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REVIEW

For whom and what outcomes does cognitive-behavioral-therapy work among cancer survivors: a systematic review and meta-analysis

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Abstract

Objective To perform a systematic review and meta-analysis of CBT for individuals diagnosed with cancer across a broad range of outcome domains, i.e., functional health, psychological health, health behaviors, social relational, and general wellness.

Methods A comprehensive search of 7 databases, 91 published reviews, and 4 professional websites was performed on August 30th, 2021. English-language clinical trials of CBT for cancer patients/survivors were included. Studies were independently screened, and data were extracted by 2 reviewers, and discrepancies were resolved by consensus among the investigative team. A total of 151 clinical trials (154 articles) published between 1986 and 2021 were included in the analysis.

Results CBT was overall effective for cancer patients/survivors in the domains of functional health, $g = 0.931$, $p < 0.001$, psychological health, $g = 0.379$, $p < 0.001$, and general wellness, $g = 0.257$, $p < 0.001$, but *ineffective* in domains of health behaviors, $g = 0.792$, $p > 0.05$, and social relational outcomes, $g = 0.319$, $p > 0.05$. Additional subgroup and moderator analyses further revealed CBT's differential treatment effect for different within domain outcomes, across different cancer disease stages, and CBT delivery format.

Conclusions Findings of the study showed that CBT is an effective treatment for individuals diagnosed with cancer. However, treatment effects differ by important disease- and intervention-related factors, which should be considered when recommending CBT for cancer patients/survivors.

Keywords Cancer · Cognitive-behavioral therapy · Meta-analysis · Systematic review

Backgrounds

Cognitive-behavioral therapy (CBT) is an evidence-based psychosocial treatment for a range of mental health and psychosocial problems in the general population [1]. CBT has been increasingly used among individuals with cancer, with numerous clinical trials evaluating CBT's effectiveness across populations with different cancer diagnoses, across the age spectrum, and targeting various patient outcomes [2–6]. For example, Getu and colleagues [7] reported an overall moderate treatment effect of CBT ($g = 0.39$, $p < 0.001$) for quality of life among breast cancer patients. Based on the published review articles of CBT for cancer patients, CBT has received the strongest evidence supporting its effectiveness among breast cancer patients, primarily for treating depression or insomnia outcomes [8–10]. Besides, CBT has also been found effective for cancer patients' psychological distress, post-traumatic growth, and general quality of life, with clinical trials and/or systematic reviews and

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meta-analyses supporting its effectiveness [7, 11–13]. For example, CBT studies constitute close to 50% of the clinical trials for psychological treatment targeting emotional distress in breast cancer patients, with an overall statistically significant and moderate to large treatment effect [14].

Despite a strong body of research synthesis literature available, several salient gaps exist in the existing psycho-oncology literature evaluating CBT. First, most existing review studies focused on limited patient reported outcomes (PROs) among individuals diagnosed with specific types of cancer, such as CBT's effect for insomnia among breast cancer patients or CBT's effect for psychological stress among prostate cancer patients [15, 16]. While valuable evidence, these reviews fail to reflect the complex symptom profile of cancer patients, which includes multiple symptoms across a broad range of outcome domains, e.g., a lung cancer patient with comorbid anxiety and insomnia, and in need of smoke cessation [17, 18]. Such gap can lead to the overgeneralization of CBT's treatment effect, which, in turn, may misguide oncological providers' treatment referral for their cancer patients' PROs. Second, with recent advances in technology, technology-assisted CBTs (*t*CBTs) have been increasingly common in cancer care settings to reduce access barriers to mental health interventions [19, 20]. Yet, evaluations of *t*CBTs' treatment effectiveness are often separated from those in-person CBT interventions, preventing clinical providers from making the best treatment recommendations when patients have access to CBT being delivered in more than one format.

Finally, most, if not all, existing CBT review studies failed to evaluate the potentially different treatment effects of CBT across cancer stages, i.e., newly diagnosed, active treatment, and post-treatment survivorship [6, 21]. This represents a significant gap in the existing literature because adverse PROs persist across cancer patients' disease stages whereas CBT may not be equally effective in different stages. For example, Sun and colleagues [10] found that, for early-stage breast cancer patients, CBT was only effective for anxiety but *not* for depression or quality of life outcomes. Zhang and colleagues [22] argued that during the time of initial diagnosis, many cancer patients are overwhelmed with their distressing emotions in reaction to cancer, which interferes with validated CBT techniques such as cognitive restructuring or behavioral activation. As a result, it is possible that CBT may have low treatment effects for newly diagnosed cancer patients and would regain its efficacy after cancer patients are further along with their disease experiences with greater acceptance of their diagnosis.

To address these gaps, a comprehensive review of CBT interventions for all cancer patients across outcome domains is warranted to answer these important questions. In this paper, we report findings from a comprehensive systematic review and meta-analysis of all CBT interventions for patients with any cancer diagnosis across five broad outcome domains, including (1) functional health, (2) psychological health, (3) health behaviors, (4) social relational outcomes, and (5) general wellness. Within each outcome domain, we evaluated for an overall treatment effect of CBT for that domain as well as investigated common within domain subgroup outcomes, e.g., depression, anxiety, and psychological distress within the psychological health outcome domain. Most importantly, when feasible and appropriate, we will conduct important subgroup and moderator analyses testing (1) cancer stage and (2) CBT delivery format for each domain to explore the potential difference in CBT's treatment effect for individuals diagnosed with cancer.

Methods

A comprehensive search of English-language literature was performed in 7 electronic databases, on 91 published relevant review articles and four professional websites (see Supplement 1). Inclusion criteria were (1) delivered cognitive-behavioral therapy (CBT); (2) used a controlled trial design (with or without randomization); (3) targeted individuals diagnosed with cancer; (4) assessed at least one PROs from any functional, behavioral, and symptom domain; (5) written in English; and (6) provided statistical information needed for meta-analysis. Studies without a control condition and those with interventions did not evaluate CBT were excluded. Studies that contained duplicate reports of overlapping datasets were only included when additional longitudinal data were reported and analyzed.

Each study's eligibility for evaluating CBT was operationalized based on either of the two sets of criteria. First, if a study explicitly reported the use of CBT, or cognitive-behavioral theory as the intervention's underlying change mechanism, or included two or more out of the three core elements of CBT (i.e., cognitive restructuring, behavioral activation, and problem-solving), then a study would meet the inclusion criterion for CBT. Second, if a study evaluated mindfulness-based cognitive therapy (MBCT), which is a form of third-wave CBT [23, 24], that study was also eligible. The reason we decided to include MBCT studies in this review was because of the increasingly popular use of MBCT as an alternative to traditional (second wave) CBT for cancer patients' PROs across diagnoses and clinical populations [23, 25–29]. Potential differences in treatment effect between second versus third wave CBT were explored in data analysis.

Potentially eligible studies were first screened based on title and abstract by two independent screeners. After excluding those articles that clearly did not meet our inclusion criteria, two reviewers independently reviewed each remaining full text article to determine their eligibility

for final inclusion and analysis. When the two screeners/reviewers disagreed on a study's eligibility, a third reviewer reviewed the study and discussed it with the team to finalize a decision. Title/abstract and full text screening were completed using Cochrane Collaboration recommended platform COVIDENCE. The initial literature search concluded on August 30th, 2021, and title/abstract screening occurred between September and October 2021. Full text screening completed in November 2021, and data extraction occurred from December 2021 to February 2022. Data analyses and manuscript preparation were completed by March 2022.

Risk of bias was assessed using Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) and Risk of Bias In Non-Randomized Studies of Interventions (ROBINS-I) [30, 31]. Efforts were made to contact authors when an eligible study had missing statistics needed for effect size calculation. A pre-designed coding sheet (Supplement 2) was used to extract bibliographical information, study design, patients' demographic and clinical characteristics, intervention characteristics, and outcome measures. Outcome domains were categorized into conceptual groupings after all eligible studies were reviewed and discussed which included (1) functional health, (2) psychological health, (3) health behaviors, (4) social relational outcomes, and (5) general wellness (Supplement 3).

Publication bias was visually inspected using the funnel plot by plotting individual effect size estimates against their corresponding standard errors [32]. A symmetric funnel plot indicates the absence of publication bias, whereas an asymmetric funnel plot would suggest concerns for publication bias [33]. The study followed Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and was pre-registered in PROSPERO: CRD42021267116. Institutional review board approval was not required.

Statistical analysis

All analyses were conducted in R Statistical Software (version 3.5.3) with the *metafor* and *robumeta* package, using robust variance estimation (RVE) in meta-regression [34]. In addition to descriptive statistics at the study level, we first extracted standardized mean differences and calculated small sample sizes corrected Hedges' *g* as treatment effect sizes from primary studies [34]. Specifically in this study, we refer to those Hedges' *g* effect size after the small sample size correction as "*g*" in the result section. Then, for meta-analysis, we first calculated overall treatment effect sizes for all five outcome domains separately, i.e., (1) functional health, (2) psychological health, (3) health behaviors, (4) social relational outcomes, and (5) general wellness. Next, if feasible and appropriate, we further investigated CBT's treatment effects for common subgroup outcomes within each domain, such as depression, anxiety, and psychological distress within the psychological outcome domain; or insomnia, fatigue, and pain within the functional health domain. Besides, if data allows, we also conducted subgroup analysis within each outcome domain to evaluate CBT's treatment effect by cancer stage, delivery format, and waves of CBT (second wave versus MCBT).

Finally, for moderator analyses, for each of the five outcome domains, if feasible and appropriate, we conducted domain-specific univariate meta-regression analyses evaluating if cancer disease stage (i.e., newly diagnosed, active treatment, post-treatment survivorship, mixed stages) or CBT's delivery format (i.e., in-person, mixed in-person and technology, technology-assisted interpersonal, pre-programmed *t*CBT) significantly moderated CBT's treatment effect within each outcome domain.

We selected the RVE in meta-regression analytical framework over classic meta-analysis methods for several important reasons. First, RVE in meta-regression allows us to include multiple effect sizes from the same study (greater statistical power) while effectively addressing the within-study dependence among those effect sizes [35]. Second, the classic meta-analysis method evaluates the between-study (or effect size) heterogeneity, e.g., often with the *Q* statistic, to determine if a fixed- versus a random-effects model should be used to carry out the meta-analysis [36]. In contrast, RVE in meta-regression produces valid estimations of the sampling variance regardless of the distributional assumption of the effect size estimates, meaning that it *removes* the need to select between a fixed- versus a random-effects model based on the between-study heterogeneity (e.g., Q statistic or I^2) while still making valid inference [35, 37].

Finally, in order to produce a most comprehensive meta-analysis on this topic, our inclusion criteria allowed us to include a heterogeneous set of studies, including (1) randomized and non-randomized controlled trials and (2) second wave CBT and MBCT (third wave). For all analyses outlined above, we conducted sensitivity analyses to see if findings would change by excluding non-randomized controlled trials and/or by excluding MBCT trials. We conducted subgroup analyses of RCTs and controlled trials without randomization separately, and moderator analysis between RCT studies and controlled trial studies without randomization. No significant difference in treatment effect was identified. Because all findings remained the same as indicated by the sensitivity analyses, we report the set of findings included both RCTs and non-randomized controlled trials as well as included both second wave CBT and MBCT. Sensitivity analysis results are available upon request to the corresponding author.

Results

Characteristics of included studies

From an initial pool of 2649 potentially eligible studies, we identified a total of 151 clinical trials (154 articles/dissertations), published between 1986 and 2021 (Fig. 1). The 154 studies reported 1627 effect sizes comprising 18,340 cancer patients. Most studies were published by authors from the USA ($n = 60$, 39%), Netherlands ($n = 18$, 12%), Canada ($n = 13$, 8%), and Australia ($n = 13$, 8%). Only three studies were dissertations, and all others were peer-reviewed journal articles. Twenty-five studies were published in the journal *Psycho-Oncology* (16%), 14 in the *Journal of Clinical Oncology*, and 71 in a diversity of journals. Participants' age averaged 53.36 years old, and most were female patients ($n = 14{,}700$, 80.16%) and two-thirds non-Hispanic White ($n = 12{,}313$, 67.14%). Close to half of the studies delivered CBT to patients receiving on-going curative/active treatment ($n = 66$, 43%) and about one third delivered CBT to post-treatment cancer survivors ($n = 47$, 30%). Almost all were randomized controlled trials ($n = 138$, 93%) and the majority evaluated CBT as the study intervention arm ($n = 138$, 90%). A brief study summary table is presented in Table 1, and a detailed study table and a reference list of included studies were included in Supplement 4.

Publication bias and risk of bias

Publication bias was assessed using funnel plot (Fig. 2). Visual inspection did not reveal any major pattern of asymmetry, supporting the absence of publication bias. Risk of bias assessed using RoB2 and ROBINS-I revealed overall low risk of bias for both randomized controlled trials and controlled trials without randomization (Supplement 5). The most concerning area of risk of bias was primary studies' handling of missing data, although the overall risk remained relatively low. Studies reported very low risk of bias in other areas, including randomization procedure, intervention procedure, measurement, and selective reporting. Only one study (out of 154) was scored with a moderate risk of bias.

Functional health outcomes

There were 95 clinical trials (including 596 effect size estimates) that evaluated CBT's treatment effect on functional health outcomes among individuals diagnosed with cancer. An overall treatment effect of CBT was $g = 0.391$, 95% *CI* (0.285, 0.496) for cancer patients' functional health, which represented a moderate and statistically significant effect. Studies evaluated 2nd wave CBT (84 clinical trials and 561 effect size estimates) reported a moderate and statistically significant treatment effect, $g = 0.342$, 95% *CI* (0.240, 0.445),

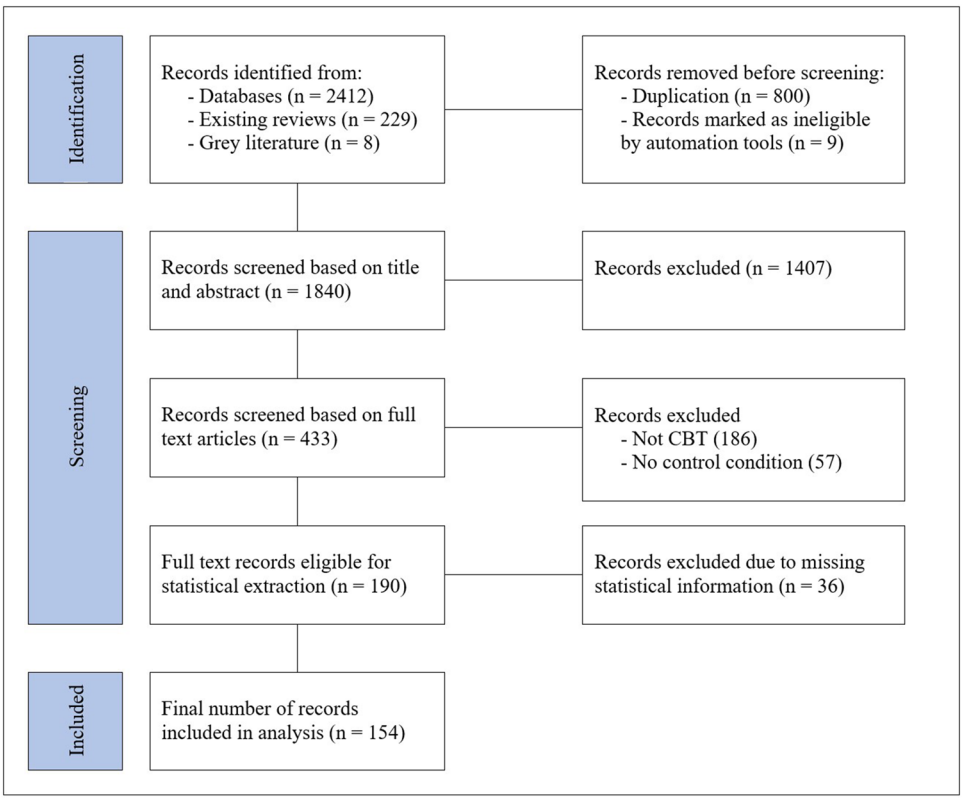

Fig. 1 PRISMA 2020 flow diagram for literature search

Table 1 Study characteristics summary table ($n = 154$)*

Characteristics (number of studies)	Mean (SD)	Frequency (%)
Country of publication		
USA		60 (39%)
Netherlands		18 (12%)
Canada		13 (8%)
Australia		13 (8%)
UK		7 (5%)
China		6 (4%)
Others		37 (24%)
Journals where studies published		
Psycho-Oncology		25 (16%)
Journal of Clinical Oncology		14 (9%)
Journal of Pain and Symptom Management		6 (4%)
Oncology Nursing Forum		6 (4%)
Other sources (69 journals and 3 dissertations)		103 (67%)
Age (weighted mean)	53.36	
Female patients		14,700 (80.16%)
Non-Hispanic White patients		12,313 (67.14%)
Cancer treatment phase		
Newly diagnosed		6 (4%)
On-going curative/active treatment		66 (43%)
Post-treatment survivorship		47 (30%)
Mixture of patients in different phases		15 (10%)
Others		20 (13%)
Study design		
Randomized controlled trial		143 (93%)
Controlled trial without randomization		11 (7%)
Waves of CBT (2nd wave)		138 (90%)
Mindfulness-base cognitive therapy		16 (10%)
CBT as the primary intervention tested		
Yes		138 (90%)
No		16 (10%)

*SD, standard deviation

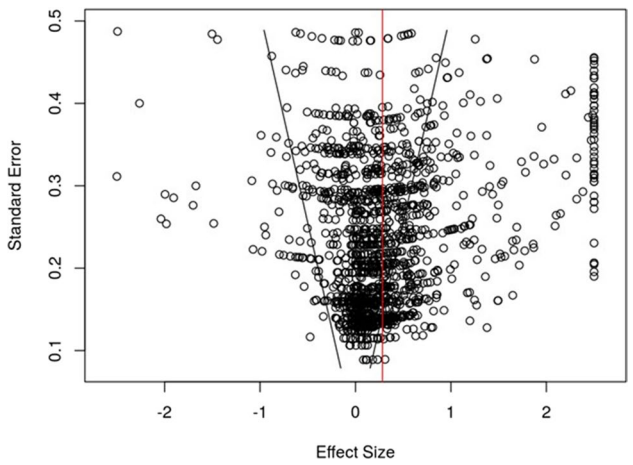

Fig. 2 Funnel plot

whereas studies evaluated MBCT (11 clinical trials and 35 effect size estimates) reported a large and statistically significant treatment effect, $g = 0.759$, *95% CI* (0.287, 1.230). The difference between the 2nd wave CBT and MBCT for functional health outcomes was statistically *non-significant* (Table 2).

Subgroup analysis of common outcomes within the functional health domain (Table 2) revealed statistically significant treatment effects across all subgroups. Specifically, moderate to large treatment effects were observed for insomnia, $g = 0.544$, 95% *CI* (0.310, 0.778), and fatigue, $g = 0.320$, 95% *CI* (0.096, 0.545). Statistically significant though small treatment effects were observed for pain, $g = 0.209$, 95% *CI* (0.051, 0.367), cognitive impairment, $g = 0.232$, 95% *CI* (0.039, 0.424), general functional health, $g = 0.252$, 95% *CI* (0.141, 0.363), and other functional outcomes, $g = 0.274$, 95% *CI* (0.109, 0.438).

Table 2 Overall treatment effects for each outcome domain and within domain subgroup analysis[1]

	2nd and MBCT combined					2nd wave CBT only					MBCT only					diff
	Estimate	df[2]	N	K	95% *CI*	Estimate	df[2]	N	K	95% *CI*	Estimate	df[2]	N	K	95% *CI*	
Functional health	0.391***	91.4	95	596	0.285, 0.496	0.342***	79.8	84	561	0.240, 0.445	0.759***	9.97	11	35	0.287, 1.230	No
Insomnia	0.544***	29.6	31	95	0.310, 0.778	0.482***	26.3	28	88	0.273, 0.691	1.10	2	3	7	−2.070, 4.270	No
Fatigue	0.320**	44.1	46	115	0.096, 0.545	0.318***	40.5	43	111	0.138, 0.498	−0.043	3	4	4	−3.270, 3.190	No
Pain	0.209*	12.4	15	61	0.051, 0.367	0.127*	9.23	13	47	0.018, 0.236	0.624	1	2	14	−0.934, 2.180	No
Cognitive impairment	0.232*	6.79	9	30	0.039, 0.424	0.232*	6.79	9	30	0.039, 0.424	–	–	–	–	–	–
General functional health	0.252***	34.5	39	202	0.141, 0.363	0.208***	29.5	34	192	0.101, 0.315	0.565*	3.8	5	10	0.004, 1.130	No
Other functional outcome	0.274**	24.9	28	93	0.109, 0.438	0.272**	24	27	92	0.103, 0.442	–	–	–	–	–	–
Psychological health	0.379***	104	112	779	0.285, 0.473	0.347***	92.5	100	717	0.249, 0.444	0.636**	10.3	12	62	0.285, 0.987	No
Depression	0.426***	58.7	62	140	0.260, 0.592	0.399***	53.9	57	132	0.224, 0.573	0.754*	3.68	5	8	0.165, 1.340	No
Anxiety	0.307***	55.2	61	159	0.199, 0.414	0.294***	49.9	55	146	0.177, 0.410	0.415*	4.48	6	13	0.037, 0.792	No
Distress	0.435***	42.5	46	125	0.253, 0.617	0.439***	35.9	39	110	0.227, 0.650	0.426*	5.6	7	15	0.012, 0.840	No
Posttraumatic stress	0.335	9.79	11	28	−0.314, 0.983	0.243	8.8	10	26	−0.439, 0.925	–	–	–	–	–	–
General mental health	0.292***	55.2	61	327	0.203, 0.381	0.251***	50.4	56	303	0.166, 0.336	0.755*	3.68	5	24	0.096, 1.410	No
Health behaviors[3]	0.792	2.99	4	10	−0.391, 1.980	0.743	2	3	8	−1.410, 2.890	–	–	–	–	–	–
Social relational[3]	0.319	2.41	5	10	−0.213, 0.851	0.234	1.16	4	9	−1.170, 1.640	–	–	–	–	–	–
General wellness	0.257***	58.6	61	232	0.142, 0.373	0.262***	52.9	55	221	0.131, 0.392	0.219*	4.61	6	11	0.025, 0.412	No
Quality of life	0.238***	45.4	48	166	0.109, 0.367	0.243***	40.8	43	157	0.095, 0.392	0.202	3.63	5	9	−0.048, 0.452	No
General wellness	0.249	13.9	15	56	−0.077, 0.576	0.245	12.9	14	54	−0.110, 0.599	–	–	–	–	–	–
General health	0.319	2.9	4	10	−0.021, 0.658	0.319	2.9	4	10	−0.021, 0.658	–	–	–	–	–	–

[1]*df*, degrees of freedom; *N*, number of studies and *K*, number of effect sizes; 95% *CI*, 95% confidence interval; *diff*, if an overall treatment effect is different between 2nd wave CBT only and MBCT only, whereas *MBCT*, mindfulness-based cognitive therapy. [2]When df is ≤ 4, a *p* value of 0.01 should be considered significant but not a *p* value of 0.05. [3]For health behaviors domain and social relational domain, not enough studies or effect sizes to allow further subgroup analyses. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Subgroup analysis by cancer disease stages (Table 3) revealed statistically significant treatment effects of CBT for functional health among cancer patients receiving active/on-going cancer treatment, $g = 0.270$, 95% *CI* (0.134, 0.407), in different/multiple disease stages, $g = 0.343$, 95% *CI* (0.139, 0.547), and in the post-treatment survivorship phase, $g = 0.585$, 95% *CI* (0.352, 0.819). However, CBT's treatment effect for functional health was statistically *non-significant* for patients newly diagnosed with cancer, $g = 0.063$, 95% *CI* (−0.099, 0.226). Notably, univariate moderator analysis evaluating cancer disease stage as a moderator (Table 4) indicated that CBT's treatment effect for functional health outcomes was significantly greater among post-treatment survivors than that among newly diagnosed cancer patients and those receiving active/on-going cancer treatment, $b = -0.505$, $p < 0.05$, and $b = -0.307$, $p < 0.05$, respectively.

Subgroup analysis by CBT delivery format (Table 3) revealed statistically significant treatment effects of CBT for functional health across different delivery formats. A statistically significant though small treatment effect of CBT was identified for cancer patients' functional health when being delivered with a mixed format of in-person and technology-assistance, $g = 0.281$, 95% *CI* (0.131, 0.431). Statistically significant and moderate treatment effects of CBT were identified for cancer patients' functional health when being delivered as a pre-programmed computer intervention, $g = 0.274$, 95% *CI* (0.159, 0.569), as an interpersonal intervention via technology, $g = 0.333$, 95% *CI* (0.062, 0.603), and as an in-person intervention, $g = 0.462$, 95% *CI* (0.290, 0.633). Univariate moderator analysis evaluating delivery format as a moderator did not reveal any significant between group differences in CBT's effect size for functional health outcomes, suggesting CBT is equally effective for cancer patients' functional health across different delivery formats (Table 4).

Table 3 Within domain subgroup analysis by cancer stage and CBT delivery format[1]

	Functional health domain			Psychological health domain			General health domain		
	Estimate	df[2]	N/K	Estimate	df[2]	N/K	Estimate	df[2]	N/K
Cancer stage									
Posttreatment survivorship	0.585***	32.7	34/173	0.410***	28.9	31/193	0.391**	15.4	17/48
Newly diagnosed	0.063	1.61	3/27	0.151†	2.49	5/33	−0.184	1.00	2/4
On-going active treatment	0.270***	36.1	39/287	0.392***	40.5	45/348	0.202†	22.7	24/100
Mixture of multiple phases	0.343**	10.1	12/83	0.436**	11.2	14/101	0.626*	3.96	5/31
CBT delivery format									
In person	0.462***	52.9	55/307	0.392***	59.1	66/489	0.251**	38.4	40/165
Mixed in person and technology	0.281***	23.3	25/179	0.305**	22.7	24/154	0.157†	10.3	12/42
Tech-assisted interpersonal	0.333*	5.71	7/46	0.308	9.7	11/78	0.478	2.90	4/8
Pre-programmed technology only	0.364**	9.5	11/52	0.546**	9.94	11/53	0.287	4.97	6/17

[1]*df*, degrees of freedom; *N*, number of studies and *K*, number of effect sizes; 95% *CI*, 95% confidence interval. [2]When df is ≤ 4, a *p* value of 0.01 should be considered significant but not a *p* value of 0.05. †$0.05 < p < 0.06$, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Table 4 Within domain univariate moderator analysis results[1]

	Functional health domain			Psychological health domain			General health domain		
	Estimate	df[2]	N/K	Estimate	df[2]	N/K	Estimate	df[2]	N/K
Cancer stage (*ref*: posttreatment survivor)	0.578***	32.3	95/596	0.411***	29.1	110/761	0.410***	15.7	58/218
Newly diagnosed	−0.505*	2.2	95/596	−0.224	4.8	110/761	−0.578	1.25	58/218
On-going active treatment	−0.307*	67.9	95/596	−0.015	63.5	110/761	−0.204	34.3	58/218
Mixture of multiple phases	−0.218	18.8	95/596	0.030	20.0	110/761	0.189	6.2	58/218
Not described	−0.239	8.39	95/596	−0.080	26.8	110/761	−0.333*	18.3	58/218
Delivery format (*ref*: in person)	0.459***	52.0	95/584	0.394***	59.0	111/774	0.252	38.2	61/232
Mixed in person and technology	−0.170	47.2	95/584	−0.082	43.7	111/774	−0.050***	17.6	61/232
Tech-assisted interpersonal	−0.113	7.5	95/584	−0.074	14.1	111/774	−0.196	3.3	61/232
Pre-programmed technology only	−0.127	13.0	95/584	0.146	13.7	111/774	−0.040	6.7	61/232

[1]*df*, degrees of freedom; *N*, number of studies and *K*, number of effect sizes; 95% *CI*, 95% confidence interval. [2]When df is ≤ 4, a *p* value of 0.01 should be considered significant but not a *p* value of 0.05. *$p < 0.05$, ***$p < 0.001$

Psychological outcomes

There were 112 clinical trials (including 779 effect size estimates) that evaluated CBT's treatment effect on psychological outcomes among individuals diagnosed with cancer. An overall treatment effect of CBT was $g = 0.379$, 95% *CI* (0.285, 0.473) for psychological outcomes, which represented a moderate and statistically significant effect. Studies evaluated 2nd wave CBT (100 clinical trials and 717 effect size estimates) reported a moderate and statistically significant treatment effect, $g = 0.347$, 95% *CI* (0.249, 0.444), whereas studies evaluated MBCT (12 clinical trials and 62 effect size estimates) reported a large and statistically significant treatment effect, $g = 0.636$, 95% *CI* (0.285, 0.987). The difference between 2nd wave CBT and MBCT for psychological health outcomes was statistically *non-significant* (Table 2).

Subgroup analysis of common outcomes within the psychological health domain (Table 2) revealed statistically significant treatment effects across all *but one* subgroup. Specifically, moderate treatment effects were observed for depression, $g = 0.426$, 95% *CI* (0.260, 0.592), anxiety, $g = 0.307$, 95% *CI* (0.199, 0.414), and psychological distress, $g = 0.435$, 95% *CI* (0.253, 0.617). A statistically significant though small treatment effect was observed for general mental health outcomes, $g = 0.292$, 95% *CI* (0.203, 0.381), and the treatment effect of CBT for cancer patients' post-traumatic stress was statistically *non-significant*, $g = 0.335$, 95% *CI* (−0.314, 0.983).

Subgroup analysis by cancer disease stages (Table 3) revealed statistically significant treatment effects of CBT for psychological health among cancer patients receiving active/on-going cancer treatment, $g = 0.392$, 95% *CI* (0.233, 0.550), in different/multiple disease stages, $g = 0.436$, 95% *CI* (0.088, 0.785), and in the post-treatment survivorship phase, $g = 0.410$, 95% *CI* (0.218, 0.601). However, CBT's treatment effect for psychological health was statistically *non-significant* for patients newly diagnosed with cancer, $g = 0.151$, 95% *CI* (−0.008, 0.310). Univariate moderator analysis evaluating cancer disease stage as a moderator (Table 4) did not reveal any significant between-group differences in CBT's treatment effects for psychological outcomes.

Subgroup analysis by CBT delivery format (Table 3) revealed statistically significant treatment effects of CBT for psychological health across different delivery formats, except for interpersonal CBT delivered via technology. Specifically, a large and statistically significant treatment effect of CBT was identified for cancer patients' psychological health when being delivered as pre-programmed CBT interventions, $g = 0.546$, 95% *CI* (0.255, 0.837). Statistically significant and moderate treatment effects of CBT were identified for cancer patients' psychological health when being delivered as an in-person intervention, $g = 0.392$, 95% *CI* (0.261, 0.522), and with a mixed format of in-person and technology-assistance, $g = 0.305$, 95% *CI* (0.127, 0.483). When CBT was delivered as an interpersonal treatment via technology, an overall treatment effect was statistically *non-significant* for psychological health among patients with cancer, $g = 0.308$, 95% *CI* (−0.090, 0.706). Univariate moderator analysis evaluating delivery format as a moderator did not reveal any significant between group difference in CBT's effect size for psychological outcomes (Table 4).

Health behavior and social relational outcomes

There were 4 clinical trials (10 effect sizes) and 5 clinical trials (10 effect sizes) evaluating CBT for cancer patients' health behavior outcomes and social relational outcomes, respectively. Statistically *non-significant* treatment effects of CBT were identified for cancer patients' health behavior outcomes, $g = 0.792$, 95% *CI* (−0.391, 1.980) as well as for cancer patients' social relational outcomes, $g = 0.319$, 95% *CI* (−0.213, 0.851). Given the small number of studies (and effect sizes) evaluating these two outcome domains, further subgroup and moderator analyses by CBT waves (2nd wave CBT versus MBCT), cancer disease stages, and delivery format were not feasible.

General wellness outcomes

There were 61 clinical trials (including 232 effect size estimates) that evaluated CBT's treatment effect on general wellness outcomes among individuals diagnosed with cancer. An overall treatment effect of CBT was $g = 0.257$, 95% *CI* (0.142, 0.373) for cancer patients' general wellness, which represented a statistically significant though small treatment effect. Studies evaluated 2nd wave CBT (55 clinical trials and 221 effect size estimates) reported a small and statistically significant treatment effect, $g = 0.262$, 95% *CI* (0.131, 0.392), as well as those evaluated MBCT (6 clinical trials and 11 effect size estimates) for cancer patients' general wellness, $g = 0.219$, 95% *CI* (0.025, 0.412). The difference between 2nd wave CBT and MBCT for general health outcomes was statistically *non-significant* (Table 2).

Subgroup analysis of common outcomes within the general wellness domain (Table 2) revealed a statistically significant treatment effect only for cancer patients' quality of life, $g = 0.238$, 95% *CI* (0.109, 0.367). CBT's treatment effects were statistically *non-significant* for general wellness outcomes, $g = 0.249$, 95% *CI* (−0.077, 0.576), and for general health outcomes, $g = 0.319$, 95% *CI* (−0.021, 0.658) among individuals diagnosed with cancer.

Subgroup analysis by cancer disease stages (Table 3) revealed statistically significant treatment effects of CBT for

general wellness among cancer patients in the post-treatment survivorship phase, $g = 0.391$, 95% *CI* (0.174, 0.607), and for those in different/multiple disease stages, $g = 0.626$, 95% *CI* (0.006, 1.250). In contrast, CBT was overall statistically *non-significant* for cancer patients who are newly diagnosed, $g = -0.184$, 95% *CI* (−4.980, 4.680), and those who are receiving active/on-going cancer treatment, $g = 0.202$, 95% *CI* (−0.005, 0.409).

Subgroup analysis by CBT delivery format (Table 3) revealed a statistically significant treatment effect of CBT for general wellness outcomes only when being delivered in person, $g = 0.251$, 95% *CI* (0.088, 0.413). CBT's treatment effects were statistically *non-significant* when being delivered with a mixture of in-person and technology-assistance, $g = 0.157$, 95% *CI* (−0.009, 0.323), as an interpersonal intervention via technology, $g = 0.478$, 95% *CI* (−0.419, 1.380), and as a pre-programmed computer intervention only, $g = 0.287$, 95% *CI* (−0.185, 0.759).

Discussion

In this systematic review and meta-analyses, we identified 154 studies inclusive of 18,340 cancer patients and 1627 effect sizes of CBT for cancer patients' (1) functional health, (2) psychological health, (3) health behaviors, (4) social relational outcomes, and (5) general wellness outcomes. Results revealed statistically significant moderate treatment effect sizes of CBT for cancer patients' functional health, psychological health, and general wellness outcomes but not for their health behaviors and social relational outcomes. In addition, findings identified important subgroup differences and moderators which included cancer disease phase and CBT delivery format.

Study findings of CBT's effectiveness for cancer patients are consistent with the general CBT literature and published meta-analyses with several important differences. First, as consistently documented in the CBT literature for both general and cancer populations, CBT is effective with a small to moderate treatment effect supporting cancer patients in three out of five outcome domains [1, 8]. Second, reflecting the robust literature of CBT for insomnia both among the general and cancer populations [1, 8, 11, 16, 38], findings of this review found the largest treatment effect estimate of CBT for cancer patients' insomnia outcomes. Third, though statistically significant, we identified an estimated *moderate* treatment effect of CBT for cancer patients' psychological outcomes, which was smaller in magnitude than the general CBT literature indicating large treatment effect size for individuals without cancer [1, 39]. Studies appraised an expected reduction in treatment effect size of CBT for cancer patients' psychological outcomes [40, 41]. Greer and colleagues, for example, argued that many thoughts and feelings considered irrational among healthy individuals are often rational, yet still distressing, to cancer patients [40]. Therefore, key techniques of CBT, e.g., cognitive restructuring or behavioral activation, should be tailored for the unique needs and challenges confronting cancer patients. Finally, findings revealed that CBT was not effective for cancer patients' health behavior outcomes and their social relational outcomes, both of which are important gaps in the CBT literature for cancer patients and therefore, warrant further study [42, 43].

Several important findings based on subgroup and moderator analyses have important clinical implications for delivering CBT to cancer patients/survivors. First, while CBT in general remains effective for cancer patients across treatment phases, *non-significant* treatment effects were consistently identified among studies delivering CBT to newly diagnosed cancer patients. As patients are processing the shocking news of a cancer diagnosis, a cognitive-based approach may not work efficaciously for these patients, as they are overwhelmed with highly distressing emotions and feelings in reaction to a traumatic health diagnosis during the initial stage. Second, although CBT was generally effective for psychological health outcomes and for general wellness outcomes, subgroup analyses revealed that CBT was ineffective for cancer patients' post-traumatic stress, general wellness, and general health outcomes. One possible reason contributing to these non-significant findings was due to the relatively small number small of studies (and effect size estimates) focusing on these outcomes, leading to reduced statistical power. Alternatively, studies have considered post-traumatic stress and general wellness as distal outcomes, meaning these outcomes take longer periods of time to improve after the patients' immediate outcomes (e.g., depression, distress, quality of life) improve first [44, 45]. Therefore, it is important for future trials to include both immediate and distal PROs and have long-term follow-up assessments to evaluate the impact of CBT on these outcomes. Finally, this study revealed important differential treatment effects of CBT across delivery formats. Across the three outcome domains for which CBT is overall effective, i.e., functional health, psychological health, and general wellness, only in-person CBT was consistently identified as an effective approach. Interpersonal CBT delivered via technology platforms was ineffective for both the psychological health and general wellness domains. A relatively small number of studies (and effect size estimates) may have contributed to these non-significant findings. Besides, our investigative team were not necessarily surprised by such finding because there was a robust growth in the literature focusing on pre-programmed, and often self-help, CBTs among cancer patients. In comparison, studies evaluating CBT's treatment effect delivered by a human therapist over technology-platforms (e.g., zoom or iPad)

have not been extensively evaluated and reported, which may contribute to the low treatment effect of this delivery format. While it may be reasonable to expect in-person CBT to remain its efficacy when being delivered virtually, empirical studies are needed to further support the efficacy of interpersonal CBT delivered via technology platforms.

Strengths and limitations

A strength of this study is that findings are supported by the large sample size of effect sizes and virtually all studies with very low risk of bias. As a result, the study was sufficiently powered to conduct subgroup and moderator analyses, which provided a more thorough understanding of the unique role of cancer disease stage and delivery format impacting CBT's treatment effect. Nevertheless, several limitations should be mentioned. First, given the extensiveness of this project, only a few eligible trials ($n \leq 3$) have been published since the completion of the initial search in August 2021, which were not included in the final analysis [2, 46]. Given the large number of studies and effect sizes included in the current analysis, we are confident that the main study findings will hold without these new studies. Second, due to space limitations, we only reported major subgroup and moderator analysis results, omitting additional important moderator analyses within each outcome domain, e.g., the potential moderating role of time or study design in relation to CBT's treatment effects. Future studies should report these findings to further inform the delivery of CBT to cancer patients. Finally, as race/ethnicity data were not reported in many studies, we were unable to consider race/ethnicity as a moderator, preventing the investigation of potential racial/ethnic disparities in health outcomes. This limitation should be revisited in the future when these data become available.

Conclusion

Results of this systematic review and meta-analysis demonstrate that CBT is effective for cancer patients across a diversity of outcome domains, including functional health, psychological health, and general wellness. When delivering CBT to cancer patients, providers should be mindful of a patient's current cancer treatment stage (newly diagnosed versus other stages) and the delivery format of CBT to be employed.

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Data availability Full data and codes are submitted for peer review and can be made available upon request to the corresponding author.

Declarations

Ethics approval This is an empirical evaluation of published data only and involves no human subject, therefore, IRB approval is not applicable.

Consent to participate No human participants were involved in the study and, therefore, consent to participate was not applicable.

Consent for publication Consent to publish is not applicable.

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