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The effects of acceptance and commitment therapy (ACT) on psychological and physical outcomes among cancer patients and survivors: An umbrella review

Christina Sauer a,b,*, Alexander Haussmann Gregor Weissflog d,e

- a Department of General Internal and Psychosomatic Medicine, University Hospital Heidelberg, Heidelberg, Germany
- b Institute of Medical Psychology, University Hospital Heidelberg, Heidelberg, Germany
- ^c Division of Physical Activity, Prevention, and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany
- ^d Department of Medical Psychology and Medical Sociology, University Medical Center, Leipzig, Germany
- ^e Comprehensive Cancer Center Central Germany (CCCG) Leipzig-Jena, Leipzig, Germany

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ABSTRACT

Background: Acceptance and Commitment Therapy (ACT) is a promising approach in psycho-oncology that has led to an increasing number of studies and reviews. This systematic umbrella review provides a comprehensive overview of the results of existing systematic reviews and meta-analyses to investigate the trans-symptomatic (i.e., psychological and physical symptoms) efficacy of ACT in the context of cancer. The study addresses both physical and psychological outcomes, aiming to identify existing research gaps and delineate potential focal points for future studies exploring the application of ACT in psycho-oncological settings.

Methods: A systematic literature search was conducted in Pubmed, Ebsco Host Academic Search Complete (incl. APA PsycInfo), Web of Science, Cochrane Library, website of the Association of Contextual Behavioral Science (ACBS), and Prospero. To be included, studies had to meet the following criteria: 1) be a systematic review and/or meta-analysis focusing on ACT and its impact on psychological and physical outcomes in cancer patients or survivors; 2) include only patients with oncological conditions; 3) be published in English. The quality of the reviews and meta-analyses was assessed using the AMSTAR 2 criteria.

Results: We included eight systematic reviews and meta-analyses in our synthesis. Results of the reviews and meta-analyses indicate that ACT interventions increase the health-related quality of life (HRQoL) and psychological flexibility, and reduce depression, anxiety, and psychological distress in cancer patients and survivors. The best evidence exists regarding psychological distress and HRQoL. The efficacy of these interventions concerning other psychological outcome measures (e.g., fear of progression/recurrence, hope) and biological parameters has not yet been well investigated. Moderator analyses revealed larger effects for younger patients, individuals from Eastern countries (Iran, China), and after longer intervention durations. Results suggest potential differential effects based on the cancer stage. According to the AMSTAR 2 criteria, the quality of the included reviews was low or critically low.

Conclusion: Recent meta-analyses and reviews suggests that ACT interventions are an effective and evidence-based treatment for increasing HRQoL and reducing psychological distress in patients with cancer. However, the results should be interpreted with caution, as the quality of the included reviews was generally low. Our synthesis highlights the need for more high-quality randomized controlled trials, reviews, meta-analyses, and mediator analyses in this research area.

1. Introduction

A cancer diagnosis is associated with a wide range of consequences and changes on the physical, psychological, financial, and social levels. Cancer patients, survivors, and their families must cope with and adjust to the drastic challenges this presents. About 50% of patients with cancer report increased levels of distress and various symptoms like fatigue, sleep disturbances, mobility impairment, pain, and

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^{*} Corresponding author. Heidelberg University Hospital Institute of Medical Psychology Bergheimer Str. 20 69115 Heidelberg Germany. E-mail address: christina.sauer@med.uni-heidelberg.de (C. Sauer).

psychological burdens like worry, fear, sadness, and nervousness (Carlson et al., 2019; Mehnert et al., 2018). One-third suffer from a diagnosable co-morbid mental disorder (Mehnert et al., 2014). Psycho-oncological interventions that support the adaption to all these challenges are therefore needed to reduce symptoms of psychological distress like depression and anxiety and improve well-being and health-related quality of life (HRQoL).

Acceptance and Commitment Therapy (ACT) is a transdiagnostic functional-contextual approach of third-wave cognitive-behavioral therapy (CBT) (Hayes et al., 2006). It was shown to be effective in various psychological disorders (e.g., Ferreira et al., 2022; Gloster et al., 2020), chronic pain (Hughes et al., 2017), insomnia (Ruan et al., 2022), and chronic physical diseases (A-tjak et al., 2015).

Based on the premise that illness, pain, and suffering are unavoidable parts of our lives, ACT conceptualizes cancer patients' distress as a normal response to the challenging experience of a serious illness. This distress is classified as primary suffering (e.g., normal levels of fear of cancer progression or recurrence, grief about loss of functional capacity). In contrast, secondary suffering results from maladaptive coping processes such as experiential avoidance or control strategies (e.g., rumination on disease-related experiences or 'positive thinking'). In cancer patients, these attempts to control or alter the form, frequency, or sensitivity of private experiences are often associated with dysfunctional behaviors, such as over- or under-utilizing of the healthcare system to reduce concerns about their condition or failure to initiate and/or maintain disease self-management behaviors (Herbert et al., 2022). Control attempts can also manifest themselves as over-focusing on one value (e.g., health) to the detriment of others (e.g., social contacts). In contrast to traditional CBT approaches (e.g. Beckian therapy), ACT offers a significantly different approach to dealing with dysfunctional thoughts and feelings. It is characterized by an acceptance- and value-based way of dealing with primary suffering (e.g. painful experiences and emotions), thereby reducing or even preventing secondary suffering, rather than changing thoughts and feelings through cognitive reconstruction. ACT therapists work with their cancer patients using six core processes, which constitute the Hexaflex of psychological flexibility, to achieve a reduction of secondary suffering. In cancer patients, this includes "acceptance" as the willingness to bear unpleasant emotions and experiences (e.g., grief over functional restrictions, fear of progression, pain, fatigue), "contact with the present moment" as the non-judgmental focus on the 'here-and-now' (which can be shaped, in contrast to an uncertain future), "defusion" as a de-literalizing of thoughts (e.g., 'The pain is certainly a sign of cancer progression.'), the contact to the unchangeable "self-as-context" (in contrast to the many changes due to the cancer illness), and the promotion of and active engagement in value-based living (e.g., "values" and "commitment"). For instance, a cancer diagnosis can lead to a re-prioritization of values. ACT, with its values-based approach, can help to clarify these values.

All these hexaflex processes are targeted in ACT treatments with the overall goal of increasing the psychological flexibility of cancer patients to help them cope with the above-mentioned substantial somatic, psychological, and social changes. Beyond psychological flexibility, ACT treatment protocols also focus on broader ACT-consistent processes like self-compassion and emotional approach coping (i.e., coping with stressors by actively acknowledging, processing, and expressing one's emotions) (Fishbein et al., 2022; Miller-Mendes et al., 2023).

In their systematic review and meta-analysis, Fawson et al. (2023) examined the relationship between distress and specific hexaflex processes (i.e., components of psychological flexibility). The strongest empirical evidence was found for the association with psychological distress in patients with cancer (Fawson et al., 2023). Higher scores on flexible processes (such as present moment awareness and acceptance) were associated with lower distress, with small to medium effects (pooled r with -0.39 and -0.24, respectively). Higher scores on inflexible processes (cognitive fusion and experiential avoidance) were associated with higher distress, with strong effects (pooled r with 0.57

and 0.58, respectively). Moderator analyses for the stage of diagnosis, time since diagnosis, age and gender did not reveal significant relationships between the individual ACT processes and distress. The results of this meta-analysis provide a rationale for ACT interventions as an effective approach for improving mental health in psycho-oncology settings. Comparable analyses for the relevant somatic outcomes in cancer patients are still lacking, and this should be investigated in future research to estimate the trans-symptomatic potential of ACT interventions in cancer patients. Physical symptoms like fatigue or sleep disorders are highly prevalent and burdensome in cancer patients and survivors (Al Maqbali et al., 2022; Pearce et al., 2017). Hence, the trans-symptomatic perspective, akin to the transdiagnostic approach in psychopathology, holds significance in psycho-oncology. In the context of the biopsychosocial model, psychological and physiological symptoms are reliably associated and interact in cancer patients (e.g., Maurer et al., 2021; McFarland et al., 2022), highlighting the need for effective *trans*-symptomatic interventions.

1.1. Aim of this umbrella review

Since 2011, the number of publications focusing on the efficacy of ACT interventions in improving psychological and physical outcomes in cancer patients and survivors increased from two studies in 2011 to 38 studies in 2022, and 31 publications in 2023 (source: Pubmed; January 2024). Despite this large number of studies, which also include systematic reviews, an overarching analysis of the current empirical evidence on the effects of ACT on psychological and physical outcomes in patients with cancer and survivors is still missing. Due to different foci and outcomes in various studies, and multiple burdens in the context of cancer, this overview is especially important in the field of psychoncology. Furthermore, this umbrella review aims to investigate the *trans-symptomatic* efficacy (i.e., psychological and physical outcomes) of ACT in cancer patients.

This systematic umbrella review provides a comprehensive overview of the results of existing systematic reviews and meta-analyses, particularly for patient groups with diverse characteristics (e.g., stages of disease), designs (RCTs vs. non-RCTs) and outcomes. The review will enable us to detect research gaps and targets for future studies investigating ACT in psycho-oncological settings.

2. Methods

A study protocol for this umbrella review was published and registered on PROSPERO (CRD42022365420).

2.1. Inclusion criteria

For this umbrella review, we searched for systematic reviews and/or meta-analyses published in English on the topic of ACT in (exclusively) patients with cancer.

The study used the Population, Intervention, Comparator, Outcome (PICO) criteria to establish the following inclusion criteria: P= patients with cancer or survivors (all entities); I= ACT interventions (i.e., all hexaflex processes were addressed) or ACT-based interventions (i.e., ACT is the rationale of the intervention, but not all processes of the hexaflex are addressed during the intervention); C= all comparators (waitlist, standard care, passive or active controls) and designs (RCTs, non-RCTs, single-arm pre-post); O= anxiety, depression, HRQoL, distress, fear of progression/recurrence, insomnia, fatigue, physiological and biological outcomes.

2.2. Data sources and search strategy

For this umbrella review, a systematic literature search of Pubmed, Ebsco Host Academic Search Complete (incl. APA PsycInfo), Web of Science, Cochrane Library, website of the Association of Contextual Behavioral Science (ACBS), and Prospero were conducted by the first author on September 29th, 2023. The following search string was used for the search (PubMed): ((acceptance and commitment therapy[Title/Abstract]) OR (ACT-based[Title/Abstract])) AND ((cancer[Title/Abstract]) OR (tumor[Title/Abstract]) OR (neoplasm[Title/Abstract]) OR (oncology[Title/Abstract]) OR (carcinoma[Title/Abstract]) OR (malignancy[Title/Abstract])) AND ((systematic review[Title/Abstract) OR (meta-analysis[Title/Abstract])). The search strings for the other data bases are available in supplement A.

2.3. Eligibility assessment and data extraction

Two authors independently screened titles and abstracts against inclusion and exclusion criteria and read all full texts of the potentially relevant reviews and meta-analyses. Data on review characteristics based on the criteria for umbrella reviews by the Joanna Briggs Institute (Aromataris et al., 2015) were independently extracted by the first and the second author, and any discrepancies were resolved by the last author.

2.4. Assessment of methodology quality

Review quality was appraised independently by two authors using the validated AMSTAR2 tool for systematic reviews and meta-analyses including RCTs and non-RCTs (Shea et al., 2017). Disagreement between the reviewers was resolved through discussion and consultation of the original publication. The AMSTAR2 consists of 16 items and results in an overall rating based on weakness in critical domains. To assess the overall quality of the included studies, we used the five-item scheme (Pieper et al., 2021), which reflects the key domains for our umbrella review. As the AMSTAR2 criteria are considered to be very conservative and may show floor effects (De Santis et al., 2022), we also looked at the number of criteria met to better distinguish the quality of the included reviews and meta-analyses.

3. Results

3.1. Prisma flow diagam

The PRISMA flow diagram (Page et al., 2021; see Fig. 1) summarizes our search. Systematic reviews and meta-analyses of ACT and 'chronic

disease', 'illness,' and 'health' (rather than 'cancer' or 'oncology') (A-tjak et al., 2015; Dochat et al., 2021; Graham et al., 2016; Herbert et al., 2022; Maunick et al., 2023) were also examined to identify studies involving oncology patients. However, these publications were excluded as they included very few primary studies ($n \le 7$) with patients with cancer and those were all already considered in the included reviews and meta-analyses, and no separate meta-analysis for cancer patients was conducted. Before screening, our search yielded nine systematic reviews and meta-analyses. One meta-analysis (Z. Li, Wu, et al., 2021) was excluded due to critical methodological issues (e.g., in this meta-analysis, one primary study included no patients with cancer). Due to the small number of included reviews and meta-analyses, pooling of effect sizes was not possible. The included eight systematic reviews (four with meta-analysis) were published in 2019 (n = 1), 2021 (n = 5), 2022 (n = 1) and 2023 (n = 1). Two reviews focused solely on advanced-stage cancer patients (Fang et al., 2023; Huiyuan Li, Wu, et al., 2021), while another review examined cancer survivors (i.e., patients who competed primary treatment and receiving no maintance treatment, p. 428, Mathew et al., 2021). A systematic review with meta-analysis (Hanting Li, Wu, et al., 2021) exclusively reviewed studies with breast cancer patients. Six reviews included both ACT and ACT-based interventions (Gonzalez-Fernandez & Fernandez-Rodriguez, 2019; Hanting Li, Wu, et al., 2021; Huiyuan Li, Wu, et al., 2021; Mathew et al., 2021; Salari et al., 2021; Zhang et al., 2023); Zhao et al. (2021) and Fang et al. (2023) focused exclusively on ACT-interventions. In addition, all reviews included individual and group therapy interventions. The meta-analysis of Zhang et al. (2023) focused on the outcomes of psychological flexibility, sleep, fatigue, and HRQoL. A total of 116 studies were included in the eight reviews. Due to overlapping inclusion criteria between the reviews (e.g., entities, stage of disease), the actual number of studies conducted between 2001 and 2022 is reduced to n = 61 studies. The primary studies were RCTs, quasi-experimental studies, uncontrolled pre-post studies, single-case studies, and case series. Control conditions varied between the primary studies. In three reviews, only RCTs were included (Fang et al., 2023; Hanting Li, Wu, et al., 2021; Zhang et al., 2023).

Table 1 summarizes the characteristics and results of the eight included reviews. More detailed information about the included reviews is provided in Supplement B.

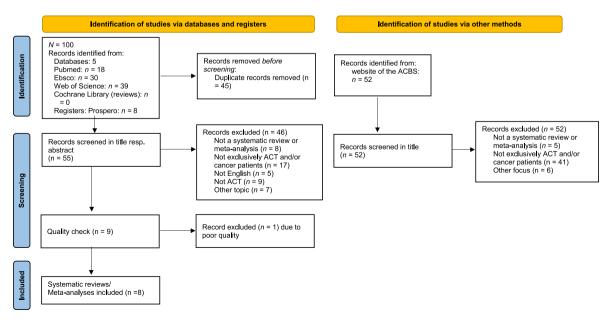


Fig. 1. PRISMA flow diagram for systematic reviews on ACT in psycho-oncology.

Table 1Description and results of the included reviews.

Citation	Objective	Type of review	Participant details	Setting/context	Types of studies	Outcomes
Zhao et al.	investigate the effects of ACT on psychological and physiological distress among cancer patients	meta-analysis with trial sequence analysis, moderating analysis	N = 2256 cancer patients (regardless of ethnicity, gender, age, type and stage)	Intervention included all six core processes of ACT, not combined with other intervention models	17× RCT and 8× non- RCT (CG: active or Waitlist)	Psychological Distress: large ES $(g=0.88; k=18)$, Psychological flexibility: medium ES $(g=0.58; k=10)$ QoL: large ES $(g=1.19; k=7)$ physical distress: no effect $(g=-0.18; k=5)$ Hope: large ES $(g=2.17, k=3)$ High heterogeneity (Q value, I2) for all outcomes Potential publication bias $(significant Egger's regression test)$ for psychological flexibility (corrected $g=0.37$) Trial sequential analysis: data to be unaffected by further studies for psychological distress and quality of live; not for psychological flexibility Moderators for effect on psychological distress: Country (eastern > western) Age (younger > older) Intervention period (longer > shorter)
Li, Wu et al.,	summarize available evidence and assess the efficacy of ACT on physiological and psychological outcomes in patients with breast cancer	Systematic review and meta-analysis	N = 487 Patients with breast cancer ≥18 years	Any form of ACT, 8 interventions group based, one telephone-based	RCTs CG: standard care, passive controls (e.g., placebo controls), or active controls (e.g., other psychological interventions)	Results quality assessment: 1 no risk of bias; 7 unclear (at least on category; 5 high risk (at least on category) Anxiety (n = 4): moderate effect (SMD = -0.58) Depression USA (n = 2): small effect (SMD = -0.30) Depression Iran (n = 4): large effect (SMD = -1.12) Stress (n = 2): moderate effect (SMD = -0.68) Hope (n = 3): large effect (in favour of control! SMD = 0.89) Physiological symptoms: no meta-analysis conducted Psychological flexibility: no meta-analysis conducted Fear of cancer recurrence: no meta-analysis conducted
Gonzalez- Fernandez & Fernandez- Rodriguez	Investigate published studies regarding usefulness of ACT in patients with cancer	systematic review	N = 806 cancer patients (regardless of ethnicity, gender, age, type and stage)	13× individual Intervention, 6x group intervention duration: 1–14 sessions, dose: 1×/2 weeks up to 2×/week	$10 \times$ RCT, $5 \times$ CT, $3 \times$ Case study, $1 \times$ case serie Very small studies (4 < n < 55) Exception Hawkes et al. with n = 410 colorectal cancer patients	Significant Effects: Anxiety (n = 7): post-evaluation: 7 studies; follow-ups (3–12 months): 4 studies Depression (n = 8): post-evaluation: 8 studies (1 Non-RCT); follow-ups (1–12 months): 5 studies (2 Non-RCT); Emotional distress (n = 4): post-evaluation: 4 studies; follow-ups (3 month): 2 studies Quality of life (n = 6): post-evaluation: 4 studies; follow-ups (3–12 months): 3 studiesPsychological flexibility (n = 12): post-evaluation: 11 studies; follow-ups (15 days-12 months): 9 studies
Li, Wong et al.	identify the main contents, mode, fre- quency and duration of ACT in patients with advanced cancer and evaluate its effects on psychological and physical outcomes and healthrelated quality of life by systematically reviewing current studies on the application of ACT	systematic review	Cancer patients (≥18 years); diagnosed with advanced cancer	Studies implemented ACT as an independent or a major part of intervention (the number of Acceptance and Commitment Therapy hours was more than 50% of total therapy hours).	5 RCTs, 1 pre-post-design (single group) CG: usual care, education, waitlist or other therapies	Quality Assessment: One study with low RoB (apart from blinding); 3 with at least one further unclear bias; one with a further RoB; one NRSI with 1 RoB and 1 unclear Effects: Depressive symptoms (n = 5): Two studies with large effects; two non-significant effects (both active controls); one pretest- (continued on next page)

Table 1 (continued)

Citation	Objective	Type of review	Participant details	Setting/context	Types of studies	Outcomes
						posttest study with non-sig, improvements Anxiety (n = 5): One study with significant effect; 3 with non-significant effects); one pretest-posttest study with non-sig. Psychological distress (n = 4): two studies with large significant effects; two with non-significant effects (both active controls) Fatigue (n = 4): all studies with non-significant effects Sleep characteristics (n = 3): One study with significant effects; two with non-significant effects Pain/pain interference (n = 3): all studies with non-significant effects Health-related quality of life (n = 2): one study with significant effect; one non-significant
Mathew et al.	context, mechanisms, and effect of ACT among adult cancer survivors	Systematic review	N = 537 Adult cancer survivors (individuals who has received a cancer diagnosis and completed primary care treatment	Interventions based on ACT (solely or in combination with other therapies)	5 RCTs, 1 RC cross-over design 2 quasi-experimental designs Single-arm pre-post studies (3) survey, case-series	(active control) Quality rating: RCT: 4 low risk of bias; 2 high risk of bias (4 good quality rating; 1 fair; 1 poor) Non-RCTs: all fair quality rating Effects: Psychological flexibility (k = 4): 2 with significant effect; 1 no statistical analysis; 1 similar decrease in IG and CG Anxiety: significant effect post-intervention in 7 studies; in 5 studies at FU (2–6 months); 1 no statistical analysis Distress: significant effect post-intervention in 3 studies; in 3 studies at FU (1–6 months) Depression (k = 4): significant effect post-intervention in 3 studies; in 1 study at FU (1–6 months); 1 no statistical analysis Stress (k = 2): significant effect post-intervention in 2 studies; in 1 study at FU (1 and 6 months) Fear of cancer recurrence (k = 5): significant effect post-intervention in 5 studies; in 5 studies at FU (1–6 months) Quality of life (k = 3): significant effect post-intervention in 3 studies; in 1 study at FU (1 and 6 months); 1 no statistical analysis Further outcomes reported
Salari et al.	effect of ACT on psychological distress in patients with cancer	Systematic review	N = 965 cancer patients, mixed locations	Mostly 4–12 sessions, 3 studies <3 sessions; ACT or ACT-based	10 RCTs, CG: different comparison groups (BA, TAU) semi-experimental, open trial, preliminary study (pre-post-design)	Effects: Psychological distress (n = 7; 4 RCT): Significant effects post- intervention in 3 studies (1 study also in CG); 1 study at FU Anxiety (n = 9; 5 RCT): Significant effects in 6 studies (in 3 studies also in other groups) Depression (n = 11; 5 RCT): Significant effects in 8 studies (in 2 studies also in other groups); 1 study at FU
Zhang et al.	Effectiveness of acceptance and commitment therapy on psychological flexibility, fatigue, sleep disturbance, and quality of life of patients with cancer Exploration of moderation	Systematic review and meta-analysis of RCTs	N = 1643 cancer patients	Interventions: Face to face: 12 Online: 5 Combined 2 4-12 sessions Over 4 weeks-8 months session lengths: 40min- 2h	RCTs CG: usual care, waitlist control, supportive care, standardized talking	Quality assessment: 6 no risk of bias; 8 unclear (at least on category; 5 high risk (at least one category) Effects: Psychological flexibility: large significant effects postintervention (9 studies): MD (continued on next page)

Table 1 (continued)

Citation	Objective	Type of review	Participant details	Setting/context	Types of studies	Outcomes
	effects affecting intervention effectiveness					= -4.22, 95% CI-[-7.86, -0.58]; 3 month FU (4 studies): -4.36, 95% CI [-8.67, -0.05] Significant moderation: higher effect when higher intervention duration Fatigue: no significant effects Post-intervention (6 studies): Hedges' g = -0.03, 95% CI [-0.24, 0.18] 6 weeks FU (3 studies): Hedges' g = 0.21, 95% CI [-0.51, 0.94] No moderators Sleep disturbance: no significant effects Post-intervention (4 studies): Hedges' g = -0.26, 95% CI [-0.82, 0.30] 6 weeks FU (3 studies): Hedges' g = -0.11, 95% CI [-0.45, 0.22] Moderation: Higher effect for older study populations Quality of life: large significant effect Post-intervention (8 studies): Hedges' g = 0.94, 95% CI [0.59, 1.29]
Fang et al.	(a) examine the effectiveness of ACT on psychological flexibility and psychological symptoms in patients with advanced cancers; (b) evaluate the effectiveness of ACT on physical symptoms and QoL(c) identify the intervention characteristics of ACT	systematic review and meta-analysis	N = 488 people with advanced cancer Two studies mixed cancer types, 5 specific entities	Interventions included all six core processes, conducted by psychologists, nurses, PhD candidate in nursing, social workers Intervention duration: 6 weeks- 4 months 4-12 sessions	RCT Different CGs (see Table 1): usual care, educational support, talking control	No moderators Quality assessment: 1 no risk of bias; 6 unclear (at least on category; 1 high risk (at least on category; 1 high risk (at least one category) Effects (all post-intervention; latest available time point) Psychological flexibility (3 studies): non-significant effect (SMD = -1.22, 95% CI: -2.37 to -0.06) Anxiety (6 studies): significant effect (SMD = -1.22, 95% CI: -2.37 to -0.06); low GRADE rating Depression (6 studies): significant effect (SMD = -1.28, 95% CI: -2.37 to -0.19); low GRADE rating Psychological distress (3 studies): significant effect (SMD = -0.38, 95% CI: -0.72 to -0.04); moderate GRADE rating Pain (2 studies): no significant effect in both studies (no meta-analysis) Fatigue (4 studies): significant effect (MD = -0.69, 95% CI: -1.35 to -0.04); moderate GRADE rating Quality of Life (4 studies) significant effect (SMD = 0.74, 95% CI: 0.43 to 1.05); moderate

Abbreviations: ACT Acceptance and Commitment Therapy, BA Behavioral activation, CG Control group, CI Confidence interval, CT Controlled trial, ES Effect size, FU Follow up, GRADE Grading of Recommendations Assessment, Development and Evaluation, HRQoL Health related Quality of Life, I² Heterogeneity, IG Intervention group, k number of studies, MD Mean difference, n sample size, PF Psychological flexibility, SMD Standardized mean difference, RC/RCT Randomized controlled trial, RoB Risk of bias, NRSI = non-randomized study on intervention effect, TAU Treatment as usual.

3.2. Quality of the included reviews

Quality assessment with AMSTAR2 revealed n=2 systematic reviews/meta-analyses with low quality (one flaw in a critical domain) (Mathew et al., 2021; Zhao et al., 2021) and n=6 systematic reviews/meta-analyses with critically low methodological quality (more than one flaw in a critical domain, see Supplement C). For instance, no

meta-analyses assessed the presence and likely impact of publication bias (item 15). In one systematic review, only two of the thirteen quality domains in systematic reviews were partially met (e.g., quality assessment was missing; Gonzalez-Fernandez & Fernandez-Rodriguez, 2019).

The meta-analysis by Zhao et al (2021) (see Supplement C) showed the most fully or partially fulfilled quality criteria (81%, see Supplement C). Of the systematic reviews, the study by Huiyuan Li, Wong, et al.

(2021) met more AMSTAR2-criteria (77%) than the others.

3.3. Key findings of the included reviews

3.3.1. Psychological outcomes

Psychological distress: Seven of eight reviews investigated psychological distress as an outcome. All reviews revealed a significant reduction in psychological distress in cancer patients and survivors after ACT interventions (Fang et al., 2023; Gonzalez-Fernandez & Fernandez-Rodriguez, 2019; Hanting Li, Wu, et al., 2021; Huiyuan Li, Wu, et al., 2021; Mathew et al., 2021; Salari et al., 2021; Zhao et al., 2021). Results of the meta-analysis by Zhao et al. (2021), which was methodologically the best meta-analysis, showed that ACT interventions reduce psychological distress in patients with cancer with a large effect size (pooled effect size at post-intervention with Hedges g = 0.88; k = 18; Zhao et al., 2021). Further, Zhao et al. (2021) conducted a Trial Sequential Analysis (TSA), which allows for determining the required number of participants to achieve reliable results in a meta-analysis (Wetterslev et al., 2017). Results showed that the current trial number was sufficient to estimate the effect of ACT on psychological distress and no more studies are required.

The moderator analysis of this meta-analysis revealed that greater reductions in psychological distress were obtained among patients in Eastern countries (Iran, China with Hedges g=1.39 versus United States, United Kingdom, Spain and Australia with Hedges g=0.35), younger patients ($\beta=-0.08$; p<.01) and after longer interventions ($\beta=0.14$; p<.05) (Zhao et al. (2021).

Other reviews with lower quality revealed a medium effect size of ACT interventions on psychological distress in breast cancer patients at post-intervention or follow-up (FU) with a *Standardized Mean Difference* (SMD) = -0.68 (k=2; Hanting Li, Wu, et al., 2021). The effect on distress in patients with advanced cancer at post-intervention was small (k=3; SMD = -0.38; Fang et al., 2023).

Depression: A stable effect across seven reviews was seen regarding a reduction in depressive symptoms (Fang et al., 2023; Gonzalez-Fernandez & Fernandez-Rodriguez, 2019; Hanting Li, Wu, et al., 2021; Huiyuan Li, Wu, et al., 2021; Mathew et al., 2021; Salari et al., 2021; Zhao et al., 2021). Meta-analyses revealed a medium to large effect size at post-intervention (g=0.97, k=8; Zhao et al., 2021) and at post-intervention or FU (SMD = - 0.77, k=6; Hanting Li, Wu, et al., 2021). In patients with advanced cancer, the meta-analysis of Fang et al. (2023) showed a large effect at post-intervention (SMD=-1.28; k=6).

Health-related Quality of life: Six of eight reviews investigated HRQoL as an outcome, and all found a significant increase in cancer patients and survivors after ACT interventions (Fang et al., 2023; Gonzalez-Fernandez & Fernandez-Rodriguez, 2019; Huiyuan Li, Wu, et al., 2021; Mathew et al., 2021; Salari et al., 2021; Zhao et al., 2021). Meta-analyses revealed a large, pooled effect size for HRQoL (Hedges g = 1.19, k = 7; Zhao et al., 2021; and Hedges g = 0.94, k = 8, Zhang et al., 2023). The TSA of Zhao et al. (2021) indicated that the available evidence is strong enough to draw meaningful conclusions regarding the effect of ACT on HRQoL in cancer patients and survivors. A moderate effect and low heterogeneity were found in patients with advanced cancer (SMD = 0.74, k = 4; Fang et al., 2023).

Anxiety and fear of progression/recurrence: Seven reviews investigated anxiety as an outcome (Fang et al., 2023; Gonzalez-Fernandez & Fernandez-Rodriguez, 2019; Hanting Li, Wu, et al., 2021; Huiyuan Li, Wu, et al., 2021; Mathew et al., 2021; Salari et al., 2021; Zhao et al., 2021). They revealed that ACT interventions showed moderate to large effects in reducing anxiety at post-intervention and FU measurements in patients with cancer and survivors. Meta-analyses in overall cancer patients showed large effects (Hedges g = 0.92, k = 7; Zhao et al., 2021), and a medium effect at post-intervention or FU in patients with breast cancer (SMD = - 0.58, k = 4; Hanting Li, Wu, et al., 2021). In the meta-analysis of Fang et al. (2023) with advanced cancer patients, a large effect was revealed (SMD = 1.22, k = 6) with high heterogeneity

and a low *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) of evidence (i.e., further research is very likely to have an important impact on the confidence in the estimated effect and is likely to change the estimate (Guyatt et al., 2008)). Within the review of Huiyuan Li, Wong, et al. (2021), only one of the six primary studies focusing on advanced cancer patients demonstrated positive effects (study of Rost et al., 2012).

Two reviews investigated fear of progression/recurrence as an outcome, both indicating a significant reduction after the intervention and at FU (up to 6 months) (Hanting Li, Wu, et al., 2021; Mathew et al., 2021).

Hope: Two reviews indicated large effects for an increase of hope (Hanting Li, Wu, et al., 2021; Zhao et al., 2021), but further studies are needed due to a possible publication bias (Zhao et al., 2021).

3.3.2. Physical outcomes

Physical distress: One meta-analysis presented pooled data for physical distress including fatigue and pain with Hedges g=-0.18 (k=5; Zhao et al., 2021). Fang et al. (2023) reported no significant differences in the two included studies investigating physical distress (no meta-analysis was conducted). Within the systematic reviews, there were very few findings regarding the effects of ACT interventions on physical distress (fatigue, pain, sleep) (Huiyuan Li, Wu, et al., 2021; Hanting Li, Wu, et al., 2021).

Fatigue: The meta-analysis of Zhang et al. (2023) showed no significant improvements in the levels of fatigue after ACT compared to CG at post-intervention (Hedges' g=-0.03, p=0.75, k=6) and 6-weeks FU (Hedges' g=-0.21, p=0.56, k=4). In patients with advanced cancer, ACT showed significant effects in reducing fatigue (MD = -0.69, k=4; low heterogeneity; Fang et al., 2023).

Sleep disturbances: Only the meta-analysis of Zhang et al. (2023) investigated sleep disturbances. Results showed no significant improvements with ACT compared to a CG at post-intervention (Hedges' g=-0.26, p=0.37, n=4) and 6-weeks FU (Hedges' g=-0.11, p=0.50, k=3; Zhang et al., 2023). Moderator analysis showed that the association was influenced by age ($\beta=0.15, p=0.04$), i.e., younger patients experienced more improvements in their quality of sleep than older patients after their treatment.

3.3.3. Psychological flexibility

Seven reviews investigated psychological flexibility as an outcome (Fang et al., 2023; Gonzalez-Fernandez & Fernandez-Rodriguez, 2019; Hanting Li, Wu, et al., 2021; Mathew et al., 2021; Salari et al., 2021; Zhang et al., 2023; Zhao et al., 2021). Five of them showed positive effects of ACT interventions on psychological flexibility in patients with cancer and survivors (Gonzalez-Fernandez & Fernandez-Rodriguez, 2019; Mathew et al., 2021; Salari et al., 2021; Zhang et al., 2023; Zhao et al., 2021). One primary study indicated a mediating role of psychological flexibility for clinical outcomes (emotional difficulties and HRQoL; Gonzalez-Fernandez et al., 2018). Results of meta-analyses revealed positive effects of ACT at post-intervention (Hedges g = 0.58, k = 18, Zhao et al., 2021; and MD = -4.22, high heterogeneity, k = 10, Zhang et al., 2023) and 3-months FU (MD = -4.36 k = 4, Zhang et al., 2023). Longer intervention duration predicted higher psychological flexibility ($\beta = -1.39$; Zhang et al., 2023). In patients with advanced cancer, no significant differences were found after ACT interventions (MD = -3,42, k = 3) with high heterogeneity across the included studies (Fang et al., 2023). TSA analysis revealed that more studies are needed to evaluate the efficacy of ACT in increasing psychological flexibility (Zhao et al., 2021).

3.3.4. Further results

Beyond data aggregation, the systematic review of Mathew et al. (2021) provides additional value by presenting a conceptual framework that highlights the role of influential factors in the ACT model (see introduction). These influential factors include the context of the

intervention (e.g., sociodemographic, and cultural factors, and individual versus group intervention), participants' perspectives (e.g., level of comprehension of ACT processes and required skills, acceptance, and satisfaction with ACT) and intervention inputs (e.g., person who delivers the intervention, their training, and materials and protocols used for intervention delivery). The authors suggest that influential factors impact ACT interventions and need to be considered when designing and analyzing interventions in cancer survivors.

4. Discussion

The umbrella review aimed to provide a comprehensive overview of the current state of research on ACT in psycho-oncology and to investigate the trans-symptomatic efficacy regarding psychological and physical symptoms as well as HRQoL in patients with cancer and survivors. We identified eight systematic reviews and meta-analyses which correspond to our inclusion criteria, all published between 2019 and 2023. Two reviews focused exclusively on patients with advanced cancer (Fang et al., 2023; Huiyuan Li, Wu, et al., 2021), one review included only studies with breast cancer patients (Hanting Li, Wu, et al., 2021), and one focused exclusively on cancer survivors (Mathew et al., 2021). Four reviews provided meta-analytic data for some of the relevant outcomes (Fang et al., 2023; Hanting Li, Wu, et al., 2021; Zhang et al., 2023; Zhao et al., 2021). One systematic review and one meta-analysis showed low methodological quality (Mathew et al., 2021; Zhao et al., 2021), whereas the remaining six were of critically low methodological quality according to the AMSTAR2 quality assessment, which needs to be considered when interpreting the findings. Overall results indicate that ACT interventions reduce psychological distress, depression and anxiety, and increase HRQoL. Efficacy relating to other outcome measures (e.g., fear of progression/recurrence, hope, sleep) has not yet been well investigated. Moderator analyses indicated larger effects for younger patients, people from Eastern countries (Iran, China) and after longer intervention duration (Zhang et al., 2023; Zhao et al., 2021). In addition to high-quality RCTs, studies with longer FU periods (>6 months) are needed to investigate the long-term effects of ACT interventions among patients with cancer.

4.1. Effects on psychological and physical outcomes

Our review revealed stable results for the positive effects of ACT- and ACT-based interventions in reducing psychological distress, depression, and improving HRQoL in patients with cancer and survivors, as evidenced by meta-analytic reviews with small to large effect sizes in patients with cancer, patients with advanced cancer, and breast cancer patients. The critical methodological quality of most of the reviews and meta-analyses (see above) included in this umbrella review limits the significance of these results. Nevertheless, the findings are corroborated by the highest-quality review (Mathew et al., 2021) and meta-analysis (Zhao et al. (2021). Notably, the meta-analysis by Zhao et al. (2021), which employed appropriate meta-analytical methods, found large effects across all the outcomes named. Two meta-analyses also revealed stable effects for reducing anxiety in patients with various cancer entities and different stages as well as breast cancer patients (Hanting Li, Wu, et al., 2021; Zhao et al., 2021). However, the effects of ACT on anxiety in patients with advanced cancer were poorly evidenced and highly heterogeneous (Fang et al., 2023; Huiyuan Li, Wu, et al., 2021). This might be explained by the small number of studies included in the meta-analysis (n = 6) and review (n = 4), respectively, that focused exclusively on patients with advanced cancer. As patients with advanced cancer often show high levels of death anxiety (Hong et al., 2022) and fear of cancer progression (Butow et al., 2021), it might be particularly important to develop ACT-based interventions that focus on managing anxiety in palliative patients, as none of the included reviews focused on these aspects. Due to its acceptance- and value-based stance and its emphasis on the defusion of unhelpful thoughts, ACT offers a promising

approach for dealing with existential distress and anxiety, even in the advanced cancer phase.

Furthermore, reviews showed positive effects of ACT on psychological flexibility in patients with cancer (mixed stages) and survivors, but no effects in patients with advanced cancer. Again, more studies are needed to draw profound conclusions. It is noteworthy, that all studies used some form of the Acceptance and Action Questionnaire (AAQ, e.g., AAQ-II, AAQ-Cancer; Arch & Mitchell, 2016; Bond et al., 2011) to measure psychological flexibility. The AAQ measures the different constructs psychological flexibility, experiential avoidance, and acceptance, which is a contradiction in itself (see French et al., 2017). Per definition, a measure of psychological flexibility should contain all six hexaflex processes, and not only two (Arch et al., 2023). It is discussed that the AAQ functions more as a measure of distress than of psychological flexibility (Tyndall et al., 2019). Thus, more specific instruments for the ACT processes are needed to determine the effects of psychological flexibility according to ACT theory.

The low consideration of fear of progression or recurrence in the reviews indicates that few studies to date have investigated these fears as an outcome. As fear of progression or recurrence is one of the most common psychological burdens of patients with cancer (Herschbach et al., 2020), future studies that include this construct are worthwhile.

Our extensive review revealed a paucity of information on the effects on physical outcomes to date. Regarding fatigue, we found inconsistencies between the meta-analyses. The study of Zhang et al. (2023) in patients with different cancer stages found no effect on fatigue; however, the study of Fang et al. (2023) found a positive effect of ACT on fatigue in patients with advanced cancer. It is of note, that both meta-analyses included only four and six primary studies, respectively. Findings of another meta-analysis included eight primary studies with patients with cancer or fibromyalgia and revealed a small effect of ACT on fatigue (Maunick et al., 2023). Sleep was examined in only one meta-analysis, which found no effects of ACT for insomnia (ACT-I) in patients with cancer (Zhang et al., 2023). However, based on the promising effects of ACT-I in other clinical populations (Ruan et al., 2022), more studies in cancer patients with insomnia are needed to draw meaningful conclusions. In sum, our results reveal the need for further high-quality RCTs of ACT in cancer that investigate physical distress, such as pain, fatigue, and sleep.

Zhao et al. (2021), which was methodologically the best meta-analytic review, evaluated whether available evidence of the effect of ACT on different outcomes is sufficient to draw robust conclusions using TSA. They found that the effects of ACT on cancer patients' HRQoL and distress can be classified as sufficiently validated. However, this is not true for psychological flexibility, physical distress, and other outcomes (e.g., hope). Furthermore, this meta-analytic review identified important moderators (age, eastern versus western countries, intervention duration) and revealed no differences between the intervention format (individual vs. group, face-to-face vs. web-based) (Zhao et al., 2021). The authors explain the cultural differences with lower health literacy, poorer functioning at baseline, and lower prevalence of palliative and supportive care services in Eastern countries, leading to greater effects of ACT interventions. In addition, there were no differences between control conditions (waiting list vs. treatment as usual (TAU), p = 0.70).

4.2. Methodological and conceptual evaluation of the reviews

According to the AMSTAR2 quality assessment, six reviews were of critically low methodological quality, and two (meta-analytic) reviews of low quality. It needs to be taken into account though that 95% of meta-analyses published in psychology are considered to be of critically low quality according to AMSTAR2 (Leclercq et al., 2020). Nevertheless, the included reviews showed flaws in critical domains (e.g., assessment of publication bias) and therefore, the results of this umbrella review have to be interpreted with caution.

In all included reviews, the low methodological quality of the primary studies was frequently pointed out (e.g., no blinding of the participants, sufficient power, representativeness of the sample, reporting of adverse events; Zhao et al., 2021). For instance, only one of the 25 studies in this meta-analysis had an active control group (study of Gonzalez-Fernandez et al., 2018). This highlights the need for further high-quality RCTs to investigate the effects of ACT in psycho-oncology.

4.3. Implications of the current findings

In light of our objective to evaluate *trans*-symptomatic evidence on ACT, it can be concluded that ACT- or ACT-based interventions are effective in reducing psychological symptoms and increasing HRQoL. However, this comprehensive overview reveals research gaps regarding the effects of ACT on fear of cancer recurrence or progression, physical symptoms like pain, fatigue, and sleep in patients with cancer. More studies are needed to draw strong conclusions about its *trans*-symptomatic efficacy. There is also a need for studies with patients with advanced cancer and survivors. Several trials focusing on palliative patients (e.g., Arch et al., 2022) or survivors (e.g., van de Graaf et al., 2022) are presently underway. These endeavors promise to improve the overall research landscape regarding the efficacy of ACT in psycho-oncology and strengthen the validity of subsequent findings.

However, the differing results found in patients with cancer (of any stage) and patients with advanced cancer regarding anxiety, psychological flexibility and fatigue might indicate that the efficacy of ACT differs depending on the stage of cancer. Since the meta-analysis and systematic review focusing exclusively on patients with advanced cancer included only eight and six studies respectively, this interpretation must be considered with caution. A recent meta-analysis investigating the association between the ACT core processes acceptance, present moment awareness, self-compassion, and experiential avoidance, and psychological distress did not find any moderator effect on cancer stage (Fawson et al., 2023). Although this finding suggests that the same ACT processes are relevant to psychological distress both in curative and palliative situations, it could be that other processes (e.g., self-compassion) also play a pivotal role in patients with advanced cancer.

Currently, only one study includes objective measures or biomarkers. According to Mathew (2021, p.430) only one study looked at stress biomarkers: Gardner (2018). This study was a dissertation study and included a sample of 20 breast cancer patients. The following physiological measures and biomarkers were examined: resting heart rate, blood pressure, fasting blood glucose, salivary alpha-amylase, salivary cortisol, relative telomere length, inflammatory cytokine Interleukin-6, and allostatic load index. There was no significant reduction in almost all stress biomarkers with the exception of the allostatic load index which "was significantly reduced among participants who were waitlisted and then received the ACT-based intervention" (Mathew, 2021, p. 439 and p. 443). Future research that integrates biomarker outcomes such as altered immune function and endocrine or inflammatory responses is urgently needed to evaluate the holistic biopsychosocial effects of ACT in cancer patients (Rivest et al., 2023). A recent systematic review on the influence of mindfulness-based (not including specific ACT) interventions on biomarkers in cancer patients presents mixed results (Matiz et al., 2024). The authors state that the most promising evidence relates to a positive modification of cortisol, blood pressure, telemerase activity and pro-inflammatory gene expression, but this should be interpreted with caution due to a lack of methodological rigor within the included studies. A meta-analysis with mixed chronic conditions by Dunn & Dimolareva (2022) provides information on post-interventional reductions in C reactive protein and interleukin-6, and an increase of CD4+, telomere length and telomerase activity. Within this meta-analysis, only a single ACT intervention (besides mainly mindfulness-based interventions) was conducted with a distressed and overweight/obesity sample resulting in a significant reduction of C reactive protein (Järvelä-Reijonen et al., 2020).

The review of the studies showed that there is a lack of high-quality RCTs investigating the effects of ACT in cancer settings. 45 of the 61 included studies were RCTs, which is the majority, but studies of high methodological quality, with larger sample sizes, and longer FU are needed.

Furthermore, more mediation studies are needed to gain a better understanding of the underlying mechanisms of ACT in psychooncology. Mediation studies from clinical samples revealed the best evidence for psychological flexibility and acceptance as mediators between psychotherapy and outcomes (Stockton et al., 2019). Psychological flexibility and acceptance are also the most studied ACT processes, with fewer studies integrating cognitive defusion, present-moment, self-as-context, or value-based living. Thus, only parts of the hexaflex-model have been examined, which was previously criticized, especially since most studies used variants of the AAQ (see discussion above) (Arch et al., 2023). In the context of cancer, Fishbein et al. (2022) investigated the longitudinal change and mediation effects of ACT target processes and ACT-related processes in anxious cancer survivors. Self-compassion and emotional approach coping (i.e., coping with stressors by actively acknowledging, processing, and expressing one's emotions), two broader ACT-consistent processes, as well as values-aligned behavior were significant or marginal partial mediators of anxiety symptoms in cancer survivors. Interestingly, experiential avoidance was not a significant mediator (Fishbein et al., 2022). Other studies suggest that self-compassion plays a critical role as a mediator of the intervention effects of ACT (Ong et al., 2021). These findings might indicate that ACT-related processes are especially important in cancer survivors. In a recent paper, Arch et al. (2023) described five challenges and recommendations for addressing them in research on ACT processes and mediators: 1) distinguishing ACT processes in measurement contexts, 2) developing and validating measures of ACT processes, 3) using stronger measures of ACT processes/mediators, 4) demonstrating specificity and sensitivity, 5) performing replicable results. Given the theory-based background of ACT, the development of validated measurements that reliably assess ACT processes in patients with cancer and their integration into ACT studies is critical to understanding what works for whom in cancer patients and survivors.

4.4. Limitations

The rising number of systematic reviews and/or meta-analyses investigating ACT interventions in psycho-oncology has yielded both conclusive and inconclusive findings. In response, this umbrella review amalgamates existing evidence through a consistent and comprehensive approach. Specifically, the focus of this umbrella review is on the *trans*-symptomatic therapeutic potential of ACT, encompassing both psychological and physical symptoms, in individuals affected by cancer and survivors.

It is evident that umbrella reviews are susceptible to limitations stemming from the quality of the included 'primary' studies and reviews (Choi & Kang, 2022). In our analysis, we observed a notable deficiency in the overall quality of the included reviews, with assessments ranging from low to critically low quality. This observation leads to a dual interpretation: firstly, it could reflect the genuine methodological quality of research in the field, revealing the need for high-quality RCTs. Secondly, it may be influenced by a floor effect resulting from stringent quality criteria (Leclercq et al., 2020). Addressing the latter possibility would necessitate the adoption of refined quality criteria, particularly tailored for umbrella reviews. Due to our wide focus on physical and psychological outcomes, our inclusion criteria were rather broad (e.g. regarding cancer stage), which leads to higher heterogeneity of the studies. Further, due to the sparse body of research, some reviews included few studies or studies with poor study quality, which reduces the validity of the results. Due to the small number of systematic reviews and meta-analyses, pooling was not possible, which diminishes the

validity of the findings. In sum, our results highlight that ACT is a nascent therapeutic approach within psycho-oncology and that there is a strong need for more high-quality RCTs, valid reviews and meta-analyses.

4.5. Conclusion

This umbrella review provides a comprehensive overview of the efficacy of ACT in psycho-oncological settings. Our summary of reviews and meta-analyses suggests that ACT interventions are an effective and evidence-based treatment for increasing HRQoL and reducing psychological distress and depression in patients with cancer. They can be used cost-effectively and flexibly in a variety of settings (face-to-face, online, telephone-based, individual versus group setting). Simultaneously, the evidence regarding the reduction of physical distress, as well as other outcome parameters (e.g., fear of progression or recurrence, hope) and changes in objective biological parameters has not yet been sufficiently investigated. Further, results might indicate that the efficacy of ACT differs depending on the stage of cancer. All reviews included in this study had a (critically) low methodological quality and the quality of the included primary studies was partially low. Heterogenous results regarding anxiety, psychological flexibility, and fatigue indicate the need for studies considering the stage of the cancer disease as a moderator for the efficacy of ACT, as well as studies exploring the mechanisms of ACT interventions in psycho-oncological settings. Additionally, there is a need for rigorous, high-quality RCTs to address the identified gaps and to comprehensively examine the long-term effects.

CRediT authorship contribution statement

Christina Sauer: Writing – review & editing, Writing – original draft, Validation, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. Alexander Haussmann: Writing – review & editing, Methodology, Investigation. Gregor Weissflog: Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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