

Article

Acceptance and Commitment Therapy (ACT) in End-of-Life Care: A Meta-Analysis of Efficacy and Process of Change

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ABSTRACT

Background: Acceptance and Commitment Therapy (ACT) is an evidence-based, process-oriented psychotherapy that provides palliative care through compassionate, person-centered care for terminal illness. This study evaluates the effects of ACT on quality of life (QoL) and emotional distress and examines the role of process variables (e.g., psychological flexibility). **Method:** Systematic review with meta-analysis following searches in PubMed, SCOPUS and PsycInfo for studies measuring QoL, anxiety/depression symptoms, and process variables in ACT interventions. Random-effects meta-analyses and meta-regressions were performed. Risk of bias was assessed. **Results:** 13 studies were included (1,109 participants; $M_{age} = 61.5$; 55.7% women; 6 RCTs). ACT showed significant, moderate effects for QoL, anxiety and depression symptoms versus active controls ($SMD = 0.44$ to 0.62), sustained at 1-9 months follow-up ($SMD = 0.35$ to 0.56). Psychological flexibility emerged as the strongest predictor of QoL improvement. Face-to-face interventions demonstrated better results than remote delivery. **Conclusions:** These findings support the clinical relevance of ACT as an effective approach for addressing psychological distress and improving QoL in end-of-life care. Key limitations include self-report bias, high heterogeneity, potential overlap between measures, publication bias for QoL, and limited sample sizes in some analyses. High-quality trials are warranted, particularly in non-oncological populations, caregivers, and healthcare professionals.

Terapia de Aceptación y Compromiso (ACT) en Cuidados al Final de la Vida: Un Metaanálisis de Eficacia y Procesos de Cambio

RESUMEN

Palabras clave:

Terapia de Aceptación y
Compromiso
Calidad de vida
Enfermedad terminal
Cuidados paliativos
Revisión sistemática
Meta-análisis

Introducción: La Terapia de Aceptación y Compromiso (ACT) es una psicoterapia basada en procesos que proporciona atención compasiva y centrada en la persona en cuidados paliativos. Este estudio evalúa la eficacia de ACT en calidad de vida (CdV) y bienestar emocional, y examina variables de proceso (p.ej., flexibilidad psicológica). **Método:** Se buscó en PubMed, Scopus y PsycInfo estudios que midieran CdV, síntomas de ansiedad/depresión, y variables de proceso en intervenciones ACT. Se realizaron metaanálisis de efectos aleatorios y metarregresiones. Se evaluó el riesgo de sesgo. **Resultados:** Se incluyeron 13 estudios (1,109 participantes; $M_{edad} = 61,5$; 55,7% mujeres; 6 ECA). ACT mostró efectos moderados significativos en CdV, ansiedad y depresión frente a grupos de control activos ($SMD = 0,44$ a $0,62$), mantenidos en el seguimiento de 1-9 meses ($SMD = 0,35$ a $0,56$). Las intervenciones presenciales mostraron resultados superiores a las remotas. **Conclusiones:** Estos hallazgos apoyan la relevancia clínica de ACT para abordar malestar psicológico y mejorar CdV en cuidados al final de la vida. Las limitaciones incluyen sesgo de autoinforme, alta heterogeneidad, solapamiento entre medidas, sesgo de publicación para CdV y tamaños muestrales limitados. Se requieren ensayos de alta calidad en poblaciones no oncológicas, cuidadores y profesionales sanitarios.

The global burden of terminal illness is substantial and is expected to increase significantly in the coming decades, driven in part by sustained population aging (Lee & Zhou, 2017). It is estimated that between 69% and 82% of individuals who die each year could have required palliative care for chronic or terminal conditions (Murtagh et al., 2014). Despite the crucial role of palliative care in health systems and universal health coverage, global access remains severely limited. The Lancet Commission estimates that over 61 million people experience serious health-related suffering annually, with at least 80% lacking basic palliative care, including essential pain medication (Knaul et al., 2018; Radbruch et al., 2020). These figures illustrate the substantial mortality burden associated with terminal illnesses and highlight the urgent need for early detection, effective treatment, and integrated palliative care strategies (Yang et al., 2024; Zhao et al., 2021). Tackling this challenge requires a robust, sustainable framework that ensures equitable access to supportive services across the illness trajectory. Given the evolving, multifaceted nature of terminal conditions, updated definitions are needed to capture their medical complexity and existential dimensions, as will be further addressed below.

While major international organizations (World Health Organization, European Association for Palliative Care) have not established specific operational criteria for end-of-life status (Surges et al., 2024; World Health Organization, 2020), consensus definitions describe it as an advanced, progressive, and incurable disease with no reasonable response to curative treatment, accompanied by multiple intense symptoms and significant emotional impact on patient and family (Organización Médica Colegial & Sociedad Española de Cuidados Paliativos, 2015). The lack of universal consensus on defining end-of-life leads to heterogeneity in study populations across palliative care research, with varying operational criteria including prognosis thresholds, disease staging, or enrollment in palliative care programs.

Palliative care addresses both physical suffering and existential challenges through comprehensive, multidisciplinary approaches that emphasize symptom management while acknowledging patients' personal narratives and sense of meaning (Teoli et al., 2025). The World Health Organization highlights that palliative care should be aimed at improving the QoL of patients and their families facing life-threatening illnesses (World Health Organization, 2022). Psychotherapy interventions based on contextual models may improve care by addressing the disease and the patient's psychological and relational context (Quevedo et al., 2022; Schiele et al., 2020). These approaches can be framed within contextual behavioral science (CBS), which emphasizes understanding and influencing behavior as embedded in its historical and situational context.

QoL has increasingly been recognized as a central outcome in end-of-life care, encompassing physical comfort, emotional well-being, and social connectedness beyond mere survival (Khan et al., 2005; World Health Organization, 2022). Approaching the final stage of life due to a terminal illness evokes not only the fear of death, but also a complex array of emotional and existential challenges affecting identity, meaning, and connection (Lamont, 2005). The most common manifestations are symptoms of anxiety and depression (Secinti et al., 2019). These conditions significantly impact QoL, treatment adherence, and symptom burden. In addition, a diagnosis of terminal illness often triggers what has been termed an "existential plight" (Weisman & Worden, 1977), a heightened

awareness of mortality that encompasses profound concerns about meaning, identity, and impending death (Yalom, 2008). The medical community increasingly recognizes addressing these existential dimensions as integral to patient care (Tarbi & Meghani, 2019).

While cognitive-behavioral therapy (CBT) has demonstrated moderate efficacy in reducing anxiety and depressive symptoms in patients with advanced cancer (Wilaras, 2024; Xia et al., 2024), only a minority of CBT trials have explicitly addressed existential distress, and treatment effects in this population have often been non-significant (Campbell & Campbell, 2012). This limitation is notable given that existential concerns (such as death anxiety, loss of meaning, and spiritual suffering) are inherent to the palliative care context (Lee, 2020). Acceptance and Commitment Therapy (ACT), as both a philosophy and clinical approach (Carlsson, 2012; Kissane, 2012), may offer a more comprehensive framework for addressing these concerns. ACT targets psychological flexibility, the ability to remain open to difficult inner experiences while engaging in value-based action (Hayes, Strosahl, et al., 2006), through explicit emphasis on values clarification, acceptance of death-related anxiety, and commitment to meaningful action in the face of existential threat. Evidence suggests that psychological flexibility is a key mechanism of change, associated with decreased anxiety and depression in patients with terminal illnesses (Zhao et al., 2021), making it a central outcome in assessing ACT's efficacy in end-of-life care as a valuable complement to biomedical interventions (Kredentser & Chochinov, 2020; Sauer et al., 2024; Secinti et al., 2019).

ACT is a transdiagnostic, process-based therapy rooted in functional contextualism that emphasizes psychological flexibility, which enables patients to engage meaningfully with suffering while reorienting actions toward personal values (Hayes et al., 2013, 2022; Hayes, Strosahl, et al., 2006). The Extended Evolutionary Meta-Model identifies processes such as acceptance and values-based action as essential for addressing existential dilemmas and clinical symptoms (Ciarrochi et al., 2022; Hayes et al., 2020; Menzies & Menzies, 2024). There is evidence supporting the efficacy of ACT in managing chronic illnesses and other health conditions (Gloster et al., 2020; González-Fernández et al., 2018; Jiang et al., 2024).

Recently, ACT has expanded to include terminal illness. In their systematic review, Li et al. (2021) identified 6 studies ($n = 261$) examining the effect of ACT for patients with advanced cancer. They found that these interventions had a positive effect on emotional distress, health-related QoL and somatic issues such as sleep problems. Gibson Watt et al. (2023) conducted a systematic scoping review that also included caregivers. With a similar sample size ($k = 7$ intervention studies for patients) they found results consistent with Li et al. (2021), and expanded them with findings suggesting benefits for psychological distress in caregivers too. A recent meta-analysis (Fang et al., 2023) found 8 studies ($n = 488$) examining the effects of ACT for advanced cancer patients. They found large effects on QoL, anxiety and depression, while the effects on psychological flexibility were non-significant.

However, these reviews have important limitations that warrant an updated and more comprehensive meta-analysis. First, the only existing meta-analysis (Fang et al., 2023) excluded non-randomized controlled designs, potentially limiting the comprehensiveness of the evidence base. Second, this meta-analysis only examined immediate post-treatment effects without analyzing longer-term follow-up outcomes, leaving questions about the durability of ACT's

benefits. Third, none of the existing reviews, whether systematic reviews (Gibson Watt et al., 2023; Li et al., 2021) or meta-analysis (Fang et al., 2023), explored mechanisms of change, despite ACT theory emphasizing psychological flexibility as the key therapeutic process. Fourth, all existing reviews focused exclusively on patients with advanced cancer, whereas terminal illness encompasses a broader range of conditions including amyotrophic lateral sclerosis (ALS) and other progressive diseases that would benefit from palliative psychological interventions. Fifth, a substantial number of studies have been published in recent years, necessitating an updated synthesis. Although ACT does not pursue symptom reduction as its primary therapeutic objective, changes in process such as psychological flexibility and valued action are consistently associated with improvements in QoL and reductions in emotional distress (Gloster et al., 2020; Hayes, Luoma, et al., 2006).

The present study (a) systematically reviews and meta-analyzes the existing literature on the short- and longer-term effects of ACT on QoL and emotional distress (e.g., symptoms of anxiety and depression) in terminally ill patients, and (b) explores the mechanism of change by examining how changes in ACT process variables, particularly values-based living and psychological flexibility, may explain the potential improvements in these clinical outcomes.

Method

This systematic review with meta-analysis followed the PRISMA guidelines for systematic reviews and meta-analyses (Page et al., 2021). In addition, this review has been pre-registered in PROSPERO (CRD42024562107). The results of the selection process, with the reasons for excluding, the coding process (with the full codebook) and the fully extracted dataset can be consulted at this OSF [link](#).

Information Sources and Search Strategy

MedLine (via PubMed), Scopus, and PsycInfo were consulted using the following search terms in the title, abstract, and keywords (for the population and the intervention): (*palliativ** OR *advanced progressive illness* OR *advanced care* OR *last year* OR *terminally* OR *terminal care* OR *terminal* OR *hospice* OR *advanced cancer* OR *amyotrophic lateral sclerosis*) AND (*acceptance and commitment*)

The full search strings are available at this OSF [link](#). Where available, the search was filtered to show only studies published in peer-reviewed journals. Reference lists of identified articles were reviewed to identify additional studies. Previous reviews on the field of ACT research on patients with cancer and other potentially terminal conditions were also consulted (Fang et al., 2023; Gibson Watt et al., 2023; Li et al., 2021; Okuyama et al., 2017; Sauer et al., 2024). In addition, a forward reference search of articles citing the identified studies was conducted to potentially identify additional eligible studies. The search included articles published up to May 26, 2025. These search terms were piloted by the authors to ensure that they would cover all relevant studies comprehensively.

Eligibility Criteria

According to the PICOS strategy (Eriksen & Frandsen, 2018), studies meeting the following characteristics were included: (A)

Population: Studies with a sample of adults (+18) who are terminally ill, including patients explicitly described as having advanced cancer or equivalent terminology (minimum stage III or IV with low survival rates, typically <50% five-year survival), advanced ALS, or patients receiving palliative care, both men and women; (B) Intervention: Studies in which at least one of the experimental groups received ACT. Combining ACT with other interventions was permitted, as long as the primary focus of the treatment remained addressing the ACT processes; (C) Comparison: For controlled trials, at least one of the arms did not receive ACT, allowing to isolate the specific effects of this intervention. Both active (e.g., treatment as usual, other psychological interventions, support groups) and inactive (e.g., waitlist, no interventions) control groups are accepted; (D) Outcomes: In order to address the main objective, studies had to include quantitative measures of depression symptoms, anxiety symptoms, and/or QoL as outcome variables. To address the question about the mechanism of change, they also had to include a measure of the main process of change variable proposed by ACT (e.g., psychological flexibility) or one of the six core process variables (e.g., valued action, cognitive fusion); (E) Study Designs: Both RCTs, nonrandomized controlled trials, and uncontrolled single-arm trials were included. Sensitivity analyses were conducted in order to control the randomization of the controlled trials. All study designs were included to provide a comprehensive synthesis of the literature. Between-group and within-subject analyses were conducted and reported separately to distinguish controlled from uncontrolled treatment effects; (F) Additional criteria: Priority was given to peer-reviewed articles in scientific journals, although doctoral theses were also included. Articles had to be written in English or Spanish, as these were the languages understood by the authors.

Selection Process

The initial title/abstract screening was conducted by a single reviewer using a conservative criterion that retained any potentially relevant study for full-text review, thereby minimizing the risk of premature exclusion. The final selection was made independently by two independent researchers by applying the selection criteria to the full texts. Agreement between the researchers was considered to be substantial, with a Cohen's kappa coefficient of .78. Disagreements were resolved by consensus.

Data Collection and Data Items

After the final selection of studies, the second and the last author independently coded the following variables: (A) study design (e.g., RCT, nonrandomized controlled trials, uncontrolled single-arm trials) and study characteristics (author, year, country); (B) population diagnosis (e.g., advanced cancer, amyotrophic lateral sclerosis); (C) sample mean age and percentage of women; (D) intervention type (e.g., ACT, ACT combined with other intervention), delivery (e.g., delivered by a therapist or self-delivered; face-to-face or remote), format (e.g., individual or group), and number of sessions; and (E) comparison (e.g., active control, inactive control). Discrepancies between the two researchers were resolved by consensus. The final author then extracted the sample size, means and standard deviations for each study arm. In cases where standard deviation values were not provided, they were calculated using the formulas recommended

by Higgins and Green (2011). For studies with insufficient data to calculate the ES, or in cases of uncertainty, the corresponding authors were contacted.

Methodological Quality Assessment

The Cochrane Risk of Bias Tool 2 (Sterne et al., 2019) was used to assess the risk of bias in RCTs, while risk of bias in nonrandomized controlled trials and uncontrolled single-arm trials was assessed with ROBINS-I (Sterne et al., 2016). RoB 2 evaluates the following five domains: (1) bias arising from the randomization process, (2) bias due to deviations from intended interventions, (3) bias due to missing outcome data, (4) bias in the measurement of the outcome, and (5) bias in the selection of the reported result. Each domain in RoB 2 was judged as having low, high, or some concerns risk of bias. ROBINS-I assesses seven domains: (1) bias due to confounding, (2) bias in the selection of participants into the study, (3) bias in the classification of interventions, (4) bias due to deviations from intended interventions, (5) bias due to missing data, (6) bias in the measurement of outcomes, and (7) bias in the selection of the reported result. Each domain in ROBINS-I was judged as having low, moderate, serious, or critical risk of bias, or no information. Two researchers assessed each study independently. Discrepancies were resolved by consensus.

One of the researchers evaluated publication bias by visually inspecting the symmetry of funnel plots. This was also assessed using the trim-and-fill method (Duval & Tweedie, 2000), to estimate the number of potentially missing studies and adjust effect size estimates accordingly, and the Egger test (Egger et al., 1997), to statistically assess funnel plot asymmetry, with $p < .05$ indicating potential publication bias.

Data Analysis

First, effect sizes (ESs) and their associated variances were estimated using Morris's proposal for within-subject (Morris, 2000) and between-group outcomes (Morris, 2008), adjusted with a small sample factor correction (Morris, 2000, 2008). The standard error was derived from the square root of the estimated variance. ES values of 0.2, 0.5, and 0.8 were interpreted as indicating small, moderate, and large effects, respectively (Cohen, 1988). Outcomes were extracted at post-treatment (first assessment immediately after treatment) and at follow-up. When multiple follow-up assessments were reported for the same outcome, we extracted the longest available follow-up time point.

A random effects model meta-analysis was then performed for each outcome by weighting the ESs by their inverse variance. This random effects model was chosen because of the expected high heterogeneity between studies and the assumption that the true effect size may vary across studies (Borenstein et al., 2010). To measure this heterogeneity among studies, the I^2 index was estimated for each outcome (Higgins et al., 2003). I^2 values of 25%, 50%, and 75% were interpreted as indicating low, moderate, and high heterogeneity, respectively.

Additional Analyses

Finally, to assess the mediating role of process variables of ACT (e.g., psychological flexibility model), meta-regressions were

conducted for each outcome. In these meta-regression models, process variables were set as predictors, while QoL and depression and anxiety symptoms were selected as dependent variables. Meta-regressions were not conducted for outcomes with fewer than three studies because this number is insufficient to estimate between-study variance or fit a meaningful model (Thompson & Higgins, 2002). At least three studies are needed for minimal interpretability; however, higher numbers are preferred for reliable results. To assess other potential sources of heterogeneity, subgroup analyses were performed using χ^2 tests. Studies were grouped according to the coded variables listed above. Significance was set at $p = .05$. Sensitivity analyses excluding studies mixing stage III and IV cancer patients were performed. Meta-analyses and meta-regressions were performed using the *meta* package (Balduzzi et al., 2019) in R (R Core Team, 2025). The R code and database are available at this OSF link.

Results

Five corresponding authors were contacted for further information. Two studies were excluded because not all individuals in their sample were in the terminal stage of cancer (Ksiksou et al., 2024; Lanthéaume et al., 2020). The other three studies did not respond and were therefore excluded because we could not be sure whether they met the eligibility criteria (Han et al., 2019; Páez et al., 2007; Yusuf et al., 2023).

Finally, six RCTs, two nonrandomized controlled trials, and five uncontrolled single-arm trials, with a total of 1,109 participants, met the eligibility criteria and were included (see Table 1 and Figure 1). The mean age of the participants was 61.5 years ($SD = 3.9$), with the majority having been diagnosed with advanced cancer ($n = 9$). On average, 55.7% of the participants were women. Regarding the intervention, most studies employed standalone ACT ($n = 11$), which was predominantly delivered by a therapist ($n = 10$) and conducted in a face-to-face ($n = 6$) and individual ($n = 9$) setting. All control groups were active ($n = 9$). The mean number of sessions in the intervention was 6.8 ($SD = 2.3$). Eight studies included at least one follow-up assessment ($M = 4.1$ months, range: 1–9 months, $SD = 2.64$).

Risk of Bias Assessment Results

For all studies, there were some concerns about the measurement of the outcome, as all were self-reported (see Figure 2a and 2b). Overall, the remaining domains for controlled trials were considered to be at low risk of bias. For uncontrolled single-arm trials, several studies did not report enough information to assess the risk of bias due to deviations from the intended interventions, and there were some concerns about the management of missing data in some studies.

Regarding publication bias, the Egger test was not significant for all outcomes. This suggests no evidence of publication bias; however, tests may be underpowered and these results should be interpreted cautiously. Trim-and-fill adjusted ES for several outcomes, but ES remained statistically significant for all outcomes. Finally, visual inspection of funnel plots with 10 or more studies suggests some asymmetry only for within-subject depression at post-treatment. Trim-and-fill imputed two studies, but the adjusted ES remained significant. Therefore, the combined results for publication bias risk assessment suggest no overall evidence of unpublished studies with negative results.

Table 1
Main Characteristics of the Included Studies

Study	Country	Design	Allocated participants (n)		Sample characteristics			Intervention characteristics						Control group	
			Treated	Controls	Diagnosis	Mean age (SD)	% of females	Type	Sessions planned	Mean sessions received (SD)	Applied by	Delivery	Format		
(Arch et al., 2019)	United States of America	Uncontrolled trial	35	-	Metastatic gastrointestinal, breast, gynecologic, prostate, myeloma and lung cancer	61.8 (11.9)	62.9	ACT	7	6.2 (0.8)	Combined	Combined	Combined	Usual care: medication, symptom-management treatment, and hospital/community services Usual care (routine inpatient care, brief emotional support, patient education, and management of chemotherapy side effects) + personalized nutrition and usual care only	
(Gould et al., 2023)	United Kingdom	Uncontrolled trial	30	-	Amyotrophic lateral sclerosis	58.4 (13.8)	48.0	ACT	8	5.5 (3.4)	Combined	Combined	Individual		
(Gould et al., 2024)	United Kingdom	RCT	97	94	Amyotrophic lateral sclerosis	63.1 (11.0)	58.0	ACT	8	N/A	Therapist	Combined	Individual		
(Hu et al., 2024)	China	Nonrandomized controlled trial	76	75	Advanced gastric cancer	57.0 (N/A)	33.8	ACT	N/A	N/A	Therapist	Face-to-face	N/A		
(Hulbert-Williams et al., 2021)	United Kingdom	Uncontrolled trial	10	-	Non-curative breast, esophageal, prostate, cervical, lung, pancreatic, bladder, colon with liver metastases, digestive/peritoneal cancers	65.7 (11.5)	40.0	ACT	5	N/A	Therapist	Face-to-face	Individual		
(Li et al., 2024)	China	RCT	80	80	Advanced lung cancer	59.5 (7.6)	20.6	ACT	4	3.4 (N/A)	Therapist	Face-to-face	Individual		Usual care: brief lung cancer/treatment education and daily care, medication & side-effect instructions, routine physical checks, plus discharge advice on diet/exercise and retesting
(Martin & Pakenham, 2024)	Australia	Nonrandomized controlled trial	52	54	Palliative care patients: lung, breast, colorectal, gynecological, pancreatic, head & neck, hematological, bone/soft tissue, prostate, skin, urological cancers; cardiovascular disease, respiratory failure, liver failure, renal failure, motor neuron disease	69.1 (9.4)	52.6	ACT	4 (modules)	N/A	Combined	Remote	Individual		Usual care: usual specialist multidisciplinary palliative care from the same service

Study	Country	Design	Allocated participants (n)		Sample characteristics			Intervention characteristics						Control group
			Treated	Controls	Diagnosis	Mean age (SD)	% of females	Type	Sessions planned	Mean sessions received (SD)	Applied by	Delivery	Format	
(Mosher et al., 2022)	United States of America	RCT	20	20	Advanced gastrointestinal cancer, including colorectal, pancreatic, stomach and liver	58.5 (10.0)	55.0	ACT	6	4.8 (2)	Therapist	Remote	Combined	Education support: 6 weekly ~50-min telephone sessions with <i>supportive listening</i> plus practical/health information and referrals (contact info for support services)
(Mosher et al., 2024)	United States of America	RCT	116	120	Metastatic breast cancer	59.0 (11.5)	100	ACT	6	5.4 (1.5)	Therapist	Remote	Individual	Education support: 6 weekly 50-min telephone sessions delivered by therapists with supportive-counseling experience
(Plumb Vilardaga et al., 2020)	United States of America	Uncontrolled trial	24	-	Advanced prostate, colorectal, lung, renal, breast, appendiceal, gallbladder cancer	66.0 (10.8)	29.0	ACT + Coping skills training	4	3.9 (0.6)	Therapist	Remote	Individual	
(Ramos et al., 2018)	United States of America	Uncontrolled trial	39	-	Palliative care patients with a life-limiting illness: advanced prostate and lung cancer; end-stage renal disease, advanced neurological or autoimmune disorders	63.1 (8.6)	N/A	ACT + CBT	6-8	N/A	Therapist	Face-to-face	Group	
(Rost et al., 2012)	United States of America	RCT	25	22	Late-stage ovarian cancer	56.0 (N/A)	100.0	ACT	12	N/A	Therapist	Face-to-face	Individual	Active CBT-style protocol (12 face-to-face sessions) including relaxation training, problem-solving, and a “five-column” cognitive restructuring
(Serfaty et al., 2019)	United Kingdom	RCT	20	20	Advance breast, colon, myeloma, prostate, bowel, non-Hodgkin lymphoma cancer	62.0 (11.5)	74.0	ACT	8	N/A	Therapist	Face-to-face	Individual	Talking Control: up to 8 sessions of structured empathic/neutral supportive conversation, explicitly avoiding active therapeutic techniques (e.g., mindfulness, cognitive restructuring, problem-solving)

Note. RCT = Randomized controlled trial; ALS = Amyotrophic lateral sclerosis; N/A = Not available; ACT = acceptance and commitment therapy; CBT = Cognitive behavioral therapy.

Figure 1
PRISMA Flow Diagram

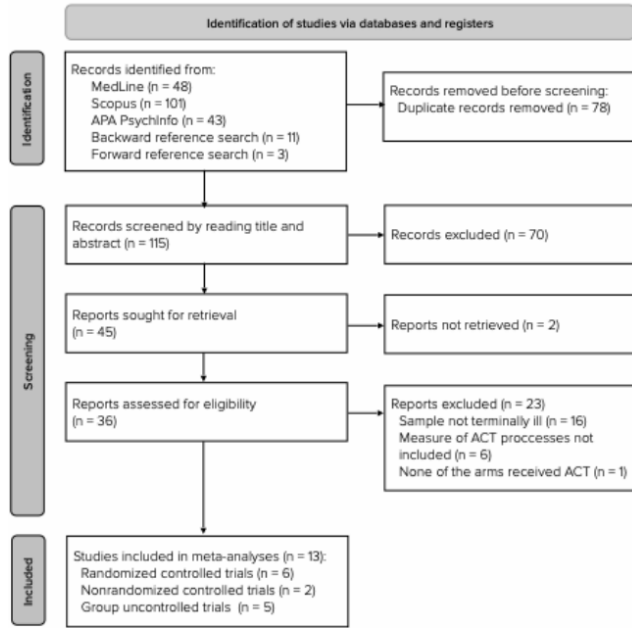


Figure 2a
Risk of Bias Summary: RoB 2 (Upper Panel)

		Risk of bias domains				
		D1	D2	D3	D4	D5
Study	Gould 2024	+	+	+	-	+
	Li 2024	+	+	+	-	+
	Mosher 2022	+	+	+	-	+
	Mosher 2024	+	+	+	-	+
	Rost 2018	+	+	+	-	+
	Serfaty 2018	+	-	+	-	+

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
- Some concerns
+ Low

Table 2
Standardized Mean Differences (SMD), 95% Confidence Intervals, Heterogeneity Analyses (I^2), and Risk of Bias for Between-Groups and Within-Subject Outcomes

Variable		Between-groups outcomes						Within-subject outcomes				
		Time point	k	n	SMD	95% CI	I^2	k	n	SMD	95% CI	I^2
Outcome variables	Quality of Life	PT	9	1051	0.44	0.10 to 0.79	90%	10	477	0.46	0.09 to 0.84	92%
		FU	5	615	0.56	0.17 to 0.95	89%	6	314	0.52	-0.02 to 1.07	94%
	Anxiety symptoms	PT	4	442	0.62	0.06 to 1.19	93%	8	305	0.41	0.26 to 0.56	60%
		FU	2	305	0.40	0.21 to 0.60	22%	3	180	0.45	0.25 to 0.64	56%
	Depression symptoms	PT	4	442	0.58	0.33 to 0.82	59%	8	305	0.25	0.15 to 0.35	47%
		FU	2	305	0.35	0.13 to 0.58	36%	3	180	0.19	0.03 to 0.36	43%
Process variables	Psychological flexibility	PT	6	515	0.49	0.08 to 0.90	80%	10	332	0.51	0.02 to 1.01	92%
		FU	4	372	0.55	0.04 to 1.07	89%	5	209	0.73	-0.27 to 1.74	96%
	Valued action	PT	4	318	0.62	-0.17 to 1.41	94%	6	199	0.57	-0.32 to 1.46	92%
		FU	3	214	0.69	-0.50 to 1.89	95%	5	149	0.60	-0.45 to 1.66	97%

Note. PT = post-treatment; FU = follow-up; k = number of studies; n = number of participants; SMD = standardized mean differences; CI = confidence intervals

Figure 2b
Risk of Bias Summary: ROBINS-I (Bottom Panel)

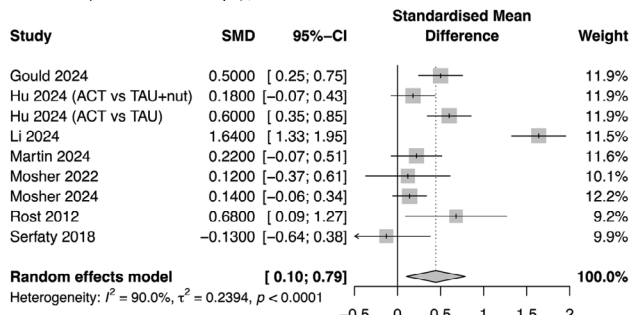
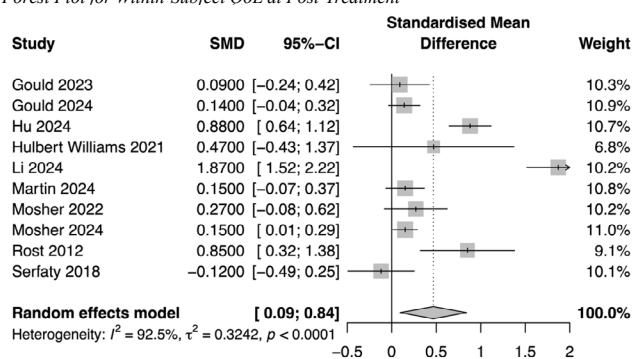
		Risk of bias domains						
		D1	D2	D3	D4	D5	D6	D7
Study	Arch 2019	+	+	+	?	+	-	+
	Gould 2023	+	+	+	+	-	-	+
	Hu 2024	+	+	+	?	?	-	+
	Hulbert-Williams 2021	+	+	+	+	+	-	+
	Martin 2024	+	+	+	+	-	-	+
	Plumb Viladarga 2020	+	+	+	+	+	-	+
	Ramos 2018	+	+	+	?	+	-	+

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
+ Serious
- Moderate
+ Low
? No information

Meta-Analyses Results

The full results of the meta-analysis are shown in Table 2, while Figures 3 and 4 show forest-plots for post-treatment QoL. See the rest of the forest-plots in Supplementary Material. Between-group analyses showed that, compared with participants in active control groups, those who received ACT improved significantly more on all outcome variables, with approximately moderate ESs (SMDs = 0.44 to 0.62). These improvements remained significant at follow-up, increasing for QoL (SMD = 0.56), while for anxiety and depression symptoms decreased (SMDs = 0.35 to 0.40). In terms of within-subject change, ES estimates were similar for QoL (post-treatment SMD = 0.46; follow-up SMD = 0.52) but smaller for anxiety and depression symptoms (SMDs = 0.19 to 0.45). However, the effect was non-significant for within-subject QoL at follow-up (CI 95% [-0.02 to 1.07], $p = .06$). Heterogeneity was high for QoL ($I^2 = 89\%$ to 94%) and low-to-moderate for anxiety and depression ($I^2 = 22\%$ to 60%, except between-group anxiety: $I^2 = 93\%$).

Figure 3*Forest Plot for Between-Group OoL at Post-Treatment***Figure 4***Forest Plot for Within-Subject OoL at Post-Treatment*

Regarding process variables, those who received ACT improved significantly more than active controls on psychological flexibility, with moderate ESs ($SMD = 0.49$) that were maintained at follow-up ($SMD = 0.55$). The ES for within-subject change was similarly moderate ($SMD = 0.51$) but became non-significant at follow-up for this variable ($CI\ 95\% [-0.27\ to\ 1.74]$, $p = .15$). However, ES for the valued action were moderate to large ($SMDs\ 0.57\ to\ 0.69$), but confidence intervals were very wide, mainly due to the small sample size, and results were not statistically significant for both between-group and within-subject outcomes. Heterogeneity was high for all process variable outcomes ($I^2 > 80\%$).

Examining the Role of the Process Variables in QoL and Anxiety and Depression Symptom Improvement

Valued action and psychological flexibility were the best predictors of QoL improvements (see Table 3, and Figures 5 and 6). These process variables significantly predicted all QoL outcomes, explaining between 75% and 100% of the variance. However, meta-regression using changes in between-group psychological flexibility as predictor after the treatment was not significant ($p = .18$) and explained only 18% of the variance.

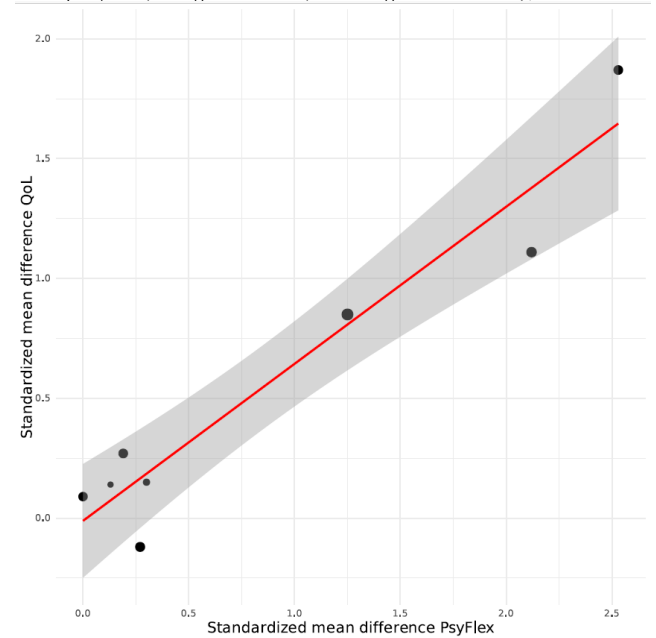
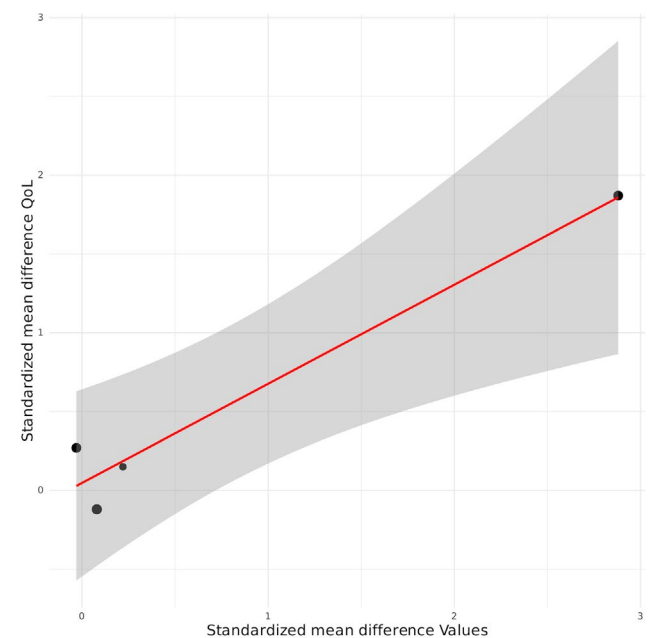
Figure 5*Scatterplot for Psychological Flexibility Predicting Post-Treatment OoL***Figure 6***Scatterplot for Values Predicting Post-Treatment QoL*

Table 3
Meta-Regression Results

Outcome	Covariates																			
	Percentage of women				Age of participants				Number of sessions				Psychological flexibility				Valued action			
	B	SE	p	R ²	B	SE	p	R ²	B	SE	p	R ²	B	SE	p	R ²	B	SE	p	R ²
BG QoL (post-treatment)	-0.01	0.01	.17	.14	-0.02	0.05	.63	0	-0.04	0.09	.67	0	0.61	0.45	.18	.18	0.98	0.12	<.001	1
BG QoL (follow-up)	-0.01	0.01	.01	.73	0.03	0.10	.78	0	-0.09	0.14	.51	0	0.71	0.19	<.001	1	0.44	0.23	.04	.75
WS QoL (post-treatment)	-0.01	0.01	.13	.16	-0.05	0.05	.29	.02	-0.05	0.09	.60	0	0.72	0.08	<.001	1	0.63	0.08	<.001	.98
WS QoL (follow-up)	-0.01	0.01	.09	.31	-0.06	0.11	.60	0	-0.25	0.16	.13	.26	0.63	0.08	<.001	0.98	0.53	0.16	<.001	.87
BG anxiety (post-treatment)	-0.01	0.01	.29	.09	-0.05	0.06	.35	.06	-0.05	0.10	.61	0	0.32	0.59	.59	0	Not enough studies			
BG anxiety (follow-up)	Not enough studies for all the covariates																			
WS anxiety (post-treatment)	0.01	0.01	.19	0	-0.03	0.02	.07	.18	0.05	0.04	.28	0	0.13	0.05	<.01	.99	0.06	0.05	.19	1
WS anxiety (follow-up)	-0.01	0.01	.88	0	-0.05	0.05	.29	.11	-0.04	0.07	.59	0	0.03	0.11	.77	0	Not enough studies			
BG depression (post-treatment)	-0.01	0.01	.35	.28	-0.03	0.03	.24	.28	-0.02	0.05	.66	0	0.32	0.24	.18	.54	Not enough studies			
BG depression (follow-up)	Not enough studies for all the covariates																			
WS depression (post-treatment)	0.01	0.01	.38	0	-0.01	0.02	.54	0	0.05	0.03	.14	0	-0.01	0.07	.98	0	-0.05	0.05	.29	0
WS depression (follow-up)	-0.04	0.02	.11	.28	-0.01	0.21	.46	0	-0.37	0.31	.22	.11	Not enough studies				Not enough studies			

Note. BG = between-group, WS = within-subject; not enough studies (n = 2)

Meta-Regression Results

On the other hand, for the remaining meta-regressions, the other covariates (e.g., percentage of women in the sample, mean age of participants, number of sessions) did not significantly predict any of the outcomes, with the only exception of between-group QoL at follow-up ($p = .01$, $R^2 = .73$).

Subgroup Analyses Results

These analyses must be interpreted with caution due to the small sample sizes in most subgroups. The clearer subgroup differences were found in favor of face-to-face intervention delivery (compared to remote or combined deliveries) in improving QoL outcomes, both after treatment ($\chi^2(2) = 10.36$; $p < .01$ for between-group and $\chi^2(2) = 7.81$; $p = .02$ for within-subject outcomes) and at follow-up ($\chi^2(2) = 35.43$; $p < .01$ for between-group and $\chi^2(2) = 29.04$; $p < .01$ for within-subject outcomes). In addition, advanced cancer patients improved significantly more than ALS patients in depression outcomes at post-treatment ($\chi^2(1) = 12.28$; $p < .01$). Subgroup analyses were not statistically significant for the remaining outcomes.

Sensitivity Analyses Results

Sensitivity analyses revealed no statistically significant differences between randomized and non-randomized controlled trials (all $p > .05$). In addition, sensitivity analyses showed that effects on within-subject depression at follow-up became non-significant (SMD = 0.26, 95% CI [-0.13 to 0.65], $p = .19$) after removing studies that included mixed stage III and IV cancer patients

(see Supplementary Table 1). All the other effects on outcome and process variables remained significant after removing those studies, and the heterogeneity was overall decreased ($I^2 = 0\%$ to 75% versus $I^2 = 22\%$ to 97%).

Discussion

This review had two primary objectives. First, it aimed to quantitatively synthesize evidence on the effects of ACT on QoL and depression and anxiety symptoms in people with advanced progressive illness. Second, it examined the role of process variables, such as psychological flexibility and values-based action, in their association with these clinical improvements. This meta-analysis found that ACT showed moderate effects in improving QoL and emotional symptoms in terminally ill patients when compared to active controls and in pre-post comparisons, though heterogeneity was high across outcomes. These effects were generally maintained at follow-up; psychological flexibility and valued action were associated with QoL improvements and emerged as candidate process-related correlates.

Our study showed that ACT was associated with statistically significant improvements in QoL in both controlled comparisons (e.g., usual care or educational support) and within-subject analyses. In some cases, these gains were maintained over time. These findings are consistent with Fang et al. (2023), who also reported a large ES for QoL improvement in advanced cancer patients. This may be because they included fewer studies and participants. These findings have been confirmed by other systematic reviews in similar populations (Li et al., 2021). However, our review uniquely expands the scope to include a broader range of terminally ill patients, such as those in palliative care and those with ALS.

The findings showed that increases in psychological flexibility were associated with QoL improvements, consistent with ACT's theoretical model, which proposes that improvements in clinical outcomes occur as consequences of changes in underlying psychological processes rather than as direct therapeutic targets (Hayes, 2020). Future research should examine whether ACT's emphasis on acceptance and values may help address existential concerns often present in end-of-life care, such as fear of death or uncertainty, which fall outside traditional diagnostic frameworks (Lee, 2020). Importantly, values work should be individualized and evaluated in terms of contextual fit and behavioral function, as rigid rule-following may also contribute to distress in some cases. However, the meta-regression analyses examining valued action as a predictor should be interpreted with considerable caution, as the R^2 values of 1.00 for several outcomes (QoL at post-treatment, and within-subject anxiety at post-treatment) suggest potential overfitting, likely due to the limited number of studies ($k = 2-8$ across models) relative to the complexity of the model, which may have resulted in perfect separation or multicollinearity issues rather than genuine moderation effects.

Research has highlighted the health benefits of having supportive relationships, which may promote physical and mental well-being (Cacioppo & Patrick, 2008). Conversely, loneliness and social isolation have been associated with increased mortality risk, with effect sizes comparable to well-established risk factors (Holt-Lunstad et al., 2015). These findings suggest ways to develop therapeutic interventions that can alleviate the adverse effects of social stress and improve overall QoL during critical life stages.

Although our meta-regression analyses for valued action were limited by small sample sizes and should be interpreted with caution, the theoretical framework of ACT suggests that value-based interventions may be clinically useful when they are workable in context and guided by the functional analysis of the individual's behavior (Menzies & Menzies, 2024; Wersebe et al., 2017). While previous evidence suggests that values clarification and valued action often precede a reduction in symptoms (Gloster et al., 2020), our findings for valued action as a predictor were inconclusive due to limited data and potential overfitting.

According to our results, psychological flexibility was an important predictor of long-term QoL improvement, particularly in the context of terminal illness. Improvements in psychological flexibility, which encompasses acceptance of difficult internal experiences, may have a cumulative positive impact on QoL over time. Our findings showed near-large effect sizes for psychological flexibility, both compared to active controls and within subjects, with slight improvements noted at follow-up. These results are consistent with a potentially important role of psychological flexibility in improving QoL.

Our findings differ from previous reviews by Fang et al. (2023), which reported no significant effect of psychological flexibility in the context of cancer and advanced cancer. The absence of clear findings on psychological flexibility in these studies could reflect methodological limitations. Many trials focus primarily on clinical outcomes such as anxiety, depression, or QoL, rather than directly assessing flexibility through validated tools, such as the AAQ-II. Furthermore, the heterogeneity of populations and interventions, coupled with limited process-focused measures, constrains the ability to detect significant effects. In our paper, we acknowledge these gaps and emphasize the importance of future research to

systematically include flexibility assessments to capture ACT's core processes of change in end-of-life contexts. In contrast, Zhao et al. (2021) found a moderate ES for this variable. Our estimates for valued action were moderate but not statistically significant across all outcomes. This is likely due to the limited sample size in studies assessing these variables and the high heterogeneity of the results. The analysis shows that improvements may co-occur with, or be associated with, increases in psychological flexibility and, to a lesser extent, valued action. However, valued action should not be assumed to be uniformly beneficial, as its impact depends on the function of the behavior and the contextual contingencies in which it occurs. These findings suggest that psychological flexibility may be an important therapeutic process in end-of-life care, though further research with larger samples is needed to confirm this relationship.

Some argue that ACT promotes psychological flexibility by encouraging acceptance of thoughts and emotions rather than attempting to suppress them (Hayes & Hofmann, 2021). As early as the 1980s, research showed that attempting to control or suppress thoughts can paradoxically intensify them (Wegner et al., 1987). Conversely, accepting the symptoms often leads to their reduction (Hayes, Strosahl, et al., 2006). Together, these findings and the long-term effect on QoL highlight the need to consider delayed response patterns when evaluating the efficacy of ACT. This may help clinicians set realistic expectations that focus on improving QoL rather than immediate symptom relief. Our results are consistent with previous studies that have emphasized the importance of acceptance when coping with distress associated with terminal illness (Davis et al., 2017; Secinti et al., 2019). Our consistent results across between-group and within-subject outcomes align with previous reviews in cancer patients (Fang et al., 2023; Li et al., 2021) and advanced illness patients (Gibson Watt et al., 2023), though the ESs were smaller. Unlike QoL, ACT process variables did not consistently predict improvements in these emotional symptoms. Anxiety and depression in terminal illness may arise from specific fears, such as mortality and loss of autonomy (Butow et al., 2021; Hong et al., 2022), which are not fully addressed by reducing experiential avoidance. Overall, while ACT moderately reduces anxiety and depression in terminally ill patients, these symptoms are multifaceted and may be influenced by factors beyond psychological flexibility.

First, it is important to note that the results suggest that none of the other continuous variables (e.g., age, percentage of women, number of sessions) significantly predicted treatment outcome. These null findings may suggest that effects do not vary markedly by age or gender, although tests may be underpowered. Furthermore, even shorter interventions (e.g., four sessions) may yield similar ES to longer treatments (e.g., 12 sessions). Subgroup tests suggested larger effects for face-to-face delivery, though these results require cautious interpretation. This finding may suggest that face-to-face interactions may play an important role for terminally ill patients, perhaps by strengthening the therapeutic relationship, reducing distractions, and providing richer nonverbal communication (Berle et al., 2015). In contrast, therapy format (e.g., individual versus group therapy) does not appear to affect treatment outcomes. Finally, ACT's versatility is further supported by its potential benefits in treating terminally ill patients with different diagnoses (e.g., advanced cancer and ALS).

Our results suggest that ACT was associated with statistically significant improvements in QoL among people with advanced

progressive illnesses, with potential benefits beyond advanced cancer, though data for non-oncological diagnoses, such as ALS, remain limited. These findings suggest that ACT may be a promising approach for addressing some of the complex challenges of end-of-life care. Clinicians may consider ACT as one therapeutic option for terminally ill patients, particularly when the goal is to enhance psychological flexibility and QoL. Furthermore, ACT has shown utility for caregivers, addressing a critical gap in care systems (Gibson Watt et al., 2023). However, improving the QoL of people in palliative care does not necessarily improve family well-being, underscoring the necessity for tailored interventions for caregivers (Dionne-Odom et al., 2015).

There are several limitations to the present study that should be noted. First, a potential source of bias was identified primarily due to the self-reported nature of the measurement of the variables. However, it has been argued that in the context of psychotherapy research, there is limited evidence of an overestimation of effects due to self-reported outcomes (Munder & Barth, 2018). Future studies should incorporate multi-method assessment of outcomes and intervention-related change (e.g., behavioral/observational indicators of change process, or informant reports) to strengthen inferences beyond self-reported change. Second, we observed a high heterogeneity across studies for most outcomes, which is consistent with prior reviews in studies on ACT for cancer patients (Fang et al., 2023; González-Fernández & Fernández-Rodríguez, 2019; Sauer et al., 2024). This may complicate the interpretation of the true overall effect and limit the generalizability of the findings. Third, some evidence suggests that one of the main measures of psychological flexibility is highly correlated with psychological distress (Langer et al., 2024). This could limit the interpretation of meta-regression analyses examining the relationship between psychological flexibility and symptoms of anxiety and depression. In this sense, the meta-regressions using valued action as a predictor with R^2 values of 1 should be interpreted with caution, because of the risk of potential overfitting and multicollinearity issues. Fourth, the trim-and-fill test revealed some evidence of publication bias for QoL at the follow-up. Conversely, we did not detect evidence of publication bias for the other outcomes. Fifth, the small sample size in some meta-regressions and some groups in the subgroup analyses may affect the validity of these analyses and should be interpreted with caution. Sixth, the inclusion of stage III cancer patients in some studies may have introduced heterogeneity, though sensitivity analyses confirmed the robustness of the findings. Seventh, the inclusion of single-arm trials in within-subject analyses limits causal inferences for these estimates, though our primary conclusions are based on controlled between-group comparisons from controlled studies. Eighth, the inclusion of different study designs (RCTs, quasi-experimental, and single-arm studies) may limit direct comparability and requires cautious interpretation. However, we addressed this by separating controlled (between-group) from uncontrolled (within-subject) analyses and conducting sensitivity analyses comparing randomized versus non-randomized studies. Finally, although RCTs can reduce several threats to internal validity and provide estimates of average effects, they may have limited ecological validity for individualized, function-guided clinical practice (Pérez Álvarez, 2020); therefore, future research should complement group trials with idiographic, repeated-measures designs (e.g., single-case experimental designs and intensive time-series assessment) to evaluate clinically

meaningful change at the individual level. Relatedly, these findings should not be interpreted as supporting a one-size-fits-all protocol; in end-of-life care, intervention components, particularly values work, should be individualized and evaluated with respect to behavioral function and contextual constraints.

In conclusion, integrating ACT interventions and addressing key psychological processes may improve our understanding of psychotherapy's potential to mitigate psychological distress in palliative care. ACT's emphasis on addressing existential dilemmas through values-based interventions provides a distinctive approach to preparing patients for the end-of-life. Although it is often difficult to feel fully prepared for the ethical and existential challenges of terminal illness, an existential perspective may offer a framework through which individuals can be guided by their values toward an authentic, dignified, and humane farewell. This, in turn, may be associated with improved QoL, even in the final moments. Our findings are broadly consistent with evidence suggesting that ACT can be a promising approach in palliative care, highlighting links between process-based interventions and process-related correlates of change. Taken together, these findings suggest that ACT may be associated with improvements in QoL and psychological distress, potentially by addressing existential dilemmas and fostering adaptive behaviors. This integration paves the way for future research at the intersection of psychotherapy and change processes, particularly values-based action, in end-of-life care. In this context, values work should be understood as clinically relevant when it is workable in the person's situation and informed by functional assessment, rather than assumed to be inherently beneficial. By promoting values-driven behavior and psychological flexibility, ACT may offer a compassionate, evidence-based approach that could support terminally ill patients, although more rigorous and adequately powered trials are needed to confirm effects and clarify mechanisms across settings and diagnoses.

Author Contributions

Juanjo Macías: Conceptualization, Writing - Original Draft.
Lucía Lara-Merín: Writing - Review & Editing, Investigation.
Carlos López-Pinar: Conceptualization, Writing - Original Draft, Investigation, Methodology, Formal Analysis, Visualization, Project Administration.

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Conflict of Interest

In recent years, Carlos López-Pinar has received financial compensation for conducting training in behavioral therapies. This background is acknowledged as a potential source of bias when

interpreting some of the topics discussed in this article. The rest of the authors have no conflict of interests to declare.

Data Availability Statement

Both the database and R code used for data analysis are available at Open Science Framework in this link: https://osf.io/3jwty/?view_only=9b988d4f6be14fa8b4999360747a3dee

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