

Psychosocial Outcomes in Informal Caregivers of the Critically Ill: A Systematic Review*

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Objective: The objective of the review was to evaluate and synthesize the prevalence, risk factors, and trajectory of psychosocial morbidity in informal caregivers of critical care survivors.

Data Sources: A systematic search of MEDLINE, PsychInfo, PubMed, CINAHL, Cochrane Library, Scopus, PILOTS, EMBASE, and Physiotherapy Evidence Database was undertaken between January and February 2014.

Study Selection: Citations were screened independently by two reviewers for studies that investigated psychosocial outcomes (depression,

anxiety, stress, posttraumatic stress disorder, burden, activity restriction, and health-related quality of life) for informal caregivers of critical care survivors (mechanically ventilated for 48hr or more).

Data Extraction: Data on study outcomes were extracted into a standardized form and quality assessed by two independent reviewers using the Newcastle-Ottawa Scale, the Physiotherapy Evidence Database, and the National Health and Medical Research Council Hierarchy of Evidence guide. Preferred Reporting Items for Systematic Reviews guidelines were followed.

Data Synthesis: Fourteen studies of 1,491 caregivers were included. Depressive symptoms were the most commonly reported outcome with a prevalence of 75.5% during critical care and 22.8–29% at 1-year follow-up. Risk factors for depressive symptoms in caregivers included female gender and younger age. The greatest period of risk for all outcomes was during the patient's critical care admission although psychological symptoms improved over time. The overall quality of the studies was low.

Conclusions: Depressive symptoms were the most prevalent in informal caregivers of survivors of intensive care who were ventilated for more than 48 hours and persist at 1 year with a prevalence of 22.8–29.0%, which is comparable with caregivers of patients with dementia. Screening for caregiver risks could be performed during the ICU admission where intervention can be implemented and then evaluated. Further high-quality studies are needed to quantify anxiety, stress, caregiver burden, and posttraumatic stress disorder outcomes in informal caregivers of long-stay patients surviving ICU. (*Crit Care Med* 2015; 43:1112–1120)

Key Words: caregivers; critical care; depression; posttraumatic stress disorder; psychological outcomes

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More patients are surviving intensive care although the legacy of critical illness can be long lasting, affecting survivors' physical, cognitive, and psychological functioning and health-related quality of life (HRQoL) (1). This constellation of patient outcomes has been recognized as "postintensive care syndrome" by an international task force

(1) and may result in an increased requirement for care following hospital discharge, rising over time due to the burgeoning demands on healthcare services in the context of an ageing population (1). To provide this support, Western healthcare systems typically rely on the support of family members to adopt the role of informal caregiver for their loved one. As a result, family members are at increased risk of mental health morbidity, such as anxiety, depression, and posttraumatic stress disorder (PTSD) (1–3). This cluster of family complications in response to critical illness has been recognized and termed “postintensive care syndrome–family” (1, 3).

Psychological responses of informal caregivers to critical illness may contribute to secondary social stressors, such as burden and lifestyle interference (2, 4). Informal caregivers are thought to buffer the physical and/or social limitations of survivors of intensive care (5) by acting as “social assistive” devices (6) although the cost to caregivers is unknown. Given the significant resources invested in critical care patients during their ICU and hospital admission, it is important to consider patient care beyond hospital discharge and its effect on informal caregivers, so that mitigation strategies can be employed. To date, no systematic review has investigated the prevalence and trajectory of symptoms and risk factors nor the degree of burden experienced by informal caregivers following an ICU admission. Therefore, the aim of this review was to identify, evaluate, and synthesize the prevalence, risk factors, and trajectory of psychosocial morbidity (depression, anxiety, stress, PTSD, burden, activity restriction, and HRQoL) in informal caregivers of survivors of ICU who received mechanical ventilation for more than 48 hours.

MATERIALS AND METHODS

This systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (7).

Information Sources and Search Strategy

The Cochrane Library and Physiotherapy Evidence Database (PEDro) were initially searched to ensure a similar systematic review had not been published. Nine electronic databases accessed via the University of Melbourne, Australia, were searched by a single reviewer (K.J.H.) and included the following: MEDLINE (1950–2014), PsychInfo (1920–2014), PubMed (1949–2014), Cumulative Index to Nursing and Allied Health Literature (1982–2014), Cochrane Library (2014), Scopus (1960–2014), Published International Literature of Traumatic Stress (1973–2014), Excerpta Medica Database (1980–2014), and PEDro (1999–2014).

A systematic and comprehensive search strategy (Table 1) was used to search databases from January 14, 2014, with searches completed February 1, 2014. The reference lists of retrieved articles and personal files of the investigators were also searched to identify additional relevant citations.

Study Selection

Titles and abstracts were assessed against eligibility criteria (Table 2) by two independent reviewers (K.J.H., E.H.S.). Full-text articles were sourced where the abstract contained insufficient information. Relevant full-text articles were retrieved and independently reviewed by both reviewers. Corresponding authors were contacted by a single investigator (K.J.H.) to ascertain whether studies met inclusion criteria (e.g., duration of mechanical ventilation or caregiver bereavement) if necessary. Discrepancies were resolved by consensus between the two reviewers, but where consensus could not be reached, a third independent reviewer (S.B.) adjudicated. Studies were included if over two thirds of the cohort met inclusion criteria (e.g., if 66% or more of the cohort were mechanically ventilated > 48 hr).

TABLE 1. Search Strategy to Identify Relevant Articles

Type of Database	Database	Search Fields	Search Terms
MESH indexing	CINAHL, EMBASE, MEDLINE,	Title, abstract, key words	Caregiver/s; carer; family; spouse; next of kin; partner; relative Intensive care; intensive care unit; critical care; critical illness; mechanical ventilation; respiration, artificial Psychological (psychol*); psychology; mental health; morbidity; postintensive care syndrome–family; postintensive care syndrome family; depression; anxiety; posttraumatic stress disorder; stress; health-related quality of life; quality of life; burden; lifestyle restriction; activity restriction; limitations; function; activities of daily living; time; survivors; survivorship; disability
Non-MESH indexing	Cochrane, PubMed, PsychINFO, Pilots	Title, abstract, key words	Caregiver, family, intensive care, critical care, critical illness
Non-MESH indexing	Physiotherapy Evidence Database	Title, abstract, key words, topic	Caregiver, critical care

Participant, intervention, and outcome terms were combined within-group with the Boolean operator OR and then the “participant” terms yield was combined between-group with the “intervention,” and “outcome” terms yields using the Boolean operator AND.

TABLE 2. Eligibility Criteria for Inclusion and Exclusion of Articles

Characteristics	Inclusion	Exclusion
Design	Randomized, quasiexperimental (parallel control group trials and pre-post intervention trials), observational, or qualitative studies	Case report, reviews, editorials, theses, descriptive commentary
Participants	Informal caregivers (unpaid family member who is involved in or provides any aspect of care to patient for independent ADLS or ADLS, e.g., physical, financial, emotional assistance before, during, or after ICU) of adult (> 18 yr) intensive care patients mechanically ventilated > 48 hr	Pediatric, long-term home ventilated patients Bereaved caregivers, children participants
Intervention	Any	Nil
Outcome measures	Psychosocial (anxiety, depression, stress, posttraumatic stress disorder, health-related quality of life, and activity restriction)	
Publication status	English only; no publication restrictions	

ADLS = activities of daily living.

Data Collection Process, Data Items, and Appraisal (Including Risk of Bias)

Data were extracted by a single author (K.J.H.) into a standardized form. Data items included 1) study details—author, publication year, geographic location of the study, study design, and patient group; 2) participant (both caregiver and patient)

demographics, eligibility criteria, and sample size; 3) intervention and staff who delivered intervention; and 4) relevant outcomes (anxiety, depression, stress, PTSD, activity restriction, and HRQoL) and data collection time points. Narrative findings from qualitative studies were extracted. For the purpose of this review, the negative aspects of the caregiver experience were the focus, as described in the model by Van Pelt et al (8).

Two independent reviewers (K.J.H., E.H.S.) assessed risk of bias using the Newcastle-Ottawa Scale (NOS) (9) (non-randomized trials) and the PEDro scale (10) (randomized trials) for quantitative studies. Studies were also ranked using The Australian National Health and Medical Research Council Hierarchy of Evidence Scale (11).

Two independent reviewers (K.J.H., E.H.S.) assessed risk of bias using the Newcastle-Ottawa Scale (NOS) (9) (non-randomized trials) and the PEDro scale (10) (randomized trials) for quantitative studies. Studies were also ranked using The Australian National Health and Medical Research Council Hierarchy of Evidence Scale (11).

Analysis

Agreement between reviewers was measured using the κ statistic, interpreted according to Landis and Koch (12). All references and data extraction were stored in Excel for Mac 2011 (Version 14.1.0; Microsoft Corporation, Santa Rosa, CA). Analyses were performed using SPSS for Macintosh statistical software package (Mac SPSS Statistical Version 20; IBM, New York, NY).

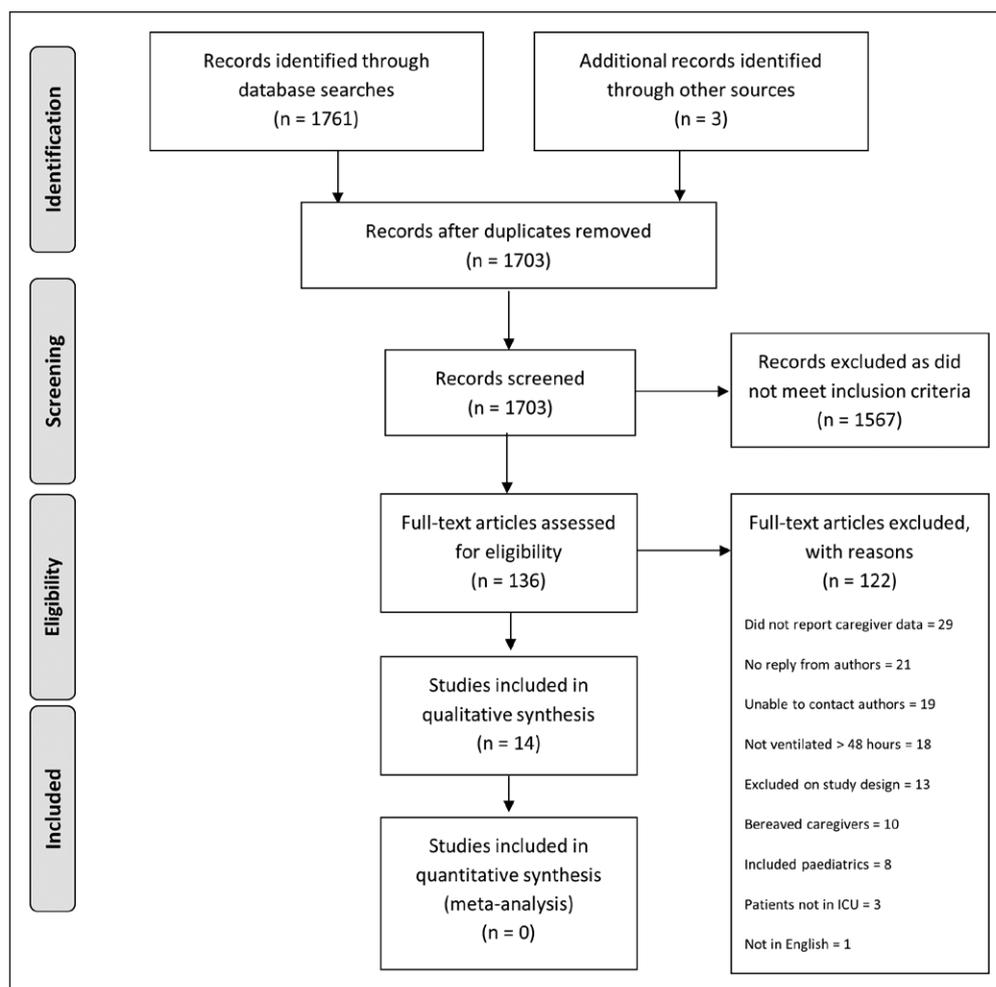


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram—selection of articles according to inclusion and exclusion criterion.

RESULTS

Study Selection

The searches retrieved 1,764 citations. Four hundred and sixty-five abstracts and 136 full-text articles were reviewed (Fig. 1). Fourteen full-text articles were included. κ for abstract and full-text review agreement were 0.76 ($n = 465$, $p < 0.001$) and 1.00 ($n = 139$, $p < 0.001$), indicating substantial agreement and almost perfect agreement, respectively (12).

Characteristics of Included Studies

The majority of studies were conducted in North America and Canada (2, 4, 13–23). Most studies were prospective observational cohorts (2, 13–17, 19–22, 24) with a single study each of a prospective experimental (18), randomized controlled trial (RCT) (24), cross-sectional survey (4), and a qualitative study (semistructured interviews) (23). The 14 studies enrolled a total of 1,491 caregivers and 1,487 patients (Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/B176>; and Supplemental Table 2, Supplemental Digital Content 2, <http://links.lww.com/CCM/B177>). The majority of caregivers were middle-aged, female, spouses/partners, with an education level of high school or less and in current employment (Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/B176>). Patients were mostly male, middle-aged, moderately to severely unwell, and primary ICU diagnostic groups included respiratory failure, sepsis, cardiovascular, trauma, and neurological conditions (Supplemental Table 2, Supplemental Digital Content 2, <http://links.lww.com/CCM/B177>). Many of the studies treated caregivers and patients as dyads at enrolment. Four studies had unequal caregiver and patient numbers due to refusal of patient consent (14, 16), incomplete data at long-term follow-up (4), and reasons unknown (23).

Caregiver prior psychiatric/psychological history was not routinely measured, and three studies reported on this with approximately 40% experiencing prior emotional problems (14–16). Timing of outcome measurement varied greatly. Three studies performed acute measures solely in ICU (14). Other studies measured outcomes across a trajectory during the acute stage (ICU admission to ICU discharge) (25) and from acute (ICU) through to subacute stages (2- to 4-mo follow-up) (15, 16, 19). Other studies' measurement ranged from hospital discharge to 2- to 12-month follow-up (2, 13, 17, 18, 21, 24). Two studies performed single measures in the subacute phase at 2 months (20) or 2 years (the longest follow-up period) (4).

Despite being included in our review *a priori*, it should be noted that none of the studies included in this review reported on anxiety and stress.

Prevalence, Time Course, and Measurement of Depression

Depressive symptoms in caregivers were the most commonly reported psychological outcome (11 studies) (Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/B178>) (2, 4, 14–22). Depressive symptoms were measured using two tools, the full (seven studies) (2, 4, 17–21) and short version (four studies) (14–16, 22) of the Centre for Epidemiological Studies-Depression (CES-D). A majority of studies used a cutoff score of at least 16 or more to define the at-risk population (two used a cutoff score of 15 or more) with the full CES-D (4, 19). Caregivers were at highest risk for the presence of clinically significant depressive symptoms during the patient's ICU admission (Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/B178>). Only one study measured depressive symptoms in the ICU, reporting a prevalence of 75.5% in 370 caregivers (19). Two months following ICU, the prevalence of depressive symptoms ranged from 33.9% of 115 caregivers in two studies (2, 20) to 43.3% of 278 caregivers in single study (19). Two studies reported on prevalence at longer term follow-up ranging from 22.8% of 92 caregivers (2) to 29% of 48 caregivers (21) at 1 year and 31.9% of 47 caregivers (4) at 2 years following ICU (Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/B178>).

The studies using the CES-D short version (14–16, 22) used a cutoff score of at least 8 to define clinical risk (Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/B178>). During ICU, the risk of clinically significant depressive symptoms ranged from 90% in two studies (14, 16) with separate cohorts of 50 caregivers to 80.1% in a cohort of 47 caregivers (15). The prevalence of depressive symptoms decreased with 46.2% of 27 caregivers affected 4 months post ICU (15).

Prevalence, Time Course, and Measurement of Burden, Activity Restriction, and HRQoL

Caregiver burden, activity restriction or lifestyle interference, and HRQoL were the next most common outcomes reported, in six (14–18, 22), five (2, 4, 13, 20, 21), and three (4, 18, 22) studies, respectively (Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/B178>).

The majority of studies measuring caregiver burden, all led by the same author, used the Brief Zarit Burden Interview, where a cutoff score of more than 17 indicated substantial burden (14–16, 22). The prevalence of caregiver burden was 36% of 50 caregivers during ICU (14, 16) and of 31 caregivers at 2 months after ICU (16) (Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/B178>). The other two studies used the Caregiver Reaction Assessment (18) and an Objective/Overload Burden Scale (17), though neither of these studies reported a cutoff score and prevalence data were unable to be extracted.

Most studies measuring activity restriction or lifestyle interference used the Activity Restriction Scale (ARS) (26) and although one study used the Caregiver Impact Scale, scores for the cohort were not reported (4). On the 11-item ARS, caregivers are asked to report the degree of restriction they experienced due to providing care. Possible scores ranged from 11 to 44, where a score of 20, for example, indicates slight restriction in activities such as caring for self or others, visiting friends, and working on hobbies. However a definitive cutoff score has

not been described in the literature. Caregivers' scores indicated a slight activity restriction, which improved over time. Mean scores ranged from 23 at 1 month post ICU (13) to 22.1 at 2 months post ICU (2, 20) and continued to decrease over time to 20 in two studies which repeated measures a year following initiation of mechanical ventilation (2, 21).

Three studies measured HRQoL using the Short Form (SF)-8 (18), the Vitality Subscale of the SF36 (22), and the SF36 (4). As each study used different outcome measures at different time points, results were not easily synthesized, and trajectories appeared to differ, which may be attributable to the variability in outcome measures used. The Physical subscale scores (of the SF-8) appeared to remain stable between hospital discharge and 2 months follow-up (18), whereas Vitality subscale scores appeared to improve slightly from ICU admission to 4 months following ICU discharge (22) (Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/B178>). The last study measuring HRQoL reported solely 2-year outcomes, with lower scores in all domains compared with population values (4).

Prevalence, Time Course, and Measurement of PTSD

Only one study reported PTSD (24) and used the Post Traumatic Stress Scale (PTSS) (Supplemental Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/B178>). The caregivers of patients in the intervention group, which received a diary outlining details of the patients' stay in ICU, had lower PTSS scores from 1 to 3 months following ICU discharge compared with those who did not receive a diary, although the authors did not report a cutoff score or corresponding prevalence at any time point (24).

Risk Factors for Psychological Morbidity

The risk factors for depressive symptoms were the most commonly reported (Supplemental Digital Table 4, Supplemental Digital Content 4, <http://links.lww.com/CCM/B179>). Four studies completed univariate analyses and three studies

completed multivariate analyses. The most frequently reported were caregiver specific (female gender and greater health risk behaviors) and related to patient characteristics, specifically functional dependency, and institutionalization post-hospital discharge. Other significant risk factors included younger caregiver, older patient, overload, fatigue, and whether they received paid help (Supplemental Table 4, Supplemental Digital Content 4, <http://links.lww.com/CCM/B179>).

The main risk factor for caregiver burden was in those who experienced high health risk behaviors, for example, inadequate rest, exercises, and skipping meals, and the other main risk factor was the longer term institutionalization of the patient (Table 3). A number of differing statistical methods were utilized in individual studies making synthesis of risk factors for caregiver burden difficult. Two studies were not able to be included in Table 3. Douglas and Daly (17) reported that caregivers of patients residing in an institution reported higher burden scores at 6 months than did caregivers of patients residing at home; however, statistical testing to identify risk factors was not reported. Similarly, Choi et al (15) reported caregiver burden scores but did not report any associated risk factors.

Van Pelt et al (21) reported the most comprehensive risk factors for caregiver lifestyle disruption using univariate and multivariate analyses. On multivariate analyses, the main risk factors for lifestyle disruption were patient male gender (at 2 and 12 mo), functional dependency (at 12 mo), patient education at least 12th grade (at 2 mo), and patient tracheostomy (at 12 mo). An earlier article by the same research team/investigators (2) did not identify risk factors using statistical analyses but descriptively reported that when stratified by pre-ICU functional status, lifestyle disruption tended to be higher in caregivers of those with pre-ICU functional dependency, although this was significant for 6 months lifestyle disruption. Although Im et al (20) reported activity restriction scores, they did not report associated risk factors, as it was not their primary outcome of interest. Choi et al (13) used Bonferroni post hoc comparison and showed that the lifestyle disruption scores were higher in

TABLE 3. Risk Factors for Caregiver Burden

Author (Reference)	Study (n) ^a	High Caregiver Health Risk Behaviors	Child Caregiver to Care Recipient	Patient Institutionalized Post Discharge	Caregiver Fatigue
Choi et al (14) ^b	50	Yes (Spearman $\rho = 0.50$) ^c	NR	NR	NR
Choi et al (16) ^d	50	Yes (ICU admission, ICU discharge, and 2 mo post ICU) ^c	NR	NR	NR
Douglas et al (18)	290	NR	Yes (Kruskall-Wallis test) ^c	Yes (repeated-measures analysis of variance) ^e	NR
Choi et al (22)	47	NR	NR	NR	Yes (Mann-Whitney U test) ^c

NR = not reported.

^aCaregiver = n at recruitment.

^bStatistical analyses were conducted using correlations (Spearman ρ or Pearson).

^cYes = factor statistically significant ($p \leq 0.05$) on univariate analysis.

^dStatistical analyses explored different trends in patient and caregiver characteristics by trajectory group (high risk of depression and low risk of depression) instead of identifying predictors of group membership—data displayed for high-risk group.

^eYes = factor statistically significant ($p \leq 0.05$) on multivariate analysis.

caregivers of patients who never recovered to their functional status before ICU admission compared with caregivers of patients did, by 6 months after ICU discharge. Cameron et al (4) reported risk factors for emotional distress and found that caregivers experienced more lifestyle interference when they were caring for acute respiratory distress syndrome survivors with more depressive symptoms, but that lifestyle interference was not associated with psychological well-being.

Qualitative Findings

The key findings from the single qualitative study identified a lack of support for caregivers following discharge, and caregivers suffered emotional strain balancing caregiver, work, and child care duties, which resulted in relationship strain and increased distance. Supporting quotes included: “Once we were out of the hospital, we were on our own. Nobody realizes that leaving the hospital is not the end for some people. The next place is just as hard, sometimes worse”; “He is better, but I’m exhausted. I am working and then taking care of him and the kids—and we could not get home healthcare for some insurance reason. Day and night, something is always going on. Nobody could know how bad I have it” and “I do not think we have a real normal marriage now.” Regret and hopelessness were also key themes: “You turn around and your life is changed forever”; “It is just too much sometimes, overwhelming. What will I do if he gets worse? We are sinking” (23).

Risk of Bias Within Studies

The overall methodological quality of the studies included in this review was low (Table 4). The κ for the two randomized controlled studies (18, 24) assessed using the PEDro scale was 0.71. The RCT by Jones et al (24) scored 5 of 10 on the PEDro scale indicating “fair quality” (10). The RCT by Douglas et al

(18) scored 3 of 10 on the PEDro scale indicating “poor quality.” The κ for the observational studies (2, 4, 13–17, 19–22) assessed using the NOS (9) was 0.45, indicating moderate agreement (12). The NOS scores for the observational studies ranged from 2 to 4 with a less than 4 rating on the NOS indicating limited evidence or low quality. Consensus was achieved on all occasions, and no studies were excluded from this review based on the assessed risk of bias.

Quantitative Synthesis of Results

Meta-analyses could not be conducted due to the predominant methodological design being observational cohort studies.

DISCUSSION

This systematic review describes psychological outcomes for informal caregivers of longer stay ICU survivors, from ICU admission to long-term follow-up. Fourteen studies were identified for inclusion with the majority of studies using quantitative research methodology and only one using qualitative inquiry. The overall quality of the studies was low as graded by the risk of bias tools and the National Health and Medical Research Council Grade of Evidence levels. High-quality studies are needed to quantify the degree of impairment in psychosocial outcomes in informal caregivers.

Depression was the most commonly investigated and reported outcome across the studies with symptom prevalence that ranged from 75% during ICU to 22.8–31.9% at 1 year following ICU. It should be noted that the majority of studies used screening tools to identify depressive symptoms rather than diagnostic tools. Risk factors for depressive symptoms specific to the caregiver included female gender and younger age, whereas patient-specific risk factors included older age, functional dependency, and institutionalization

TABLE 4. Risk of Bias for Cohort Studies Scored Using Newcastle-Ottawa Scale

Author (Reference)	Design	Selection	Comparability	Outcome	Total	National Health and Medical Research Council Grade of Evidence
Choi et al (14)	Cohort	1	0	1	2	III-2
Choi et al (16)	Cohort	1	0	3	4	III-2
Douglas et al (19)	Cohort	1	0	2	3	III-2
Van Pelt et al (21)	Cohort	1	0	1	2	III-2
Van Pelt et al (2)	Cohort	1	0	3	4	III-2
Im et al (20)	Cohort	1	0	3	4	III-2
Douglas and Daly (17)	Cohort	1	0	2	3	III-2
Choi et al (15)	Cohort	1	0	3	4	III-2
Choi et al (13)	Cohort	1	0	1	2	III-2
Cameron et al (4)	Cross-sectional survey	1	0	2	3	III-2
Choi et al (22)	Cohort	2	0	2	4	III-2

Strong evidence, consistent findings among multiple high-quality studies 6/9; moderate evidence, consistent findings among multiple lower quality studies and/or one high-quality study 4–5/9; limited evidence, one lower quality study < 4; conflicting evidence, inconsistent findings among multiple studies; and no evidence, no evidence among studies.

post-hospital discharge. Epidemiological findings indicate a female preponderance for depression with the burden reported as 50% higher for women than men (27). In this review, caregivers were predominantly women, the spouse/partner of the patient, and employed, which is consistent with the literature describing possible reasons for gender differences for depression. Social roles and cultural norms have been suggested to contribute to a female predisposition for depression where women traditionally adopt caregiving roles within the family unit. It is suggested that demands of these traditional roles may place women at greater risk for depression leading to the hypothesis of “role strain” (28). This was supported by the qualitative findings of Cox, where a key theme was emotional strain from balancing caregiver, work, and childcare responsibilities (23).

It was understandable that patient factors such as functional dependency and greater comorbidities were associated with increased caregiver depressive symptoms due to the likely increased physical care requirements. These may translate to increased burden although this was not specifically measured in the studies. Qualitative findings supported this and one of the key themes identified was “lack of support following hospital discharge” (23). Conversely, institutionalization (where a paid/professional carer usually provides the necessary physical care) was associated with increased risk for depressive symptoms in caregivers of those patients institutionalized post-hospital discharge. This suggests that there may be other psychological factors specific to institutionalization of a loved one that contributes to depressive symptoms. Some of these have been described by researchers evaluating dementia care and include guilt that the patient could not be cared for at home, grief, and loss (29). There may also be an interaction within the dyad where the psychological functioning of the patient may influence the caregiver with regard to depression outcomes (4). This may also contribute to “relationship strain,” which has been reported by others (23). There is more extensive literature describing the outcomes and risk factors for depressive symptoms in other caregiver populations, such as dementia (30), stroke (31), and cancer (32). Although the evidence for outcomes of caregivers for the critically ill is still an emerging field, the longer term depressive symptom rate of 22.8–31.9% was comparable with caregivers of patients with dementia (30) and stroke caregivers (31) although greater than the prevalence of depression in caregivers of patients with colorectal cancer (32). However, this long-term rate of depressive symptom remains higher than reported lifetime prevalence rates of 8.3–14.9% in the general population (33). It should be noted that as women were overrepresented in the caregiver cohort of this review, this could contribute to these differences, as depression is more prevalent in women than men (33). Caregiver characteristics and risk factors such as female gender and younger age are also similar across reviews (30, 31), whereas patient functional dependence was similar to depression in dementia caregivers (30). This is important to identify an at-risk group for the targeting of intervention in future studies.

Caregiver burden and lifestyle interference was also commonly investigated across the studies. Less than half of the

caregivers experienced burden during ICU and at 2-month follow-up, although it was difficult to interpret the findings as different outcome measures were used and not all had cutoff scores. It is, therefore, possible that the degree of burden caregivers face may be underrepresented in this review. Institutionalization of the patient following hospital discharge was a main risk factor for burden. Lifestyle interference was highest while the patient was in ICU and decreased over time; this may be a sign of the caregiver’s adaptation and coping. Alternatively this could also be attributable to patient recovery; future studies should aim to distinguish between these two concepts. Patient functional dependency in the longer term also carried a degree of risk for caregiver lifestyle disruption. This could be due to the ongoing care requirements that functionally dependent patients require, which consequently leads to greater lifestyle interference for the caregiver. This may be of particular concern for the younger, female caregiver who potentially has to manage domestic tasks, employment, and other dependents such as children (28).

In this review, the primary period of risk for psychological morbidity was during the patients’ admission to ICU, which is often a high stress time. Symptoms of psychological morbidity in caregivers decreased overtime following the patient’s discharge from hospital. However, the majority of studies had relatively short follow-up periods, and adverse psychological outcomes may still be present over a longer term but are as yet undetected. This trajectory of symptoms is consistent with stress process models, which have been more commonly described in other caregiver populations such as Alzheimer disease (34). Stress process models have been used to describe the interaction between caregiver stressors, possible psychosocial resources and caregiver well-being (34). The trajectory seen in this review could also be related to other psychological factors such as resilience, which is considered by some authors to be a relatively stable personality trait characterized by the ability to navigate and spring back from adversity (35, 36). Resilient individuals tend to draw on positive emotion-eliciting coping strategies, such as benefit finding, positive reappraisal, and humor to control negative emotions (35, 36). Traits such as psychological resilience may strengthen resistance to stress by allowing greater access to positive emotional resources (35, 36) and would be useful for future studies to include.

Studies to date have used a myriad of outcome measures at variable time points making synthesis of this literature and comparison between studies difficult. This is an important area to further define to develop timely and relevant interventions. Many of the studies did not define informal caregiving, which is a common problem in other systematic reviews of caregiver outcomes (30, 37). Within the critical care literature, Choi et al (13) have consistently defined it as individual who provided the majority of emotional, financial, and physical support for the patient or the individual primarily responsible for caring of the patient on an unpaid basis. Due to the acute nature of critical illness, the definition of caregiving may need to be expanded or adapted for the critical care population as some patients may

admit to ICU without preexisting care needs but then go on to require informal caregiver assistance. It could be argued that a family member responsible for or involved in care decisions during the acute phase is providing a form of caregiving. These may be the very family members who go on to adopt the role of informal caregiver post hospital discharge although it is difficult to identify in ICU whether patients will require informal caregiving assistance once they are discharged.

Heterogeneity in reporting was a limitation of the included studies. The scope of this review was narrow, and articles where participants were not ventilated or ventilated for less than 48 hours were excluded. However, the inclusion criteria of at least 48 hours of mechanical ventilation was used to attempt to identify the longer stay patient, while recognizing there is no formal definition of this in the literature. We hypothesized that this patient group was more likely to be affected by their critical care experience, culminating in more complex care needs, with resultant implications for caregivers. Another potential limitation of the review was the exclusion of bereaved caregivers. We chose to focus this review on those patients who survive and their caregivers in order to further describe the potential burden of survivorship. However, psychological outcomes of bereaved caregivers are also important to consider but may be better addressed in a separate review.

We chose to base our review around the concept of burden and outcome measures as described in the model by Van Pelt et al (8). This review has focused only on describing informal caregiver morbidity associated with providing care for longer stay critical care survivors in order to begin to understand the complexities of recovery post ICU. This review focused on the negative aspects of caregiving as the measurement and investigation of positive psychology is relatively new for this area of research. As future studies begin to include measures of positive psychology, it would be an interesting area for a further systematic review to address, as it should be acknowledged that there are positive aspects to providing care. Caregiver outcomes are also likely to be affected by the psychological and social resources they possess, as well as factors such as resilience and coping abilities. Future studies could consider using measures of resilience in order to account for the positive aspects of psychology and not just the negative outcomes. This may be useful for design of interventional studies where interventions might be tailored toward less resilient and at-risk individuals. Future research could also investigate screening for caregiver risks during the ICU admission where intervention could be implemented and then evaluated.

CONCLUSIONS

Depression was most prevalent in informal caregivers of survivors of intensive care who were ventilated for more than 48 hours and was the most commonly investigated psychological outcome. Symptoms of depression were highest during the acute phase of the patients' illness and improved over time. However, depression persists and was 22.8–29% at 1 year, which was comparable with caregivers of patients with dementia.

Highest risk for depression occurred in younger female caregivers, although it should be noted that overall study quality was low. Further high-quality studies are needed to quantify anxiety, stress, caregiver burden, and PTSD in informal caregivers of long-stay patients surviving ICU.

REFERENCES

1. Needham DM, Davidson J, Cohen H, et al: Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. *Crit Care Med* 2012; 40:502–509
2. Van Pelt DC, Milbrandt EB, Qin L, et al: Informal caregiver burden among survivors of prolonged mechanical ventilation. *Am J Respir Crit Care Med* 2007; 175:167–173
3. Davidson JE, Jones C, Bienvenu OJ: Family response to critical illness: Postintensive care syndrome-family. *Crit Care Med* 2012; 40:618–624
4. Cameron JI, Herridge MS, Tansey CM, et al: Well-being in informal caregivers of survivors of acute respiratory distress syndrome. *Crit Care Med* 2006; 34:81–86
5. Iwashyna TJ, Netzer G: The burdens of survivorship: An approach to thinking about long-term outcomes after critical illness. *Semin Respir Crit Care Med* 2012; 33:327–338
6. Holt-Lunstad J, Smith TB, Layton JB: Social relationships and mortality risk: A meta-analytic review. *PLoS Med* 2010; 7:e1000316
7. Liberati A, Altman DG, Tetzlaff J, et al: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *J Clin Epidemiol* 2009; 62:e1–34
8. Van Pelt DC, Chelluri L, Schultz R, et al: Less-obvious predictors of post-ICU informal caregiver burden—Response to the editor. *Chest* 2010; 138:1024–1025
9. Wells G, O'Connell D, Peterson J, et al: The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed June 22, 2014
10. Maher CG, Sherrington C, Herbert RD, et al: Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther* 2003; 83:713–721
11. Council NHMR: NHMRC Additional Levels of Evidence and Grades for Recommendations for Developers of Guidelines. Canberra, Australia, National Health and Medical Research Council, 2009
12. Landis JR, Koch GG: The measurement of observer agreement for categorical data. *Biometrics* 1977; 33:159–174
13. Choi J, Donahoe MP, Zullo TG, et al: Caregivers of the chronically critically ill after discharge from the intensive care unit: Six months' experience. *Am J Crit Care* 2011; 20:12–22; quiz 23
14. Choi J, Hoffman LA, Schulz R, et al: Health risk behaviors in family caregivers during patients' stay in intensive care units: A pilot analysis. *Am J Crit Care* 2013; 22:41–45
15. Choi J, Hoffman LA, Schulz R, et al: Self-reported physical symptoms in intensive care unit (ICU) survivors: Pilot exploration over four months post-ICU discharge. *J Pain Symptom Manage* 2014; 47:257–270
16. Choi J, Sherwood PR, Schulz R, et al: Patterns of depressive symptoms in caregivers of mechanically ventilated critically ill adults from intensive care unit admission to 2 months postintensive care unit discharge: A pilot study. *Crit Care Med* 2012; 40:1546–1553
17. Douglas SL, Daly BJ: Caregivers of long-term ventilator patients: Physical and psychological outcomes. *Chest* 2003; 123:1073–1081
18. Douglas SL, Daly BJ, Kelley CG, et al: Impact of a disease management program upon caregivers of chronically critically ill patients. *Chest* 2005; 128:3925–3936
19. Douglas SL, Daly BJ, O'Toole E, et al: Depression among white and nonwhite caregivers of the chronically critically ill. *J Crit Care* 2010; 25:364.e11–364.e19
20. Im K, Belle SH, Schulz R, et al; QOL-MV Investigators: Prevalence and outcomes of caregiving after prolonged (> or =48 hours) mechanical ventilation in the ICU. *Chest* 2004; 125:597–606

21. Van Pelt DC, Schulz R, Chelluri L, et al: Patient-specific, time-varying predictors of post-ICU informal caregiver burden: The caregiver outcomes after ICU discharge project. *Chest* 2010; 137:88–94
22. Choi J, Tate JA, Hoffman LA, et al: Fatigue in family caregivers of adult intensive care unit survivors. *J Pain Symptom Manage* 2014; 48:353–363
23. Cox CE, Docherty SL, Brandon DH, et al: Surviving critical illness: Acute respiratory distress syndrome as experienced by patients and their caregivers. *Crit Care Med* 2009; 37:2702–2708
24. Jones C, Bäckman C, Griffiths RD: Intensive care diaries and relatives' symptoms of posttraumatic stress disorder after critical illness: A pilot study. *Am J Crit Care* 2012; 21:172–176
25. Paparrigopoulos T, Melissaki A, Efthymiou A, et al: Short-term psychological impact on family members of intensive care unit patients. *J Psychosom Res* 2006; 61:719–722
26. Williamson GM, Shaffer DR, Schulz R: Activity restriction and prior relationship history as contributors to mental health outcomes among middle-aged and older spousal caregivers. *Health Psychol* 1998; 17:152–162
27. Marcus M, Yasamy T, Omeren M, et al: Depression—A global public health concern 2012. Available at: http://www.who.int/mental_health/management/depression/who_paper_depression_wfmh_2012.pdf. Accessed October 3, 2014
28. Piccinelli M, Wilkinson G: Gender differences in depression. Critical review. *Br J Psychiatry* 2000; 177:486–492
29. Spruytte N, Van Audenhove C, Lammertyn F, et al: The quality of the caregiving relationship in informal care for older adults with dementia and chronic psychiatric patients. *Psychol Psychother* 2002; 75:295–311
30. Schoenmakers B, Buntinx F, Delepeleire J: Factors determining the impact of care-giving on caregivers of elderly patients with dementia. A systematic literature review. *Maturitas* 2010; 66:191–200
31. Han B, Haley WE: Family caregiving for patients with stroke. Review and analysis. *Stroke* 1999; 30:1478–1485
32. Kim Y, Carver CS, Rocha-Lima C, et al: Depressive symptoms among caregivers of colorectal cancer patients during the first year since diagnosis: A longitudinal investigation. *Psychooncology* 2013; 22:362–367
33. Richards D: Prevalence and clinical course of depression: A review. *Clin Psychol Rev* 2011; 31:1117–1125
34. Goode KT, Haley WE, Roth DL, et al: Predicting longitudinal changes in caregiver physical and mental health: A stress process model. *Health Psychol* 1998; 17:190–198
35. Ong AD, Bergeman CS, Bisconti TL, et al: Psychological resilience, positive emotions, and successful adaptation to stress in later life. *J Pers Soc Psychol* 2006; 91:730–749
36. Tugade MM, Fredrickson BL, Barrett LF: Psychological resilience and positive emotional granularity: Examining the benefits of positive emotions on coping and health. *J Pers* 2004; 72:1161–1190
37. Malonebeach EE, Zarit SH: Current research issues in caregiving to the elderly. *Int J Aging Hum Dev* 1991; 32:103–114