooled patients. To our knowledge, this work represents the most comprehensive meta-analysis to evaluate the effectiveness of psychological interventions across specific subgroups, including provider, environment, therapy type, and cancer stage. Furthermore, our work on PC is the first to combine multiple psychological constructs (depression, anxiety, distress, fatigue, and sleep disturbances) within a single study to provide a detailed synthesis of prevalence data in this population.

9.3. Limitations (including all studies)

However, several limitations must be considered when interpreting our findings. The most important issue, especially in the PC analysis, is the very high heterogeneity

among the included studies, with I^2 values consistently exceeding 90% in the prevalence estimations. This heterogeneity stems from variations in study designs, clinical settings, patient populations, cultural contexts and the definition of psychological constructs. Another major driver of heterogeneity is the variation in measurement tools. The included studies used different questionnaires, self-report scales, and clinician-administered instruments with varying severity thresholds, making direct comparisons more challenging.

Finally, the small number of studies for specific symptoms in PC study require caution. Due to these small sample sizes, we could only provide funnel plots for depression and anxiety, limiting our ability to evaluate publication bias for the other outcomes.

10. CONCLUSIONS

The systematic analyses presented in this doctoral thesis showed several definitive conclusions regarding the psychological dimensions of oncological care. First, while adjunctive psychological interventions do not significantly prolong overall survival or recurrence-free survival times in cancer patients, they demonstrate high efficacy in enhancing patient well-being. These interventions lead to significant and immediate post-intervention improvements across all primary domains of QoL, including global, emotional, physical, and social functioning.

Second, the therapeutic benefits of psycho-oncological care are heavily dependent on the clinical context and timing of delivery. Subgroup analyses indicate that psychological interventions achieve the best effect when applied during the early stages of cancer rather than in the advanced or survival phases. Furthermore, the therapeutic relationship itself appears to be the primary driver of change, as significant improvements in global and emotional QoL occur regardless of whether the treatment is delivered by a psychologist, a nurse, or another healthcare professional.

Third, the format of delivery significantly influences treatment outcomes. Personal interactions remain critical, with face-to-face and structured online individual therapies demonstrating superior efficacy in improving physical and social QoL compared to telephone-delivered interventions or group sessions. Ultimately, while the baseline improvements in QoL are substantial, these effects decrease over time and generally disappear by week 48. This decline underscores the conclusion that short, intensive psychological interventions should be standardized and repeated periodically throughout the disease course to successfully maintain their beneficial effects on patient QoL. Finally, our findings demonstrate that psychological symptoms represent a profound and highly prevalent burden in oncological populations, affecting more than a quarter of all patients diagnosed with PC. Therefore, providing psychological care from the initial diagnosis is crucial.

11. IMPLICATIONS FOR PRACTICE

Implementing scientific results in everyday clinical practice is very important and can improve the quality of healthcare.(90, 91) The established nationwide infrastructure of the Hungarian Pancreatic Study Group(92), including prospective multicenter initiatives(93) and evidence-based clinical management pathways(94), may offer a unique opportunity to incorporate routine psycho-oncological screening into pancreatic cancer care. Such integration could facilitate earlier identification and management of psychological symptoms in this highly vulnerable patient population. The high prevalence of depression, anxiety, distress, fatigue, and sleep disturbances in PC underlines the necessity of holistic patient management. Psychological support must be integrated into standard oncological care.

A universal, two-step screening model should be implemented. Instead of relying only on questionnaires, such as the Distress Thermometer for general distress, or the PHQ-9 and HADS, a semi-structured clinical interview with a psychologist should be included. This approach ensures proper case conceptualization and addresses the limited diagnostic accuracy of standalone screening tools.

Following screening, patients should receive individualized referrals to evidence-based interventions like Cognitive Behavioral Therapy, Mindfulness-Based interventions, Meaning-Centered Therapy, or Dignity Therapy, tailored to their specific needs. Clinicians must also consider the delivery format. Because personal interaction is a key driver of efficacy, face-to-face or structured online individual therapies should be preferred over telephone care or heterogeneous group settings. Finally, because the beneficial effects on QoL decrease over time, these psychological interventions should be introduced in the early stages of the disease and repeated at regular intervals to maintain their impact.

12. IMPLICATIONS FOR RESEARCH

A major methodological challenge in psycho-oncology is the extreme heterogeneity across the literature, which limits the comparability of study findings. Future research must focus on standardizing study protocols and data reporting. Investigators should establish consensus on standard intervention methods, standardized questionnaires, specific durations, frequencies, and precise reporting metrics.

Furthermore, there is a clear gap in interventional data for highly lethal cancers. Future research should prioritize randomized controlled trials that directly test the efficacy of targeted psychological therapies specifically within the PC population. Researchers should also design longitudinal studies to track how psychological symptoms change over time across different treatment phases and disease stages.

Finally, because the choice of assessment instruments remains a primary driver of statistical variance, multinational studies are needed to rigorously compare existing screening tools in real-world clinical environments. This research will help establish an international "gold standard" or validate new, brief, and cross-culturally sensitive instruments.

13. IMPLICATIONS FOR POLICY MAKERS

Policymakers must address the global disparities in access to psycho-oncological care, particularly in regions or smaller towns where psychologists are completely missing from the oncology care teams. Health authorities should establish dedicated psycho-oncology teams on every oncology ward. These teams must be adequately staffed to handle routine screening, detailed case conceptualizations, and the delivery of evidence-based psychological treatments, ensuring equitable access for all patients and their families.

Additionally, policymakers need to reevaluate how research funds are allocated. Currently, highly deadly cancers like PC receive disproportionately lower research funding relative to their high mortality rates compared to other, more well-funded malignancies.

14. FUTURE PERSPECTIVES

The future of psycho-oncology lies in transitioning from generalized psychological support to highly personalized psychosocial care. As the incidence of aggressive cancers rises among younger populations, future clinical models must account for age-related differences in psychological distress and tailor interventions accordingly.

Advancements in digital health platforms will likely play a major role in bridging current access gaps, allowing patients who are too physically ill to travel to receive high-quality, individual online therapies from home.

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16. BIBLIOGRAPHY

16.1. Publications Related to the Thesis

Psychological Intervention Improves Quality of Life, but Not Survival in Patients with Early-Stage Cancer: a Systematic Review and Meta-analysis of Randomized Clinical Trials

Sára Anna Bognár, Brigitta Teutsch, Stefania Bunduc, Dániel Sándor Veres, Bence Szabó, Beatrix Fogarasi, Olga Júlia Zahariev, Nóra Vörhendi, Omer Almog, Yael Hadani, Dorottya Gergő, Emese Mihály, Bálint Erőss, Stefania Bunduc, Katalin Márta, Peter Hegyi

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One out of Four Patients with Pancreatic Cancer Experience Psychological Symptoms: a Systematic Review and Meta-analysis

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DOI: <https://doi.org/10.1371/journal.pone.034>,

1.1. Publications not Related to the Thesis

Psychological interventions improve mental health in inflammatory digestive diseases: a systematic review and meta-analysis of randomized controlled trials

Floria Diana-Elena, Fogarasi Beatrix, Tari Edina, Szabó László, Veres Dániel Sándor, **Bognár Sára Anna**, Sikó Beáta, Eröss Bálint, Teutsch Brigitta, Hegyi Péter

Therapeutic Advances In Gastroenterology 18 Paper: 1756284825138632,21p. (2025)

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