

Mental Health Interventions to Improve Psychological Outcomes in Informal Caregivers of Critically Ill Patients: A Systematic Review and Meta-Analysis*

OBJECTIVES: Determine effect of mental health interventions on psychological outcomes in informal caregivers of critically ill patients.

DATA SOURCES: Searches conducted in MEDLINE, Embase, and other databases from inception to October 31, 2019.

STUDY SELECTION: Interventions for informal caregivers of critically ill patients in adult ICU, PICU, or neonatal ICU.

DATA EXTRACTION: Two independent, blinded reviewers screened citations and extracted data. Random-effects models with inverse variance weighting pooled outcome data when suitable. Psychologic outcomes categorized: 1) negative (anxiety, depression, post-traumatic stress disorder, distress, and burden) or 2) positive (courage, humanity, justice, transcendence, temperance, and wisdom and knowledge). Stratification according to intervention type and patient population was performed.

DATA SYNTHESIS: Of 11,201 studies, 102 interventional trials were included ($n = 12,676$ informal caregivers). Interventions targeted caregiver experience ($n = 58$), role ($n = 6$), or support ($n = 38$). Meta-analysis (56 randomized controlled trials; $n = 22$ [39%] in adult ICUs; $n = 34$ [61%] in neonatal ICU or PICU) demonstrated reduced anxiety (ratio of means = 0.92; 95% CI, 0.87–0.97) and depression (ratio of means = 0.83; 95% CI, 0.69–0.99), but not post-traumatic stress disorder (ratio of means = 0.91; 95% CI, 0.80–1.04) or distress (ratio of means = 1.01; 95% CI, 0.95–1.07) among informal caregivers randomized to mental health interventions compared with controls within 3 months post-ICU discharge. Increased humanity (ratio of means = 1.11; 95% CI, 1.07–1.15), transcendence (ratio of means = 1.11; 95% CI, 1.07–1.15), and caregiver burden (ratio of means = 1.08; 95% CI, 1.05–1.12) were observed. No significant effects of mental health interventions observed after 3 months postdischarge.

CONCLUSIONS: Mental health interventions for caregivers of critically ill patients improved short-term anxiety, depression, humanity, and transcendence while increasing burden. Clinicians should consider short-term prescriptions of mental health interventions to informal caregivers of critically ill patients with capacity to manage interventions.

KEY WORDS: critical care; informal caregivers; intensive care unit; psychology; systematic review

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Critically ill patients admitted to ICUs frequently rely on informal caregivers (e.g., family, friends) to act as surrogate decision-makers and emotional supporters (1, 2). Caregivers of critically ill patients have long-lasting negative psychological sequelae following an ICU stay including anxiety, depression, and post-traumatic stress disorder (PTSD) (3, 4).

Mental health interventions improve psychological outcomes in informal caregivers of critically ill patients (5). It is unknown whether these interventions (e.g., to improve knowledge about mental health [6] or to prevent mental disorders [7, 8]) affect informal caregivers by reducing negative (e.g., anxiety) or increasing positive (e.g., humanity) psychological outcomes.

We performed a systematic review and meta-analysis of interventional trials conducted in adult ICU, neonatal ICU, and PICU to determine how mental health interventions affect negative and positive psychological outcomes in informal caregivers of critically ill patients. We hypothesized that mental health interventions improve psychological outcomes in informal caregivers of critically ill patients.

METHODS

This systematic review was conducted and reported to the Preferred Reporting Items for Systematic Review and Meta-Analyses reporting guideline (9) (**Supplemental Table 1**, <http://links.lww.com/CCM/G288>), registered on PROSPERO (CRD42019133700) prior to data extraction.

Outcomes Measures

The main outcome was informal caregiver psychological outcomes categorized: 1) negative psychological outcomes (anxiety [state only], depression, PTSD, distress [discomforting emotional state in response to stressor or demand], and burden) as defined by the American Psychological Association (10) or others (11, 12) and 2) positive psychological outcomes (courage, humanity, justice, transcendence, temperance, and wisdom and knowledge) as defined in the Character Strengths and Virtues book (that provides a classification system and theoretical framework for six classes of positive virtues made up of 24 character strengths) (13–15). Both symptoms (i.e., self-report) and diagnoses included.

Operational definitions provided in **Supplemental Table 2** (<http://links.lww.com/CCM/G288>).

Populations, Interventions, Comparators, Settings, and Study Designs

We included quantitative and qualitative studies reporting trials targeted at informal caregivers of critically ill patients, any age. We excluded interventions for healthcare professionals. We included studies where the intervention was performed outside ICU (e.g., recovery psychology follow-up clinics). We defined: 1) a caregiver as any informal (i.e., nonclinical) person who regularly provides patient support and is in some way implicated in patient care or directly affected by patient health (e.g., family, friend) (16) and 2) critically ill patients as any persons currently or previously admitted to ICU (16).

Data Sources and Searches

Literature searches were conducted in MEDLINE (**Supplemental Table 3**, <http://links.lww.com/CCM/G288>), Embase, PsycINFO, CINAHL, and Cochrane CENTRAL Register of Controlled Trials. Search strategies were developed with a Medical Librarian (D.L.L.), revised after preliminary results. Controlled vocabulary terms and text words relating to caregivers and critical care, interventions, and psychology were used. We searched Cochrane Database of Systematic Reviews to identify related review articles; reference lists were screened to identify studies missed in search. All databases were searched from inception to October 31, 2019. Reference lists of included papers were reviewed to identify potentially missed studies. No language or date limits were applied.

Study Selection

After a subset of the team achieved 100% agreement on pilot-test of 50 random citations, titles, and abstracts were reviewed independently in duplicate (S.J.C., B.K.R.). Full abstracts of five foreign language studies (three French, two Italian) were translated by a fluent study volunteer blinded to the review objective (M.C.). Any study selected by either reviewer progressed. Full-texts were reviewed independently in duplicate (S.J.C., B.K.R.); articles selected by both reviewers were included. No foreign language abstract was progressed to full-text review. Disagreements resolved by a third

TABLE 1.
Effect of Mental Health Interventions for Informal Caregiver Psychologic Outcomes

Intervention Type ^{a,b}	Negative Psychologic Outcomes				
	Anxiety, <i>n</i> = 33 (52%) ^f	Depression, <i>n</i> = 34 (54%) ^f	Post-Traumatic Stress Disorder, <i>n</i> = 21 (33%) ^f	Distress, <i>n</i> = 22 (35%) ^f	Burden, <i>n</i> = 12 (19%) ^f
Caregiver experience ^c	18	20	13	15	6
<i>n</i> = 30 (48%) ^f	↑4 ↔14 ↓0	↑5 ↔15 ↓0	↑3 ↔9 ↓10	↑3 ↔11 ↓1	↑1 ↔5 ↓0
Preventive psychology	↑2 ↔3 ↓0	↑2 ↔3 ↓0	↑1 ↔1 ↓0	↑0 ↔3 ↓0	↑0 ↔0 ↓0
Recovery psychology	↑1 ↔2 ↓0	↑0 ↔4 ↓0	↑1 ↔4 ↓0	↑0 ↔1 ↓0	↑0 ↔0 ↓0
Skin-to-skin contact	↑0 ↔2 ↓0	↑0 ↔3 ↓0	↑0 ↔1 ↓	↑0 ↔3 ↓1	↑0 ↔1 ↓0
Caregiver role ^d	4	3	2	2	1
<i>n</i> = 6 (10%) ^f	↑0 ↔4 ↓0	↑0 ↔3 ↓0	↑0 ↔2 ↓0	↑0 ↔2 ↓0	↑0 ↔1 ↓0
Individual patient care	↑0 ↔0 ↓0	↑1 ↔0 ↓0	↑0 ↔0 ↓0	↑1 ↔0 ↓0	↑0 ↔0 ↓0
Patient advocacy	↑0 ↔1 ↓0	↑0 ↔1 ↓0	↑0 ↔0 ↓0	↑0 ↔1 ↓0	↑0 ↔1 ↓0
Caregiver support ^e	11	11	6	5	5
<i>n</i> = 20 (32%) ^f	↑4 ↔7 ↓0	↑5 ↔5 ↓1	↑1 ↔5 ↓0	↑0 ↔5 ↓0	↑0 ↔4 ↓0
Caregiver liaison	↑0 ↔3 ↓0	↑1 ↔1 ↓0	↑0 ↔1 ↓0	↑0 ↔1 ↓0	↑0 ↔1 ↓0
Psychoeducation	↑1 ↔4 ↓0	↑1 ↔4 ↓0	↑1 ↔3 ↓1	↑2 ↔2 ↓0	↑1 ↔2 ↓0

↑ = significant improvement, ↓ = significant detriment, ↔ = no effect.

^aAs reported by Finucane et al (17).

^bSelected interventions represented by at least three included studies.

^cInterventions aimed at caregiver distress, difficulty or deteriorating relationships, balancing need to relieve suffering with desire to communicate, or helplessness versus control. Preventive psychology (i.e., trauma-preventive psychology, psychologic communication strategy, creating opportunities for parent engagement). Recovery psychology (i.e., coping skills training, mindfulness training, brief-cognitive behavioral therapy, recovery programme). Skin-to-skin contact (i.e., skin-to-skin, kangaroo care).

^dInterventions aimed at caregiver detection and prevention of patient delirium, monitoring patient symptoms, or advocating for the patient. Individual patient care (i.e., newborn individualized developmental care and assessment program). Patient advocacy (i.e., family-staff communication training, patient communication training).

^eInterventions aimed at caregiver knowledge on delirium, advice on how to respond to the patient, caregiver support systems, or patient outcomes. Caregiver liaison (i.e., liaison nurse, communication facilitator, transitional consultation program). Psychoeducation (i.e., emotional support meetings, stress management interviews, psychoeducational tool, self-help manual, patient psychoeducational support).

^f*n*, number of studies that reported each objective or conclusion; %, *n* as a proportion of total randomized controlled trials (*n* = 63).

reviewer (M.A.). References managed in Endnote X9 (Clarivate Analytics, Philadelphia, PA).

Data Extraction and Quality Assessment

Two reviewers (S.J.C., B.K.R.) extracted data independently in duplicate using a data collection sheet developed and piloted by the review team

(**Supplemental Methods**, <http://links.lww.com/CCM/G289>). Discrepancies resolved by a third reviewer (M.A., K.K.). Intervention aim categorized as caregiver experience, role, or support, based on a literature review of informal caregivers of critically ill patients by Finucane et al (17). Intervention stage was categorized to Medical Research Council and National Institutes of Health Research (18). Operational

Positive Psychologic Outcomes					
Courage, <i>n</i> = 7 (11%) ^f	Humanity, <i>n</i> = 4 (6%) ^f	Justice, <i>n</i> = 0 (0%) ^f	Temperance, <i>n</i> = 2 (3%) ^f	Transcendence, <i>n</i> = 14 (22%) ^f	Wisdom and Knowledge, <i>n</i> = 2 (3%) ^f
5	2	0	0	7	0
↑1 ↔4 ↓0	↑0 ↔2 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑3 ↔2 ↓2	↑0 ↔0 ↓0
↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑1 ↔0 ↓0	↑0 ↔0 ↓0
↑0 ↔2 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0
↑0 ↔2 ↓0	↑0 ↔1 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0
1	0	0	0	2	0
↑1 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑1 ↔1 ↓0	↑0 ↔0 ↓0
↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0
↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑1 ↔0 ↓0	↑0 ↔0 ↓0
1	2	0	2	5	2
↑0 ↔1 ↓0	↑0 ↔2 ↓0	↑0 ↔0 ↓0	↑2 ↔0 ↓0	↑2 ↔3 ↓0	↑1 ↔1 ↓0
↑1 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑0 ↔1 ↓0	↑0 ↔0 ↓0
↑0 ↔1 ↓0	↑0 ↔1 ↓0	↑0 ↔0 ↓0	↑0 ↔0 ↓0	↑1 ↔1 ↓0	↑0 ↔0 ↓0

definitions provided in Supplemental Table 2 (<http://links.lww.com/CCM/G288>). We used the Adapted Cochrane Risk of Bias Assessment Tool for assessing risk of bias (19). For grading quality of evidence, we used BMJ Best Practice Grading of Recommendations Assessment, Development and Evaluation (GRADE) of Evidence Tool for quantitative studies (20) and GRADE-Confidence in the Evidence from Reviews of Qualitative research for qualitative studies (21).

Data Synthesis and Analysis

We used random-effects models with inverse variance weighting to pool outcome data from each randomized controlled trial (RCT). Pooled data are reported as ratio of means (RoM [experimental group to control group]) (22). Studies were excluded from meta-analysis if additional data was not provided and we were not able to estimate mean and SD. Two-sided *p* value of less than 0.05 was considered

statistically significant. For each outcome, we estimated the *I*² (23). Magnitude of heterogeneity was quantified using τ^2 (24). The *I*² was viewed as a proportion of variability due to τ^2 ; low (25–49%), moderate (50–74%), or high ($\geq 75\%$) (25). Estimates of heterogeneity were used to guide detailed meta-analytic stratified analyses. We performed subgroup meta-analyses according to intervention type (i.e., caregiver experience, role, or support) and patient population (i.e., adult, neonatal, or pediatric). If heterogeneity diminished upon stratification, this was interpreted as evidence that the stratification variable was a source of heterogeneity. Outcomes not amenable to meta-analysis are presented by intervention type and statistically significant effects. We synthesized results reported from included qualitative studies using thematic synthesis for reviews on health research (26). We developed discrete themes that represented the findings reported in primary studies

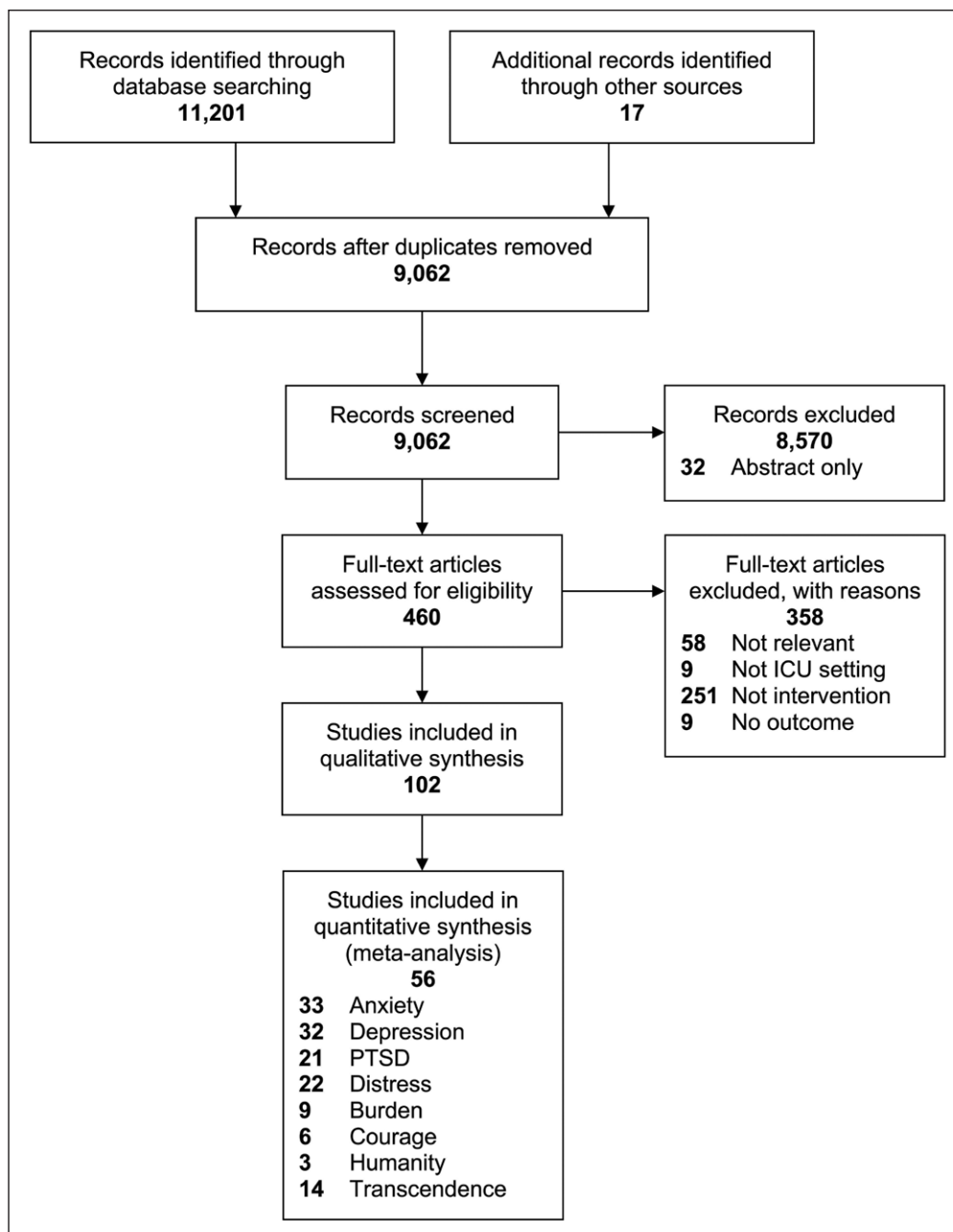


Figure 1. Study flow diagram. PTSD = post-traumatic stress disorder.

and considered these themes to generate new interpretive constructs, explanations, or hypotheses (27). We then integrated our qualitative and quantitative findings by using qualitative results to interrogate quantitative results, aiding interpretation of heterogeneity as a rich source of information and to identify research gaps (28). Data analysis was performed using STATA-IC16 (StataCorp LLC, College Station, TX) and NVivo12 (QSR International Pty Ltd., version 12, Melbourne, Australia). Additional details on

data synthesis and analysis in the Supplemental Methods (<http://links.lww.com/CCM/G289>).

RESULTS

Results of the Search

We screened 11,201 unique abstracts and reviewed 460 full-text articles; 358 full-text articles were excluded, most common reasons being the study did not include an intervention ($n = 251/358$) or was not relevant to our research question ($n = 58/358$) (Fig. 1). Hand searching identified 17 studies, of which all were excluded (zero interventions). Frequency of disagreements and agreements between reviewers for the full-text screen was calculated using Cohen's Kappa statistic ($\kappa = 0.89$).

Included Studies

Trial characteristics are in Supplemental Table 4 (<http://links.lww.com/CCM/G288>), overall results by intervention type in Table 1. Classification of trials according to intervention aim is shown in Supplemental Figure 2 (<http://links.lww.com/CCM/G288>). Among 102 studies, 63 were RCTs, 16 quasi-experimental trials, and 23 uncontrolled trials. Eight studies were qualitative, of which six studies performed thematic analysis and two studies used grounded theory. Sixty-four trials were single-centered, 38 multicentered. Fifty-eight studies were in neonatal ICUs (NICUs), 38 in adult ICUs, and two in PICUs (Supplemental Fig. 1, <http://links.lww.com/CCM/G288>). Several studies focused on specific clinical circumstances (Supplemental Table 5, [1418](http://</p>
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links.lww.com/CCM/G288) and long-term follow-up of interventions (**Supplemental Table 6**, <http://links.lww.com/CCM/G288>).

Meta-analysis included 56 RCTs; 34 RCTs (61%) in NICUs or PICUs. Caregiver outcomes were reported within (i.e., short-term, $n = 39$) or after (i.e., long-term, $n = 17$) 3 months postdischarge. Additional descriptions in the **Supplemental Results** (<http://links.lww.com/CCM/G290>). Pooled estimates from meta-analyses in **Supplemental Table 7** (<http://links.lww.com/CCM/G288>), summary of findings in **Supplemental Table 8** (<http://links.lww.com/CCM/G288>). Summary of findings from qualitative studies in **Supplemental Table 9** (<http://links.lww.com/CCM/G288>).

Negative Psychologic Outcomes

Five negative psychologic outcomes from 56 RCTs were amenable to meta-analysis (**Fig. 2A**). Meta-analysis of 33 trials ($n = 16$ [49%] in adult ICUs) demonstrated interventions to significantly reduce anxiety within 3 months postdischarge (RoM, 0.92; 95% CI, 0.87–0.97; $I^2 = 97.06%$; $n = 3,478$ caregivers). No significant effect was observed after 3 months (RoM, 0.96; 95% CI, 0.91–1.02; $I^2 = 90.17%$; $n = 2,845$ caregivers) (**Fig. 3A**). Seven studies demonstrated significant reductions in anxiety; four targeted caregiver experience (29–32) and three targeted caregiver support (33–35). Three were multisite (30, 31, 34), the largest a cluster-crossover RCT investigating flexible family visitation policies across 36 adult ICUs in Brazil (31). Two studies noted significantly positive long-term effects; Family Participation in Patient Care (35) and Family Nurture Interventions (32) improved anxiety after 3 months postdischarge.

Mental health interventions ($n = 32$ total; $n = 15$ [47%] in adult ICUs) significantly decreased depression within 3 months of ICU discharge (RoM, 0.83; 95% CI, 0.69–0.99; $I^2 = 97.09%$; $n = 3,650$ caregivers). No effect on depression after 3 months was observed (RoM, 0.99; 95% CI, 0.83–1.20; $I^2 = 98.44%$; $n = 2,870$ caregivers) (**Fig. 3B**). Six RCTs observed significant improvement, four evaluation trials within 3 months discharge (30, 31, 33, 34) and two single-site studies targeting caregiver experience (32) and caregiver support (36) at 4 and 6 months postdischarge, respectively. All six RCTs but the piloting and feasibility trial by Samuel et al (36), a Pediatric Intensive Care Follow-Up Clinic, reported significant improvements in anxiety.

Conversely, increased depression after 3 months postdischarge was reported by four trials (37–40). Kentish-Barnes et al (39) found in relatives of patients who died in ICU, condolence letters failed to alleviate psychologic distress and worsened depression and symptoms of PTSD. In addition to increased depression, the multisite evaluation RCT by Bohart et al (38) reported increased anxiety and decreased courage at 12 months postdischarge for their 3-month Recovery Programme.

Outcomes for informal caregiver PTSD were inconsistent and meta-analysis of 21 RCTs ($n = 14$ [67%] in adult ICUs) demonstrated no significant effect of interventions on PTSD symptoms at any time (**Supplemental Fig. 3a**, <http://links.lww.com/CCM/G288>). Four studies on caregiver experience interventions reported significantly decreased PTSD symptoms within 3 months discharge from adult mixed ICU (30, 41), adult medical-surgical ICU (42), or NICU (43), while two studies reported significantly increased PTSD symptoms in adult medical ICU (44) and NICU (45). Studies with longer-term follow-up reported conflicting results (36, 39, 46, 47). Two of 21 trials tested ICU Family Diaries to reduce risk of PTSD symptoms; the piloting and feasibility trial by Jones et al (41) informed the evaluation trial across four adult medical-surgical ICUs by Nielsen et al (42). Among studies reporting on symptoms of PTSD, only the evaluation RCT by Lautrette et al (30) that assessed end-of-life conferences and bereavement leaflets across 22 adult mixed ICUs observed a consistent reduction in anxiety, depression, and PTSD at 3 months postdischarge.

Meta-analysis of 22 trials ($n = 7$ [32%] in adult ICUs) identified no significant effect of on psychologic distress at any time (**Supplemental Fig. 3b**, <http://links.lww.com/CCM/G288>). Two studies reported significantly improved caregiver distress within 3 months discharge (34, 48) while two reported increased distress (49, 50); all studies conducted in NICUs. No study reported significant improvement after 3 months discharge.

Interventions pooled across five RCTs ($n = 3$ [60%] in adult ICUs) significantly increased caregiver burden [feeling need to do more] within 3 months of ICU discharge (RoM, 1.08; 95% CI, 1.05–1.12; $I^2 = 6.96%$; $n = 819$ caregivers) (**Fig. 4A**). There was no significant effect after 3 months across four trials that reported long-term outcomes (RoM, 0.81; 95% CI, 0.81–1.06; $I^2 = 0.00%$; $n = 127$ caregivers). The single study that reported significantly increased burden was the Creating

Opportunities for Parent Engagement evaluation trial by Melnyk et al (34) in two NICUs.

Positive Psychologic Outcomes

Three positive psychologic outcomes from 22 RCTs were amenable to meta-analysis (Fig. 2B). These included courage (e.g., coping, resilience) ($n = 5$ RCTs [$n = 3$; 60% adult ICUs], Supplemental Fig. 4, <http://links.lww.com/CCM/G288>), humanity (e.g., kindness, social intelligence) ($n = 3$ RCTs [$n = 0$; 0% adult ICUs], Fig. 4B), and transcendence (e.g., gratitude, satisfaction) ($n = 14$ RCTs [$n = 7$; 50% adult ICUs], Fig. 4C). Humanity (RoM, 1.11; 95% CI, 1.07–1.15; $I^2 = 0.01\%$; $n = 338$ caregivers) and transcendence (RoM, 1.04; 95% CI, 1.02–1.06; $I^2 = 74.39\%$; $n = 2,617$ caregivers) were significantly increased within 3 months postdischarge. There were no significant differences in humanity and transcendence after 3 months postdischarge or courage at any time. Findings on positive psychologic outcomes detailed in the Supplemental Results (<http://links.lww.com/CCM/G290>).

Stratified Analyses

Estimates grouped by intervention type and patient population were inconsistent; no outcome was consistently significantly improved across all interventions (Supplemental Table 10, <http://links.lww.com/CCM/G288>). Significant positive effects of mental health interventions on caregiver depression and PTSD, as well as a significant negative effect on caregiver burden, were not consistently statistically significant due to smaller number of studies in the subgroup analyses. Stratified analyses for quasi-experimental and uncontrolled studies not amenable to meta-analysis in Supplemental Figure 5 (<http://links.lww.com/CCM/G288>). Additional details in the Supplemental Results (<http://links.lww.com/CCM/G290>).

Risk of Bias and Certainty of Evidence

Risk of bias scores in Supplemental Table 10 (<http://links.lww.com/CCM/G288>). Certainty of evidence assessments summarized in Supplemental Tables 11–13 (<http://links.lww.com/CCM/G288>). Detailed

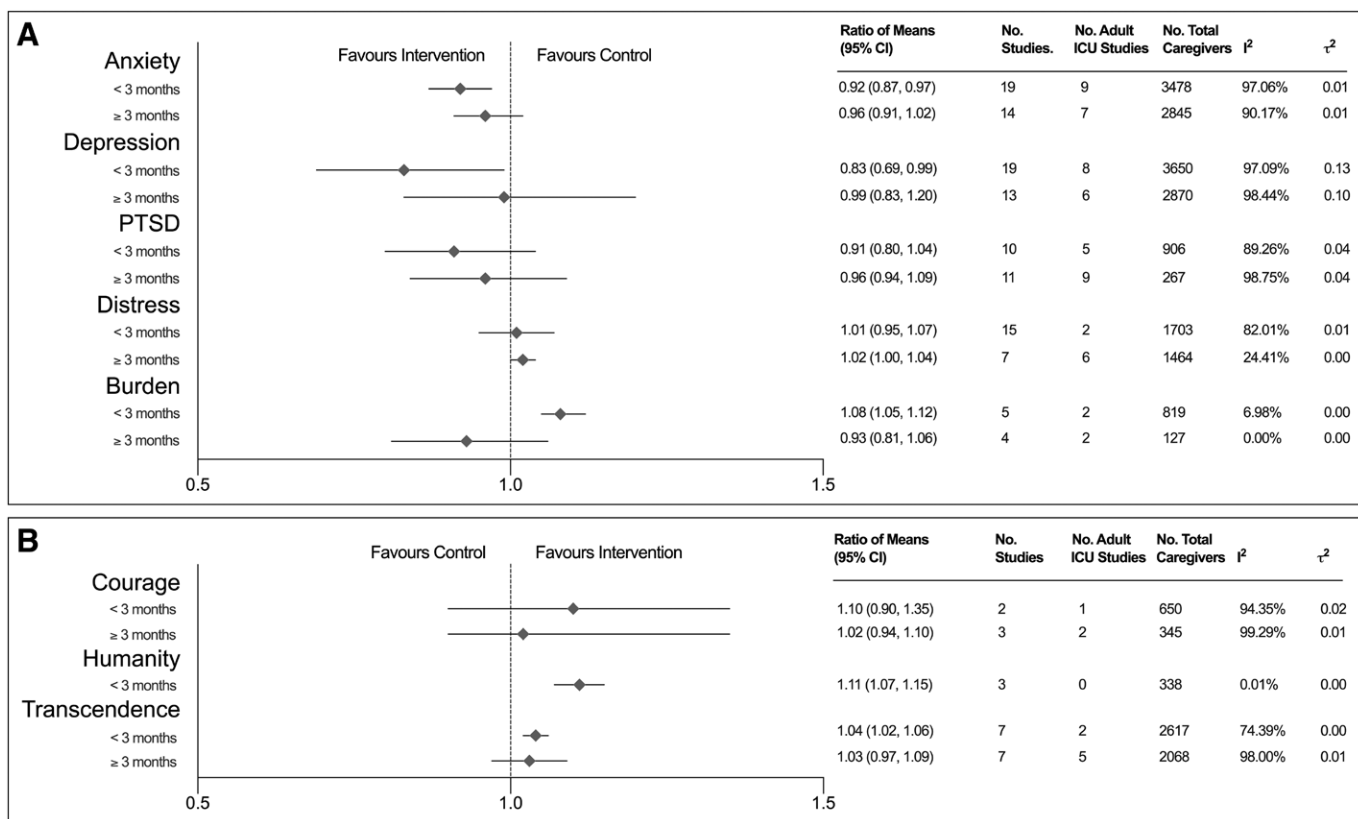


Figure 2. Ratio of means in psychological outcomes in the randomized trials amenable to meta-analysis. Ratio of means is the difference between the experimental group to the control group. Horizontal lines denote 95% confidence intervals. Diamonds represent point estimates for informal caregiver (A) negative and (B) positive psychological outcomes grouped by follow-up. PTSD = post-traumatic stress disorder.

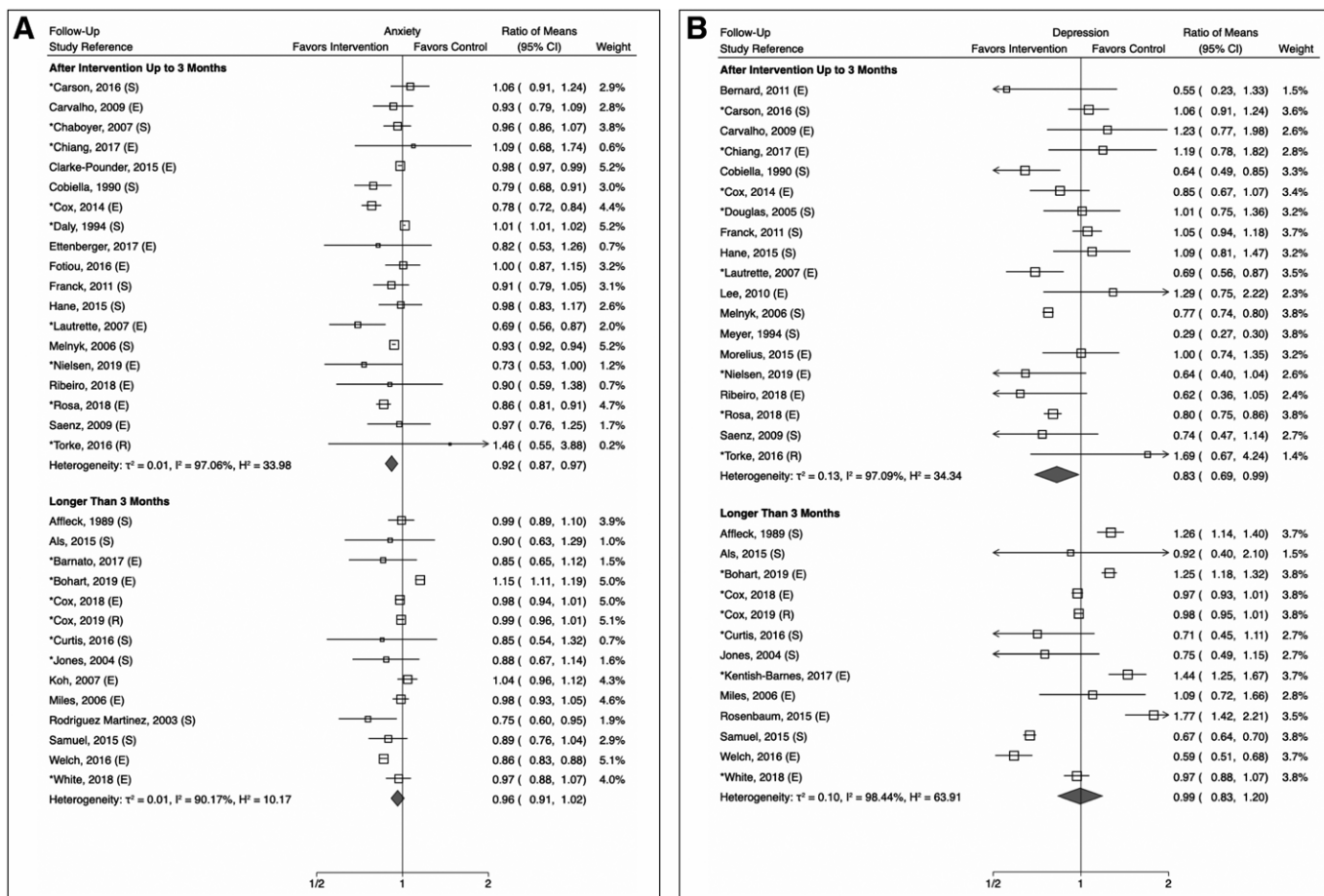


Figure 3. Ratio of means in psychological outcomes in the randomized trials amenable to meta-analysis. Ratio of means is the difference between the experimental group to the control group. *Horizontal lines* denote 95% confidence intervals. *Diamonds* represent point estimates for informal caregiver (**A**) anxiety and (**B**) depression grouped by follow-up. *Parentheses following study reference* denote intervention type: caregiver experience (E); caregiver role (R); caregiver support (S). *Asterisk* indicates adult patient population. PTSD = post-traumatic stress disorder.

results in the Supplemental Results (<http://links.lww.com/CCM/G290>).

DISCUSSION

Our systematic review of mental health interventions targeting informal caregivers of critically ill patients included 102 interventional trials, including 56 RCTs. Mental health interventions improved short-term anxiety, depression, humanity, and transcendence while increasing burden. No significant long-term effects after 3 months were observed. These findings suggest mental health interventions improve short-term but not long-term psychologic outcomes.

Three types of interventions had greatest supporting evidence for positive effects on short-term psychologic outcomes regardless of patient population. Specifically,

1) preventive psychology (i.e., to prevent negative psychologic sequelae; e.g., Trauma-Preventive Psychology [43]), 2) recovery psychology (i.e., to emphasize potential for recovery; e.g., Mindfulness Training [29]), and 3) psychoeducation (i.e., to facilitate knowledge translation for enhanced coping, treatment efficacy and adherence; e.g., Patient-Partner Psychoeducational Support [51]). Effective short-term interventions involved the critical care team (commonly nurses and/or liaisons) to enhance caregiver experience (i.e., regardless of need), as well as specialists (e.g., psychologist, psychiatrist) to provide targeted support for highly complex needs. Greater effect of mental health interventions on long-term outcomes might require including multiple levels of support (i.e., universal and targeted) to capture various levels of caregiver need while providing longer time set of supports.

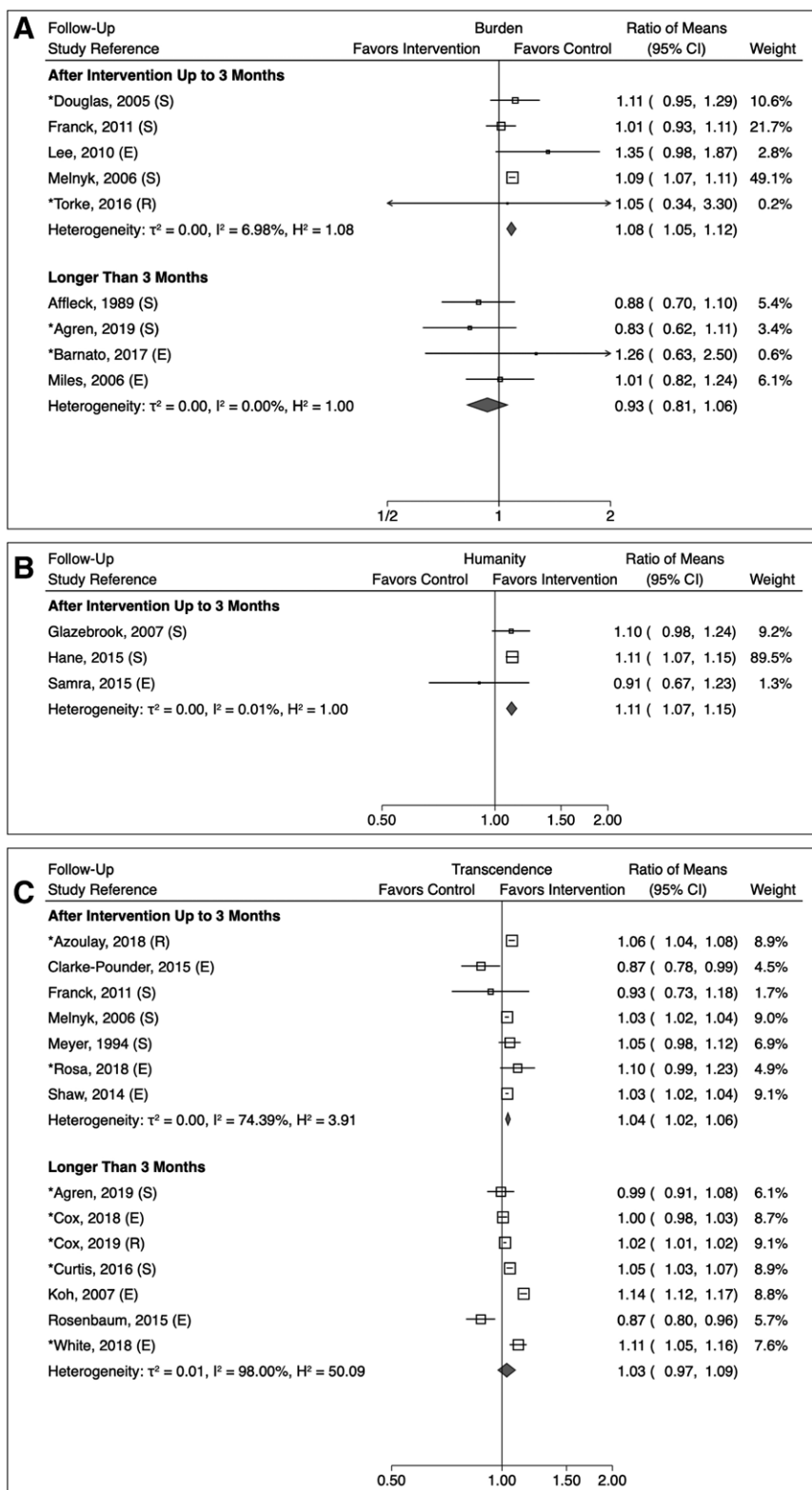


Figure 4. Ratio of means in psychological outcomes in the randomized trials amenable to meta-analysis. Ratio of means is the difference between the experimental group to the control group. *Horizontal lines* denote 95% confidence intervals. *Diamonds* represent point estimates for informal caregiver burden (A) humanity (B), and transcendence (C) grouped by follow-up. *Parentheses following study reference* denote intervention type: caregiver experience (E); caregiver role (R); caregiver support (S). *Asterisk* indicates adult patient population. PTSD = post-traumatic stress disorder.

We found significant heterogeneity our results. Some predisposing factors to poor psychologic outcomes among caregivers of the critically ill are more prominent in NICU and PICU populations, such as younger patient age and lower education, while other factors are predominantly related to adult ICU populations (e.g., being the patient's spouse) (52). Environmental factors related to the ICU setting that vary based on patient population are also known to predispose informal caregivers to poor psychologic outcomes (53).

Multiple factors may explain discordance between short- and long-term outcomes. Few studies included process evaluations to assess implementation (i.e., fidelity, dose, or reach) and outcome assessments (i.e., use of wrong tool). It is possible interventions were not reliably delivered as intended or consistently adhered to as required for mental health interventions to have full effect (4). PTSD symptoms have been reported to develop further from the time in ICU as informal caregivers process their reality of critical illness (54). Few studies designed interventions based on theories of long-term psychologic change (e.g., Post-Traumatic Growth Inventory [55]). Mental health trajectories in informal caregivers may require different outcomes targeted by different interventions at different time points. What works in immediate aftermath of critical illness may not be helpful months later.

We evaluated diverse psychologic outcomes. In addition to negative consequences, we also explored positive adaptations (56, 57). Humanity (i.e., love, kindness) and transcendence (i.e., gratitude, hope) are positive psychologic adaptations to evolving demands of stressful experiences encapsulated within psychologic

resilience (58, 59). Although highly resilient individuals proactively cultivate positive adaptations (60, 61), it is unknown whether positive adaptations are byproducts of intervention or whether they improve coping behaviors. Mental health in informal caregivers of critically ill patients should be considered holistically as the aggregate of negative and positive psychologic outcomes.

We found that some mental health interventions increased caregiver burden. Many authors noted that what constitutes appropriate mental healthcare with adequate follow-up is unclear. Individuals cope differently with critical illness such that any intervention that changes coping trajectories has the potential to both help and harm (62). Furthermore, clinicians are uncertain how to provide mental health interventions to offer support rather than to reduce negative psychologic outcomes (39). We suggest that those who provide mental health interventions should carefully weigh possible adverse effects against potential benefits (12). There is no magic bullet to improve informal caregiver mental health.

Our results need to be interpreted within context of limitations. Primarily, heterogeneity limited pooled statistical analyses. Effectiveness of interventions should be generalized with great caution to age groups other than that in which they have been studied. Second, included studies used different assessment tools. It remains uncertain which tools are most appropriate for informal caregivers (63) and theoretical frameworks to aid tool selection are scarce (64). Third, given diverse and multicomponent nature of interventions, it was not possible to determine specific components of interventions associated with more favorable caregiver psychologic outcomes in particular patient populations. Fourth, no universal definition for positive caregiver psychology added complexity to study selection. However, our broad inclusion criteria resulted in a comprehensive summary of literature assessing this concept that is understudied in critical care. Finally, perspectives from non-Western countries were under-represented. Differences in cultural values such as family responsibilities and support networks may influence caregiving experiences (65).

CONCLUSIONS

In this systematic review and meta-analysis, mental health interventions improved short-term anxiety,

depression, humanity, and transcendence among informal caregivers of critically ill patients while increasing burden. There were no significant effects on long-term psychologic outcomes. Clinicians should consider short-term prescriptions of mental health interventions for informal caregivers of critically ill patients with capacity to manage interventions.

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and Dr. Fiest affirm that this article is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained. All authors have met all four International Committee of Medical Journal Editors (ICMJE) criteria for authorship: 1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; 2) Drafting the work or revising it critically for important intellectual content; 3) Final approval of the version to be published; and 4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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All the work was developed using published data.

Statistical code will be shared upon reasonable request to the corresponding author.

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