Effectiveness of Acceptance and Commitment Therapy for people with advanced cancer: A systematic review and meta-analysis of randomized controlled trials

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Abstract

Aims: To systematically review existing evidence and assess the effectiveness of Acceptance and Commitment Therapy for people with advanced cancer.

Design: Systematic review and meta-analysis of randomized controlled trials.

Data Sources: Nine databases, including PubMed, Web of Science, Cochrane Library, Embase, CINAHL, PsycINFO, Chinese National Knowledge Infrastructure, VIP Database and Wanfang, were searched. The search covered the period between the inception of the selected databases and August 2022.

Review Methods: Two authors independently examined eligible studies and appraised the methodological quality of the included studies by applying the criteria suggested by the Cochrane Effective Practice and Organization of Care followed by data abstraction. The Template for Intervention Description and Replication (TIDieR) checklist was used to identify intervention characteristics. Meta-analysis was performed using RevMan 5.4 software, and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to evaluate the certainty of evidence.

Results: Eight studies, involving 488 people with advanced cancer, were included. The results showed significant effects of Acceptance and Commitment Therapy on the improvement of quality of life and the alleviation of anxiety, depression, psychological distress and fatigue in people with advanced cancer. However, its effects in relieving psychological flexibility and pain were not statistically significant. The certainty of the evidence was low to moderate.

Conclusion: People with advanced cancer can benefit from Acceptance and Commitment Therapy, which is conducive to improving their health outcomes.

Impact: This review provides evidence about the effectiveness of Acceptance and Commitment Therapy in people with advanced cancer. Further well-designed studies with larger sample sizes are required. This review may help nurses and researchers to design and implement Acceptance and Commitment Therapy in clinical practice, thereby improving health outcomes in this population.

PROSPERO Registration Number: CRD42021244568.
1 | INTRODUCTION

Cancer is a leading cause of death globally, with an estimated 10 million cancer-related deaths worldwide in 2020 (Sung et al., 2021). Advanced cancer refers to cancers that are unprobable to be cured or controlled with treatment (American Cancer Society, 2020). The diagnosis of advanced cancer and its complex treatment affect all domains of patients’ lives, including physical and psychological aspects. Psychological suffering is a major concern for people with advanced cancer (Wang et al., 2017). Research has shown that 31%-67% of people with advanced cancer experience various psychological problems such as depression, demoralization, anxiety and uncertainty (Huda et al., 2022; Webber et al., 2021). These problems present in combinations and can cause psychological distress, an unpleasant experience of a psychological, social or physical nature that may cripple individuals’ abilities to cope effectively with cancer, physical symptoms and treatment (Huda et al., 2022). Untreated psychological symptoms in people with advanced cancer adversely affect physical function, social activities and adherence, leading to aggravated physical symptoms and decreased quality of life (QoL) later (Chen et al., 2017; Rodríguez-Prat et al., 2017). Therefore, management of psychological symptoms is an essential part of palliative care nursing.

Non-pharmacological interventions have been recommended for symptom management in people with advanced cancer (Malakian et al., 2022). Acceptance and Commitment Therapy, a novel form of Cognitive Behavioural Therapy (CBT), has gained popularity worldwide in healthcare research and practice (Du et al., 2021a). Recent studies have touted it as a promising intervention to address the psychological symptoms of people with advanced cancer (Pan et al., 2020; Rost et al., 2012).

Nurses are ideally positioned to implement interventions for people with advanced cancer, as they have the most contact with them and can better identify their psychological problems (Malakian et al., 2022). However, nurses have insufficient experience in Acceptance and Commitment Therapy (Tyrberg et al., 2017). Equipping nurses with evidence-based Acceptance and Commitment Therapy may help them effectively support people with advanced cancer and boost the quality of holistic cancer nursing.

1.1 | Background

Acceptance and Commitment Therapy is a third-wave CBT approach (Hayes et al., 2006). Unlike traditional CBT, Acceptance and Commitment Therapy does not try to avoid or eliminate distress. Instead, it is based on a holistic perspective that assists people in obtaining psychological flexibility—the ability to fully contact the present moment as a conscious human being and to change or persist in behaviour when doing so serves valued ends (Hayes et al., 2006). Specifically, Acceptance and Commitment Therapy includes six core processes: (1) acceptance: actively embracing unwanted thoughts, emotions or experiences rather than controlling them; (2) cognitive defusion: altering the undesirable functions of thoughts rather than an immediate change in their frequency; (3) being present: non-judgmentally contacting the present moment; (4) self as context: reporting one's behaviour from a 'sense of self' perspective; (5) values: chosen qualities of purposive action; and (6) committed actions: committing to actions in the service of their chosen values (Hayes et al., 2006; Zhang et al., 2017).

Psychological flexibility plays an important role in circumstances, such as advanced cancer, over which one can exert little or no control (Davis et al., 2017). It is associated with psychological and physical symptoms and QoL in people with advanced cancer (Mosher et al., 2017, 2021; Novakov, 2021). Thus, given its aim of psychological flexibility, Acceptance and Commitment Therapy may be particularly well-suited for people with advanced cancer as it normalizes their distressing experiences and addresses existential concerns such as the loss of meaning and purpose by encouraging them to live in the present and engage in meaningful activities, thereby alleviating their psychological and physical symptoms (Moreno et al., 2022; Vehling et al., 2019).

In recent years, an increasing number of clinical trials have examined the effects of Acceptance and Commitment Therapy on different health outcomes in people with advanced cancer. Several studies (Li et al., 2022; Rost et al., 2012; Zhang et al., 2021) have shown that this therapy significantly alleviates the psychological symptoms of people with advanced cancer; however, Mosher et al. (2018, 2019) reported inconsistent results. Findings concerning the effect on psychological flexibility among this population are also conflicting (Serfaty et al., 2019; Zhang et al., 2021). A systematic review (Li, Wong, et al., 2021) summarized the relevant studies in this field; however, this review had some limitations. It completed the literature search before October 2019 and only included six studies, involving five randomized controlled trials (RCTs) and one with a single-group pretest–post-test design. The interventions in this review included Acceptance and Commitment Therapy alone or in combination with others, which may influence the evaluation of the true effect of this therapy. Furthermore, no data synthesis was performed. This review provides some insights, but the direct effectiveness of Acceptance and Commitment Therapy for people with advanced cancer remains inconclusive.

The rigorously designed RCTs (Li et al., 2022; Mosher et al., 2022; Pan et al., 2020; Zhang et al., 2021) conducted recently in this field...
may provide new and stronger evidence. Therefore, we performed a systematic review and meta-analysis of RCTs to specifically explore the effectiveness of Acceptance and Commitment Therapy for people with advanced cancer and to inform clinical nursing interventions.

Additionally, emphasis has been placed lately on better understanding the interventions characteristics in the healthcare context. Identifying intervention characteristics may provide nurses with the knowledge and skills to use this therapy and may guide them in shaping and implementing interventions to promote well-being among people with advanced cancer, thereby enhancing the quality of holistic care. Therefore, we applied the Template for Intervention Description and Replication (TIDieR) checklist (Hoffmann et al., 2014) to provide clear and detailed descriptions of the intervention elements of the included studies.

Overall, this systematic review and meta-analysis aimed to (a) examine the effectiveness of Acceptance and Commitment Therapy on psychological flexibility and psychological symptoms; (b) evaluate the effectiveness of Acceptance and Commitment Therapy on physical symptoms and QoL; and (c) identify the intervention characteristics of Acceptance and Commitment Therapy.

2 | THE REVIEW

2.1 | Aims

This study aimed to evaluate the effectiveness of Acceptance and Commitment Therapy on health outcomes among people with advanced cancer and to identify the intervention characteristics.

2.2 | Design

This systematic review and meta-analysis were performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The study protocol was registered in PROSPERO (CRD42021244568) before any analysis was conducted. The eligibility criteria for this review were modified after the protocol registration. The original target population was people with terminal illness, which may include different diseases, thus resulting in a potential bias in the meta-analysis. Since our literature screening results showed that 90% of the included studies focused on people with advanced cancer, we specifically defined the study population as people with advanced cancer. The original criterion for the intervention was to adopt at least three processes of Acceptance and Commitment Therapy. Since it was irrational and lacked sufficient scientific basis, we modified it into Acceptance and Commitment Therapy involving all six core processes, based on relevant reviews (Du et al., 2021b; Zhao et al., 2021). All other processes were conducted in line with the protocol registration.

2.3 | Search methods

A comprehensive literature search was performed in nine databases from their inception to August 2022: PubMed, Web of Science, Cochrane Library, Embase, CINAHL, PsycINFO, Chinese National Knowledge Infrastructure (CNKI), VIP Database and Wanfang. We adopted a search strategy combining indexed terms with free-text terms: (neoplasms OR cancer* OR neoplasm* OR tumor* OR tumour* OR carcinoma* OR malignan* OR oncology) AND (‘terminally ill’ OR advanced OR terminal* OR metastat* OR palliative OR hospice* OR incurable OR dying OR ‘late stage’ OR ‘end stage’ OR ‘end of life’) AND (‘acceptance and commitment therapy’ OR ‘acceptance and commitment’ OR ‘acceptance and commitment therapy’ OR ‘acceptance therapy’ OR ‘commitment therapy’ OR acceptance-based). The search terms were modified and adapted across different databases. Appendix S1 presents the search strategies for the databases. Reference lists, Google Scholar and Clinical Trials.gov were also manually searched to retrieve potential studies.

2.4 | Search outcomes

Literature screening was performed by two authors independently according to the inclusion and exclusion criteria (Box 1), and any divergence was resolved through negotiation with the third author. Figure 1 depicts the literature search and selection process. We identified 269 records via database search and Google Scholar; of these, 30 were retained after duplicate removal and screening of titles and abstracts. After full-text assessment, 22 studies were excluded. We finally included eight RCTs (six in English and two in Chinese) in the meta-analysis (Li et al., 2022; Mosher et al., 2018, 2019, 2022; Pan et al., 2020; Rost et al., 2012; Serfaty et al., 2019; Zhang et al., 2021).

2.5 | Quality appraisal

The risk of bias (RoB) tool comprising nine aspects (Cochrane Effective Practice and Organisation of Care, 2017) was adopted to assess the methodological quality of the included RCTs. Each criterion was ranked as having a low, high or unclear risk of bias. We also evaluated the potential for research fraud, misreporting or selective reporting in the included studies. The Retraction Watch Database was searched to check the integrity of the included RCTs. Prospective clinical trial registrations or protocols of the included studies were also checked. The certainty of the pooled evidence was rated using Grading of Recommendations Assessment, Development and Evaluation (GRADE) covering five domains: limitations in design, inconsistency, imprecision, indirectness and publication bias (Ryan & Hill, 2016). Evidence can be categorized into four levels: high, moderate, low and very low. GRADEpro GDT (https://grade pro.org/) was used to generate the GRADE evidence
BOX 1  Review inclusion and exclusion criteria

Studies
Included: Randomized controlled trials (RCTs).
Excluded: Studies that were repeatedly published or with full-text unavailable.

Participants
Included: Adults (≥18 years old) diagnosed with advanced cancer (stage III or IV).
Excluded: Studies involving mixed samples (people with cancer in stage I and II or non-cancer advanced illness) lacking independent data.

Interventions
Included: Acceptance and Commitment Therapy involving all six core processes.
Excluded: Studies involving intervention that combined Acceptance and Commitment Therapy with other interventions or components.

Comparison
Included: Usual care, wait-list or other treatments.
Excluded: Studies involving control that contained Acceptance and Commitment Therapy components.

Outcomes
The studies should include at least one of the primary outcomes or secondary outcomes.

Primary outcomes
Included: Psychological flexibility and psychological symptoms (e.g. anxiety, depression and psychological distress).
Excluded: Studies lacking relevant outcome data.

Secondary outcomes
Included: Physical symptoms (e.g. pain and fatigue) and QoL.
Excluded: Studies lacking relevant outcome data.

Two authors independently evaluated the methodological quality of the included studies and the certainty of evidence; disputes were resolved through discussion with a third author.

2.6  Data abstraction

A self-designed form was used to extract the following information from the included studies: (a) basic information, including authors, country and publication year; (b) participant characteristics, including type of advanced cancer, mean age and sample size of each group; and (c) outcome indicators, measurement tools, evaluation time points and statistical data. The TIDieR checklist (Hoffmann et al., 2014) was used to extract intervention characteristics such as duration, delivery format and adherence rate. Data were extracted by two authors independently, with the third author serving any disagreements (Table 1).

2.7  Synthesis

Review Manager (RevMan) 5.4 was used for data synthesis. Since all outcomes were presented as continuous variables, mean differences (MDs) or standardized mean differences (SMDs) with 95% confidence intervals (CIs) were calculated as effect sizes, based on whether the same outcome was measured by the same scale. Pooled effect sizes were measured using changes in the mean and standard deviation (SD) from baseline to post-intervention outcomes for both groups. SD change values were calculated using the following equation (Higgins & Green, 2011):

$$SD_{\text{change}} = \sqrt{SD_{\text{baseline}}^2 + SD_{\text{post}}^2 - (2 \times r \times SD_{\text{baseline}} \times SD_{\text{post}})}.$$

A correlation coefficient ($r$) value of 0.5 was employed and unavailable SDs at baseline and post-intervention were calculated based on standard errors (Higgins & Green, 2011; Saragih et al., 2021). When the study reported data at multiple time points after the intervention, the data at the latest time point were selected for analysis. Heterogeneity between studies was investigated using Higgins' $I^2$ statistic and Chi-square ($\chi^2$) test (Higgins et al., 2003). In the absence of marked heterogeneity ($p > 0.1$ and $I^2 < 50\%$) among studies, the fixed-effects model was used. Otherwise, a random-effects model was adopted to pool data, and subgroup analysis was performed to determine potential sources of heterogeneity. Based on relevant reviews (Du et al., 2021a; Li, Wu, et al., 2021) and characteristics of the included studies, we tabulated possible factors for subgrouping, such as different cultural contexts and intervention delivery formats. Sensitivity analysis was performed by removing studies unavailable in English to check whether the pooled results still hold. For data that could not be merged, a descriptive synthesis was performed. The funnel plot for assessing publication bias was not drawn, considering the limited number of included studies for each outcome.

3  RESULTS

3.1  Study characteristics

In total, eight RCTs published between 2012 and 2022 were included. These studies were conducted in the United States (Mosher et al., 2018, 2019, 2022; Rost et al., 2012), China (Li et al., 2022; Pan et al., 2020; Zhang et al., 2021), and United Kingdom (Serfaty et al., 2019).

3.2  Participant characteristics

A total of 488 people with advanced cancer were included in eight RCTs, with sample sizes varying from 40 to 122. Two studies
(Mosher et al., 2019; Zhang et al., 2021) focused on mixed cancer types, and five targeted a single type of cancer, including ovarian (Rost et al., 2012), breast (Mosher et al., 2018), lung (Li et al., 2022; Mosher et al., 2019), pancreatic (Pan et al., 2020) and gastrointestinal (Mosher et al., 2022) cancers. Participants' mean age varied from 40.2 to 62.6 years.

### 3.3 | Intervention characteristics

All studies included the six core processes of Acceptance and Commitment Therapy. The interventions were performed by psychologists (Mosher et al., 2022; Rost et al., 2012), nurses (Pan et al., 2020; Zhang et al., 2021), a PhD candidate in nursing (Li et al., 2022) and social workers with experience in using Acceptance and Commitment Therapy (Mosher et al., 2018, 2019; Serfaty et al., 2019). The interventions lasted between 6 weeks and 4 months, with the most common length being 6 or 8 weeks, delivering 4–12 sessions in total. The sessions were often delivered once a week, and the duration of each session varied from 50 to 90 min. The delivery formats included face-to-face (Pan et al., 2020; Rost et al., 2012; Serfaty et al., 2019; Zhang et al., 2021), telephone-based (Mosher et al., 2018, 2019, 2022) and face-to-face combined with video conferencing (Li et al., 2022). Seven studies (Li et al., 2022; Mosher et al., 2018, 2019, 2022; Pan et al., 2020; Rost et al., 2012; Serfaty et al., 2019) assessed participants' adherence, which ranged from 62.0% to 87.5%. Six studies (Li et al., 2022; Mosher et al., 2018, 2019, 2022; Serfaty et al., 2019) prospectively reported the average fidelity rating scores per session, ranging from 5.90 to 6.60 (rating scale: 1–7). Table 2 reports the complete intervention components of each study, based on the TIDieR checklist.

### 3.4 | Quality of included studies

Figures 2 and 3 depict the methodological quality of individual studies and the risk of bias summary respectively. All studies were rated as having a ‘low risk’ of random sequence generation bias, and four studies (Li et al., 2022; Mosher et al., 2022; Pan et al., 2020; Serfaty et al., 2019) adequately described the allocation concealment methods. Studies by Serfaty et al. (2019) and Zhang et al. (2021) were rated as exhibiting ‘high risk’ and ‘unclear risk’ of bias arising from similar baseline characteristics. All studies were judged to have a ‘low risk’ of bias for similar baseline outcome measurements, incomplete outcome data and selective outcome reporting. It was unclear whether knowledge of allocation was adequately prevented in two studies (Pan et al., 2020; Rost et al., 2012). Moreover, Li et al. (2022) and Rost et al. (2012) were rated as having a ‘low risk’ of bias arising from protection against contamination, while the bias for the other six studies was uncertain. No study was retracted as per the Retraction Watch Database. Five studies (Li et al., 2022; Mosher et al., 2018, 2019, 2022; Serfaty et al., 2019) were prospectively...
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>Population</th>
<th>Sample size (E/C)</th>
<th>Mean age (SD)</th>
<th>Experimental group</th>
<th>Control group</th>
<th>Time-point of measures</th>
<th>Outcomes (measures)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rost et al. (2012)</td>
<td>United States</td>
<td>Advanced ovarian cancer</td>
<td>47 (25/22)</td>
<td>56 (-)</td>
<td>ACT</td>
<td>Usual care</td>
<td>Baseline, end of the 4th, 8th and 12th sessions</td>
<td>Anxiety: BAI, Depression: BDI-II Psychological distress: POMS Quality of life: FACT-G</td>
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<tr>
<td>Serfaty et al. (2019)</td>
<td>United Kingdom</td>
<td>Advanced cancer</td>
<td>42 (20/22)</td>
<td>62.0 (11.5)</td>
<td>ACT</td>
<td>Talking control</td>
<td>Baseline, 1.5-month, 3-month, 4.5-month and 6-month post-intervention</td>
<td>Psychological flexibility: AAQ-II Psychological distress: K10 Quality of life: EQ-5D-5L</td>
</tr>
<tr>
<td>Pan et al. (2020)</td>
<td>China</td>
<td>Advanced pancreatic cancer</td>
<td>122 (61/61)</td>
<td>40.23 (11.67)</td>
<td>ACT</td>
<td>Usual care</td>
<td>Baseline, 8-week, and 20-week post-intervention</td>
<td>Anxiety: DASS-21 Depression: DASS-21</td>
</tr>
<tr>
<td>Zhang et al. (2021)</td>
<td>China</td>
<td>Advanced cancer</td>
<td>100 (50/50)</td>
<td>49.07 (2.13)</td>
<td>ACT</td>
<td>Usual care</td>
<td>Baseline and post-intervention</td>
<td>Psychological flexibility: AAQ-II Anxiety: SAS Depression: SDS</td>
</tr>
<tr>
<td>Li et al. (2022)</td>
<td>China</td>
<td>Advanced lung cancer</td>
<td>40 (20/20)</td>
<td>56.90 (7.05)</td>
<td>ACT</td>
<td>Usual care</td>
<td>Baseline and 1-week post-intervention</td>
<td>Anxiety: GAD-7 Depression: PHQ-9 Fatigue: FSI-I Quality of life: FACT-L</td>
</tr>
<tr>
<td>Mosher et al. (2022)</td>
<td>United States</td>
<td>Advanced gastrointestinal  cancer</td>
<td>40 (20/20)</td>
<td>58.55 (13.00)</td>
<td>ACT</td>
<td>Education/ Support care</td>
<td>Baseline, 2-week, and 3-month post-intervention</td>
<td>Psychological flexibility: AAQ-II Fatigue: FSI-I Quality of life: MQOL-R</td>
</tr>
</tbody>
</table>

Abbreviations: E, experimental; C, control; SD, Standard deviation; ACT, Acceptance and Commitment Therapy; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II; POMS, Profile of Mood States; FACT-G, Functional Assessment of Cancer Therapy-General; PROMIS, Patient-Reported Outcomes Measurement Information System; FSI-I, Fatigue Symptom Inventory-Interference; DT, Distress thermometer; AAQ-II, Acceptance and Action Questionnaire II; K10, Kessler Psychological Distress Scale; EQ-5D-5L, European Quality of Life-5 Dimension-5 Level; DASS-21, Depression Anxiety Stress Scales; SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale; GAD-7, Generalized Anxiety Disorder Scale; PHQ-9, Patient Health Questionnaire; FACT-L, Functional Assessment of Cancer Therapy-Lung; MQOL-R, McGill Quality of Life Questionnaire-Revised.
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Brief name</th>
<th>Why</th>
<th>What (materials and procedures)</th>
<th>Who provided, how and where</th>
<th>When and how much</th>
<th>Tailoring and modification</th>
<th>How well</th>
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<tbody>
<tr>
<td>Rost et al. (2012)</td>
<td>ACT</td>
<td>Yes</td>
<td>Incorporating key psychological processes typically targeted by ACT, such as mindfulness, acceptance and values. Metaphors and therapeutic strategies, such as creative hopelessness and control as the problem, were included to set up the treatment rationale.</td>
<td>• A psychologist&lt;br&gt;• Face-to-face; Individually&lt;br&gt;• Facilitator's office, chemotherapy treatment room, inpatient ward and physician exam rooms</td>
<td>• Length of intervention: 4 months&lt;br&gt;• Number of sessions: 12&lt;br&gt;• Duration per session 60 min</td>
<td>• NR&lt;br&gt;• NR</td>
<td>• Strategies: minimize travel and time requirements by scheduling appointments in line with clinic visits and/or chemotherapy treatments; patients often completed the questionnaires when waiting for their appointment.</td>
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<tr>
<td>Mosher et al. (2018)</td>
<td>ACT</td>
<td>Yes</td>
<td>Session 1: discuss patient coping strategies for managing symptoms and distress; Session 2: practice mindfulness exercise; Session 3: practice cognitive defusion; Session 4: practice acceptance; Session 5: identify personal values; Session 6: plan and practice values-consistent actions.</td>
<td>• A master’s level social worker with experience using ACT&lt;br&gt;• Telephone; Individually and dyadic&lt;br&gt;• N/A</td>
<td>• Length of intervention: 6 weeks&lt;br&gt;• Number of sessions: 6&lt;br&gt;• Duration per session 50–60 min</td>
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<tr>
<td>Mosher et al. (2019)</td>
<td>ACT</td>
<td>Yes</td>
<td>Session 1: discuss current coping strategies for managing symptoms and distress; Session 2: practice mindfulness exercise; Session 3: practice cognitive defusion; Session 4: practice self as context; Session 5: identify core values; Session 6: practice value-based actions.</td>
<td>• A master’s level social worker with experience using ACT • Telephone; Individually • N/A</td>
<td>• Length of intervention: 6 weeks • Number of sessions: 6 • Duration per session 50 min</td>
<td>• Participants learned the same skills, in-session and home practices were tailored to their cancer-related or care-related experiences and other challenges.</td>
<td>• NR</td>
</tr>
<tr>
<td>Serfaty et al. (2019)</td>
<td>ACT</td>
<td>Yes</td>
<td>The first four sessions involved helping the participant understand the concept and the core elements of ACT. The last four sessions aimed at helping patients practice them.</td>
<td>• A therapist with at least 2 years of experience using ACT • Face-to-face; Individually • Hospice day-therapy unit, patients’ home or therapist’s clinic</td>
<td>• Length of intervention: 3 months • Number of sessions: 8 • Duration per session: 60 min</td>
<td>• NR</td>
<td>• NR</td>
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<tr>
<td>Author, Year</td>
<td>Brief name</td>
<td>Why</td>
<td>What (materials and procedures)</td>
<td>Who provided, how and where</td>
<td>When and how much</td>
<td>Tailoring and modification</td>
<td>How well</td>
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<tr>
<td>Pan et al. (2020)</td>
<td>ACT</td>
<td>Yes</td>
<td>Session 1: distinguish between reality and spiritual experience; Session 2: focus on finding insights into the validity of thought and action; Session 3: focus on the present moment rather than mental distress; Session 4: oral aikido exercises to accept unwanted feelings; Session 5: learn self-compassion and self-respect; Session 6: provide guidance on how to exercise self-control to prevent future conflicts.</td>
<td>• Nurses trained by an experienced psychologist • Face-to-face; Individually • Inpatient ward</td>
<td>• Length of intervention: 8 weeks • Number of sessions: 6 • Duration per session: 90 min</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Zhang et al. (2021)</td>
<td>ACT</td>
<td>Yes</td>
<td>Help patients master six core skills of ACT, respectively, including acceptance, cognitive defusion, being present, self as context, values and committed actions.</td>
<td>• A primary nurse and a nurse with psychological consultant qualification • Face-to-face; Individually • Inpatient ward</td>
<td>• Length of intervention: NR • Number of sessions: 6 • Duration per session: NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Author, Year</td>
<td>Brief name</td>
<td>Why</td>
<td>What (materials and procedures)</td>
<td>Who provided, how and where</td>
<td>When and how much</td>
<td>Tailoring and modification</td>
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<tr>
<td>Li et al. (2022)</td>
<td>ACT</td>
<td>Yes</td>
<td>Session 1: review experiences on the struggles with cancer-related fatigue and realize the consequence of controlling fatigue and cancer experiences, thus introducing acceptance as an alternative; Session 2: separate thoughts or feelings related to the experience of fatigue and lung cancer with literal truth and view them objectively and transcendently; Session 3: clarify personal values and present the smallest value-guided goal; Session 4: emphasize the ongoing value-based goals and committed to actions for a meaningful cancer life.</td>
<td>A PhD candidate in nursing with experience in oncological and psychological care; Face-to-face and video conferencing; Individually</td>
<td>Length of intervention: 4 weeks; Number of sessions: 4; Duration per session: 60–90 min</td>
<td>NR; NR</td>
<td>Strategies: the participants received a reminder of appointments via WeChat in advance. Adherence rate: 87.5 (35/40)</td>
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<td>Fidelity: 5.90 to 6.60 (rating scale: 1–7)</td>
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</table>

Assessment and Strategies: The interventionist received ACT trainings for 15 days and online group supervision every 2 weeks. The interventionist conducted self-evaluation with a day-to-day diary and a 60-item ACT fidelity checklist to assess whether each point occurred in the session recording. Semi-monthly meeting with supervisor was held to ensure adherence to the protocol. Randomly selected 20% of the intervention audiotapes were reviewed by ACT practitioners to provide feedback to adjust the interventionist’s skills.
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Brief name</th>
<th>Why</th>
<th>What (materials and procedures)</th>
<th>Who provided, how and where</th>
<th>When and how much</th>
<th>Tailoring and modification</th>
<th>How well</th>
<th>Adherence\textsuperscript{a}</th>
<th>Fidelity\textsuperscript{b}</th>
</tr>
</thead>
</table>
| Mosher et al. (2022) | ACT | Yes | During the first session, the therapist asked about the patients' background and strategies for coping with fatigue and introduced the practice of mindfulness. During the next six sessions, patients practiced mindfulness, learned adaptive coping skills, clarified their values and set SMART goals (specific, measurable, achievable, relevant and time-bound) based on their values. | - A master's level mental health clinician and a doctoral level psychologist with experience using ACT  
- Telephone; Individually and dyadic  
- N/A | - Length of intervention: 6 weeks  
- Number of sessions: 6  
- Duration per session: 50 min | - The ACT was adapted to the dyad by including joint mindfulness practices and leveraging the relationship during discussions.  
- NR | - Strategies: NR  
- Adherence rate: 80.0% (32/40) | - Assessment and Strategies: The therapists were trained and supervised weekly by two psychologists. A master's level clinician, two psychologists and two doctoral students in clinical psychology randomly reviewed 40% of recordings for adherence to the manuals using checklists. Psychologists provided feedback on treatment fidelity and quality, and role plays were conducted to improve fidelity.  
- Fidelity rate: 98% |

Abbreviations: TIDieR, Template for Intervention Description and Replication; ACT, Acceptance and Commitment Therapy; NR, Not reported; N/A, Not applicable.

\textsuperscript{a}Adherence rate refers to the number of patients attending all sessions in ACT and control groups/total number of patients completing the baseline assessment.

\textsuperscript{b}Fidelity rate refers to the number of required topics and exercises covered in each session/total number of fidelity criteria.
registered at Clinical Trials.gov, whereas the other three studies were unregistered. Although prospective trial registration is a transparent mechanism to identify publication or reporting bias, it does not prevent low-quality trials, data manipulation or fraud, because a change or deletion of registration information could be reasonable and important problems also existed in the quality of information in trial registries (Tovey et al., 2015). Statistical checks were not performed as they cannot detect fraudulent trials (Tovey et al., 2015), and there were no reasonable grounds for suspicion about the included studies (Roberts et al., 2015). In addition to database searches, Google Scholar and Clinical Trials.gov registry websites were searched to retrieve unpublished data. Therefore, we conclude that no specific problems of research integrity were detected in the included studies and incorporated these studies into the meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation</th>
<th>Allocation concealment</th>
<th>Baseline outcome measurements similar</th>
<th>Baseline characteristics similar</th>
<th>Incomplete outcome data</th>
<th>Knowledge of the allocated interventions adequately prevented during the study</th>
<th>Selective outcome reporting</th>
<th>Protection against contamination</th>
<th>Other risks of bias</th>
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<tr>
<td>Li et al. 2022</td>
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<td>Serfaty et al. 2019</td>
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<td>Zhang et al. 2021</td>
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### 3.5 Effects of acceptance and commitment therapy

#### 3.5.1 Primary outcomes

**Psychological flexibility**

Three studies (Mosher et al., 2022; Serfaty et al., 2019; Zhang et al., 2021), involving 182 participants, measured psychological flexibility. The meta-analysis using the random-effects model suggested that Acceptance and Commitment Therapy had a non-significant effect on psychological flexibility among people with advanced cancer ($MD = -3.42, 95\% CI: -6.90$ to $0.06, p = .05$) (Figure 4). High heterogeneity was noted across these studies ($I^2 = 78\%, p = .05$).

**Psychological symptoms**

Six studies (Li et al., 2022; Mosher et al., 2018, 2019; Pan et al., 2020; Rost et al., 2012; Zhang et al., 2021), involving 363 participants, measured anxiety. The meta-analysis showed a significant difference in anxiety between the Acceptance and Commitment Therapy and control groups ($SMD = -1.22, 95\% CI: -2.37$ to $-0.06, p = .04$) (Figure 5a). High heterogeneity was noted among these studies ($I^2 = 95\%, p < .001$). Subgroup analysis based on possible grouping factors suggested that heterogeneity remained high in the subgroups (Appendix S2). A ‘low’ GRADE rating was assigned to the alleviation of anxiety using Acceptance and Commitment Therapy due to inconsistency (Table 3).

Six studies (Li et al., 2022; Mosher et al., 2018, 2019; Pan et al., 2020; Rost et al., 2012; Zhang et al., 2021), involving 363 participants, measured depression. The meta-analysis showed a significant difference in depression between the Acceptance and Commitment Therapy and control groups ($SMD = -1.28, 95\% CI: -2.37$ to $-0.19, p = .02$) (Figure 5b). High heterogeneity was noted among these studies ($I^2 = 95\%, p < .001$). Subgroup analysis based on possible grouping factors suggested that heterogeneity remained high in the subgroups (Appendix S2). A ‘low’ GRADE rating was assigned to the alleviation of depression using Acceptance and Commitment Therapy due to inconsistency (Table 3).

Three studies (Mosher et al., 2019; Rost et al., 2012; Serfaty et al., 2019), involving 139 participants, measured psychological distress. The meta-analysis suggested that Acceptance and Commitment Therapy significantly alleviated psychological distress in people with advanced cancer ($SMD = -0.38, 95\% CI: -0.72$ to $-0.02, p = .01$).
−0.04, \( p = .03 \) (Figure 5c). Low heterogeneity was observed across these studies (\( I^2 = 0\% \), \( p = .38 \)). A ‘moderate’ GRADE rating was assigned to the alleviation of psychological distress using Acceptance and Commitment Therapy due to imprecision (Table 3).

3.5.2 Secondary outcomes

Physical symptoms
Two studies (Mosher et al., 2018, 2019), involving 97 participants, measured pain. Both studies showed non-significant differences between the Acceptance and Commitment Therapy and control groups. Meta-analysis was not conducted considering the limited number of RCTs.

Four studies (Li et al., 2022; Mosher et al., 2018, 2019, 2022), involving 177 participants, measured fatigue. The meta-analysis showed that Acceptance and Commitment Therapy significantly alleviated fatigue in people with advanced cancer (MD = −0.69, 95% CI: −1.35 to −0.04, \( p = .04 \)). Low heterogeneity was observed across these studies (\( I^2 = 11\% \), \( p = .34 \)) (Figure 6). A ‘moderate’ GRADE rating was assigned to the alleviation of fatigue using Acceptance and Commitment Therapy due to imprecision (Table 3).

QoL
Four studies (Li et al., 2022; Mosher et al., 2022; Rost et al., 2012; Serfaty et al., 2019), involving 169 participants, measured QoL. The meta-analysis suggested that Acceptance and Commitment Therapy significantly improved QoL of people with advanced cancer (SMD = 0.74, 95% CI: 0.43 to 1.05, \( p < .001 \)) (Figure 7). Low heterogeneity was found across these studies (\( I^2 = 0\% \), \( p = .91 \)). A ‘moderate’ GRADE rating was assigned to the improvement of QoL using Acceptance and Commitment Therapy due to imprecision (Table 3).

3.6 Sensitivity analysis

This review included two studies (Pan et al., 2020; Zhang et al., 2021) that were not available in English; these assessed three of the seven outcomes, including psychological flexibility, anxiety and depression. Sensitivity analysis was conducted by omitting these two
studies, and the results for psychological flexibility and anxiety did not change significantly. However, the results for depression were altered, suggesting that the results were relatively unstable. Appendix S3 reports the detailed results of the sensitivity analysis.

4 | DISCUSSION

This review of eight RCTs found that Acceptance and Commitment Therapy had significant effects on anxiety, depression, psychological distress, fatigue and QoL but non-significant effects on psychological flexibility and pain in people with advanced cancer. Effective improvement in fatigue was observed in this meta-analysis. This was a new finding, as it was inconsistent with a previous review finding (Li, Wong, et al., 2021) that Acceptance and Commitment Therapy failed to alleviate fatigue in people with advanced cancer. Furthermore, our review provides new evidence on the effect of the intervention on psychological flexibility. Compared with the previous review (Li, Wong, et al., 2021), the current meta-analysis provided stronger evidence by including four
more RCTs (Li et al., 2022; Mosher et al., 2022; Pan et al., 2020; Zhang et al., 2021).

Psychological flexibility, as the general goal of Acceptance and Commitment Therapy, is the direct causal factor of this therapy (Li, Wu, et al., 2021). Contrary to our expectations, the results showed that Acceptance and Commitment Therapy had no significant effect on psychological flexibility. This finding contradicts a previous meta-analysis (Zhao et al., 2021) that involved 10 studies with 883 people with cancer and found a moderate effect of Acceptance and Commitment Therapy on psychological flexibility. Among the three studies included in our meta-analysis, Zhang et al. (2021) (involving 100 participants) found that psychological flexibility was greatly improved in the intervention group, while the remaining two studies by Mosher et al. (2022) and Serfaty et al. (2019) (involving 40 participants) showed weak and non-significant improvement in psychological flexibility. In other words, small sample sizes may have limited the measure’s sensitivity to change. Considering the limited number of studies analysing this outcome and the high heterogeneity across the three studies, we cannot draw definite conclusions. Thus, further studies with larger sample sizes are warranted to determine the effectiveness of Acceptance and Commitment Therapy on the psychological flexibility of people with advanced cancer.

Negative emotions are common in patients approaching the end of life (Lee & Ramaswamy, 2020). This review indicated that Acceptance and Commitment Therapy had significant effects on anxiety, depression and psychological distress in people with advanced cancer. These results are supported by multiple meta-analyses targeting different populations (Bai et al., 2020; Hughes et al., 2017; Zhao et al., 2021). This is probably because Acceptance and Commitment Therapy increases physical activities and social interactions among people with advanced cancer, making them focus on the present life instead of losing themselves in negative feelings (Zhao et al., 2021). However, there was high heterogeneity across the studies on anxiety and depression, which may be due to the diversity of outcome measurement tools, therapists and intervention delivery formats. Therefore, these results should be cautiously interpreted. Future studies need to carefully consider the intervenor and the format and adopt validated and preferably consistent instruments to measure the same outcomes. It is also necessary to investigate whether the aforementioned factors affect the magnitude of the intervention effect.

With the deterioration of the disease, people with advanced cancer often suffer from physical distress, commonly manifesting as pain, fatigue and other treatment-related symptoms (Henson et al., 2020). Our results showed that Acceptance and Commitment Therapy significantly alleviated fatigue in people with advanced cancer. This finding coincides with that of a systematic review involving people with fibromyalgia (Hegarty et al., 2020) and a trial involving people with chronic fatigue ( Jacobsen et al., 2017). However, this finding contradicts a previous review finding (Li, Wong, et al., 2021). Differences in findings could be due to the narrative nature of the previous review and the additional inclusion in this meta-analysis of two RCTs (Li et al., 2022; Mosher et al., 2022) measuring fatigue, compared with the previous. Only two studies (Mosher et al., 2018, 2019) measured pain in people with advanced cancer, and the results were not statistically significant; meanwhile, inconsistent conclusions were found in previous reviews of people with chronic pain (Du et al., 2021b; Hughes et al., 2017). As we included limited studies with small samples, data synthesis was not conducted; thus, the findings should be interpreted with caution. Future studies should include pain measurements to better clarify the effectiveness of Acceptance and Commitment Therapy for pain.

A good QoL for people with advanced diseases is the ultimate goal of palliative care (Chang et al., 2021). Our results revealed that Acceptance and Commitment Therapy remarkably improved QoL of people with advanced cancer, which coincides with the results of a meta-analysis involving people with cancer (Zhao et al., 2021). Notably, each of the four studies (Li et al., 2022; Mosher et al., 2022; Rost et al., 2012; Serfaty et al., 2019) included in this meta-analysis consistently presented significant improvement of QoL, and low heterogeneity was found across these studies. This is possibly because people with advanced cancer who receive Acceptance and Commitment Therapy may attempt to normalize their distressing thoughts and live in the moment. More importantly, they may re-examine their lives based on an overall perspective, identify personal values and take activities to improve their conditions and consequently their QoL (Zhao et al., 2021).

The delivery format, intervenor and intensity of Acceptance and Commitment Therapy were diverse. Due to the limited number of studies, we failed to draw definite conclusions about the optimal intervention components. It is worthwhile to discuss intervention characteristics to inform future research and practice. In the included studies, approximately 75% of the interventions did not exceed six sessions. This should be considered especially for people with advanced cancer, as they have a limited life expectancy. A further consideration is that shorter interventions with fewer sessions may facilitate participants to remember and consolidate what they have learned. Face-to-face delivery was the most adopted format in clinical settings. Three of the included studies (Mosher et al., 2018, 2019, 2022) attempted a telephone-based format and showed a higher adherence rate (76%–83%) than face-to-face format (62%–68%), possibly because telephone-based delivery is not affected by limitations of time and distance. However, face-to-face interventions in this review tended to be effective in alleviating psychological symptoms, whereas telephone-based interventions were not. Telephone-based formats may hinder interveners from understanding participants accurately and provide targeted programmes, adversely affecting patients’ access to knowledge and skills. Thus, further studies are needed to explore interventions with different delivery formats and dosages to determine the optimal Acceptance and Commitment Therapy model.

With regard to intervention providers, two of the included studies (Pan et al., 2020; Zhang et al., 2021) incorporated nurses. A qualitative study from the nurses’ perspective found that Acceptance and Commitment Therapy was useful for nurses in helping patients cope with struggles, enriching typical ward duties and dealing with
personal stress (Tyrberg et al., 2017). Nurses are the main force in caring for people with advanced cancer and can better understand their distress, as nurses have more access to them than other healthcare professionals. They may be excellent candidates for implementing interventions. Therefore, future research and practice should consider more involvement of nurses.

4.1 | Limitations

This review had some limitations. First, we only included eligible studies in English and Chinese, thereby omitting potential studies in other languages. Second, there were inconsistencies and imprecision across the studies, which caused low or moderate certainty of evidence. Third, the same parameters were measured using multiple instruments, which may cause measurement bias and effect deviation. Fourth, different control conditions may have mitigated the intervention effects. Finally, the relatively small sample sizes for most of the included RCTs could affect the accuracy of the results due to a lack of sufficient statistical power to detect the intervention effects.

4.2 | Implications for future research and practice

This meta-analysis showed the application value of Acceptance and Commitment Therapy for clinical decision-making. Given the limited number of included RCTs, more high-quality RCTs with powered sample sizes are required. Future RCTs should consider using the TIDieR checklist to ensure sufficient description of intervention characteristics, along with the CONSORT checklist, to optimize the reporting quality of RCTs. Validated and consistent instruments are recommended when measuring the effectiveness of the same outcome, and appropriate controls should be chosen to improve the internal validity of the results. Furthermore, future studies are warranted to explore an optimal intervention design. Conducting more RCTs with different intervention components is a desirable way.

Palliative care nursing emphasizes the provision of holistic care. This study showed significant improvements attributable to Acceptance and Commitment Therapy in psychological symptoms among people with advanced cancer, along with fatigue and QoL. These findings can inform clinical nursing interventions. Nurses play a critical role in providing holistic care to people with advanced cancer. Compared with other healthcare professionals, nurses usually spend most time with patients and can better identify their unmet psychological needs, which may contribute to building a therapeutic alliance. Therefore, training for nurses is necessary to help them provide evidence-based Acceptance and Commitment Therapy to support people with advanced cancer. Given patients’ limited life expectancies and the time limitations of nurses, concise and targeted intervention programmes may be feasibly integrated in daily nursing practice. This integration will allow nurses to effectively manage the psychological and physical symptoms of people with advanced cancer and promote their QoL and the quality of holistic care.

5 | Conclusions

Acceptance and Commitment Therapy is effective in improving anxiety, depression, psychological distress, fatigue and QoL in people with advanced cancer. This review highlights the need for more rigorously designed RCTs to ascertain these findings, and for further research to determine the optimal intervention model to maximize the intervention effect. Nurses play a pivotal role in caring for people with advanced cancer and are more aware of the symptom burdens experienced by patients; thus, they are better placed to implement evidence-based Acceptance and Commitment Therapy to improve patients’ well-being and promote the efficiency of palliative care nursing. Healthcare policymakers should support nurses in integrating Acceptance and Commitment Therapy in daily nursing practice, which presents an opportunity to extend this intervention to more people with advanced cancer.

Author Contributions

All authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE*): (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content.

*http://www.icmje.org/recommendations/

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Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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References


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