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Anxiety Symptoms in Survivors of Critical Illness: A Systematic Review and Meta-Analysis

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Abstract

Objectives—To evaluate the epidemiology of, and post-intensive care unit (ICU) interventions for anxiety symptoms after critical illness

Methods—We searched 5 databases (1970-2015) to identify studies assessing anxiety symptoms in adult ICU survivors. Data from studies using the most common assessment instrument were meta-analyzed.

Results—We identified 27 studies (2,880 patients) among 27,334 citations. The Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A) was the most common instrument (81% of studies). We pooled data at 2-3, 6, and 12-14 month time-points, with anxiety symptom prevalences (HADS-A 8, 95%CI) of 32%(27-38%), 40%(33-46%), and 34%(25-42%), respectively. In a subset of studies with repeated assessments in the exact same patients, there was no significant change in anxiety score or prevalence over time. Age, gender, severity of illness, diagnosis, and length of stay were not associated with anxiety symptoms. Psychiatric symptoms during admission and memories of in-ICU delusional experiences were potential risk factors. Physical rehabilitation and ICU diaries had potential benefit.

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Conclusions—One-third of ICU survivors experience anxiety symptoms that are persistent during their first year of recovery. Psychiatric symptoms during admission and memories of in-ICU delusional experiences were associated with post-ICU anxiety. Physical rehabilitation and ICU diaries merit further investigation as possible interventions.

Keywords

Anxiety; critical illness; critical care; meta-analysis; review

1. INTRODUCTION

With recent medical advances, the number of survivors of critical illness is increasing (1). There is a growing number of studies evaluating survivors' outcomes after hospital discharge (2). Critical illness survivors frequently face complicated recovery processes, including long-term impairments in physical and cognitive function, and quality of life (3,4). Psychiatric symptoms in critical illness survivors is associated with decreased quality of life (5–7). Recently, there has been increased interest in the mental health outcomes of critical illness survivors (5–7). Recent systematic reviews have focused on different aspects of mental health in this population, such as post-traumatic stress disorder (PTSD) (5) and depression (7). However, to our knowledge, no published systematic review has examined non-specific anxiety symptoms in critical illness survivors. Hence, our objectives were to: 1) examine the prevalence of anxiety symptoms in critical illness survivors, 2) evaluate the natural history and change in symptom severity during the first year after critical illness, 3) identify pre-ICU, ICU and post-ICU risk factors, and 4) assess post-ICU interventions for prevention or treatment of anxiety symptoms following critical illness.

2. MATERIALS AND METHODS

2.1. Search Strategy

To identify eligible studies, we searched 5 electronic databases (PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), PsycINFO®, EMBASE, and the Cochrane Controlled Trials Registry (CENTRAL)) from 1970 through March 2015. We searched for articles with any patient outcome assessment after hospital discharge in survivors of critical illness, since articles may measure anxiety symptoms as part of a battery of assessments of other outcomes. Our keywords for the database searches focused on the concepts of “intensive care”, “outcome assessment”, and “follow up” (Supplemental Table 1). Language of publication was not a limitation in the search strategy. In addition, we performed a manual search of reference lists of all included studies and relevant review articles.

2.2. Study Selection

In our systematic review, we included articles meeting the following criteria: 1) adult (>16 years old) study population, and 2) assessment of anxiety after hospital discharge via a validated instrument. We excluded articles if they met any of the following criteria: 1) <50% critically ill patients in study population, 2) primarily focused on a specific disease (e.g. cardiac disease, trauma, acute respiratory distress syndrome (ARDS)) and/or a specialty ICU

patient population (e.g. cardiac surgery, neurological, or trauma ICUs), 3) 20 patients at follow-up, and 4) primarily focused on evaluating psychometric properties of a questionnaire. Additionally, abstracts, dissertations not published in peer-reviewed journals, and review articles were excluded from data collection.

Trained researchers screened titles/abstracts and then full-text articles in duplicate, independently and sequentially, using DistillerSR© (2014 Evidence Partners, Ottawa, Canada). Conflicts in screening were resolved by consensus.

2.3. Data Abstraction

Two independent reviewers abstracted data from each eligible article, with conflict resolved by consensus or in consultation with the senior author (D.M.N). The following data were abstracted: study design, patient population, baseline patient characteristics, percentage of patients with pre-existing psychiatric illness, time point(s) and sample size(s) at each assessment time-point, instrument(s) used to assess anxiety symptoms including the scoring method and threshold scores (if applicable), point prevalence of anxiety symptoms, potential anxiety risk factors, and post-ICU interventions to improve outcomes. When necessary, we contacted authors for data. For collection of risk factor data, when applicable, we used results from multivariable regression analyses conducted at the first longitudinal assessment after hospital discharge. When a risk factor was evaluated in more than 1 study, we qualitatively summarized findings across studies.

2.4. Risk of Bias Assessment

We assessed for risk of bias of randomized controlled trials (RCTs) using the Cochrane Risk of Bias methodology, (8) and for observational studies using an adaptation of the Newcastle Ottawa Scale (9) (Supplemental Table 4). Data from our risk of bias assessment (specifically loss to follow-up) were used to conduct sensitivity analyses of the primary results (as described below).

2.5. Statistical Analysis

We pooled data from eligible studies for the most commonly used instrument (Hospital Anxiety and Depression Scale – Anxiety subscale: HADS-A), to synthesize: 1) HADS-A mean score and standard deviation, and 2) point prevalence based on standard cut-off thresholds of 8 and 11 that are commonly used in critical care research and recommended by the original HADS validation study (10). Pooling was conducted for data available at the three most commonly reported time-points after critical illness: 2-3, 6, and 12-14 months. For studies that measured HADS-A on the exact same group of patients in 2 consecutive time-points, we calculated the pooled change in mean HADS-A score and prevalence.

We pooled mean and prevalence data via linear and binominal random effects models, respectively, with a random intercept for the study. We used the I^2 statistic to evaluate inter-study heterogeneity, and interpreted a value $>50\%$ as substantial heterogeneity (11). We performed sensitivity analysis on results with substantial heterogeneity, first by removing studies with high risk of bias because of high loss to follow-up, and second by removing all patients who received any post-ICU interventions that might have influenced anxiety

symptoms. Since the number of studies at each time point was relatively small, publication bias was not assessed, as per prior recommendations (12).

We used STATA 13.1 (Stata Corporation, College Station, TX) to conduct all analyses. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (13) (Supplemental Checklist 1) was used for reporting the systematic review and meta-analysis results.

3. RESULTS

3.1. Description of Search and Study Characteristics

We identified 27,334 citations, and after removing the duplicates, we reviewed 18,693 unique titles and abstracts and 1,579 full-text articles. A total of 27 unique studies from 29 publications (Figure 1) met our eligibility criteria. These studies included 8 RCTs (14–21), 15 cohort studies (22–36), and 4 cross-sectional studies (37–39) (Supplemental Table 1). A total of 2,880 unique patients were assessed for anxiety symptoms in the included studies. Most assessments occurred between 1 and 12 months after critical illness (Table 1), with only 11 of 27 (41%) studies conducting assessments at >1 time point after hospital discharge. The majority of studies (25 of 27, 93%) were conducted in European countries, with 15 (56%) studies from the United Kingdom (14,15,17,19–22,25,27,28,32,33,38–40).

3.2. Risk of Bias Assessment

Among the 8 RCTs, 6 and 7 had an adequate randomized sequence generation and proper allocation concealment, respectively (Supplemental Table 3). Double-blinding was feasible in only 1 RCT. Among observational studies, 6 of 19 (32%) had adequate follow-up (Supplemental Table 4).

3.3. Measures and Prevalence of Anxiety

The most commonly used instrument was the HADS-A (22 studies, 81%), followed by the State-Trait Anxiety Inventory (4 studies, 15%) (Table 1). In-person, mail and phone assessment were used in 11 (41%), 11 (41%), and 4 (15%) of 27 studies, respectively, and assessment method was unclear in 5 (19%) studies (categories not mutually exclusive).

Past psychiatric history was considered an exclusion criterion in 3 studies, with 11 studies reporting the prevalence of psychiatric morbidities before hospital admission, which ranged from 0% to 54% (Table 1). No study specifically assessed the prevalence of anxiety symptoms at baseline prior to onset of critical illness, although one study reported a 3.5% prevalence of diagnosed anxiety disorders, such as generalized anxiety disorder (41).

The point prevalence of anxiety ranged from 5% to 73% among all eligible studies. Among 22 studies using the HADS-A, we pooled data at the 2–3 month, 6 month, and 12–14 month time-points for 1080 patients (12 studies), 760 patients (7 studies), and 1041 patients (6 studies), respectively (Supplemental Table 5). The pooled mean (95% Confidence interval (CI)) HADS-A score was 6.1 (5.5–6.6; $I^2=74\%$) at 2–3 months, 6.5 (5.8–7.2; $I^2=76\%$) at 6 months, and 5.8 (5.0–6.6; $I^2=87\%$) at 12–14 months. Anxiety symptom prevalence, using a cut-off score of 8 was 32% (27–38%; $I^2=70\%$) at 2–3 months, 40% (33–46%; $I^2=71\%$) at 6

months, and 34% (25-42%; $I^2=89\%$) at 12-14 months. When using a score of 11 as the cut-off, the pooled prevalences were 17% (14-20%; $I^2=35\%$), 20% (16-25%; $I^2=58\%$) and 17% (12-22%; $I^2=80\%$), respectively.

In sensitivity analysis, the removal of studies with high loss to follow-up, decreased heterogeneity at 6 months ($I^2 < 20\%$), but not notably at other time points. During the second sensitivity analysis that removed patients undergoing any post-ICU interventions, heterogeneity decreased for the pooled prevalence at 2-3 months and for the pooled prevalence and mean score at 6 months ($I^2 < 15\%$). Heterogeneity at 12 months remained high in both sensitivity analyses. These pooled results, during sensitivity analyses, did not materially change from the primary results, as reported above (Supplemental Table 5).

Among 390 patients from 4 studies (17,19,33,42) with HADS-A assessments at both 2-3 and 6 months, the pooled difference in mean score (95% CI) was 0.1 (0.0 to 0.2; $I^2=0\%$), and the pooled difference in prevalence (95% CI) was 5% (-1 to +12%; $I^2=0\%$) and 2% (-3 to 8%; $I^2=0\%$), for 8 and 11 thresholds, respectively. In 409 patients from 3 studies (19,32,42) with HADS-A assessments at 6 and 12 months, the pooled difference in mean score was 0.0 (-0.2 to +0.1; $I^2=0\%$), and the pooled difference in prevalence (95% CI) was 1% (-5% to +8%; $I^2=0\%$) and 0% (-6% to +5%; $I^2=0\%$), for 8 and 11 thresholds, respectively.

3.4. Risk Factors for Anxiety

For studies that reported potential risk factors, neither age nor gender were associated with anxiety in any study (0 of 5 (25,27,32,37,43) and 0 of 4 (22,27,37,43) studies, respectively). In addition, neither severity of illness, diagnosis at ICU admission, nor ICU/hospital length of stay were associated with anxiety (0 of 4 studies (25,32,35,37), 0 of 4 studies (27,29,35,37) and 0 of 4 studies (25,27,32,35), respectively).

Psychiatric symptoms in the ICU or hospital (e.g., stress reactions (27), anxiety at hospital discharge (32), and stressful nightmares and extreme fear (30)) were associated with post-discharge anxiety symptoms in 3 of 3 studies. Delirium was assessed as a risk factor for post-ICU anxiety symptoms in one study (27), with a positive association in unadjusted analyses. Memories of delusional experiences while critically ill were associated with anxiety in 3 of 3 studies (17,35,43).

Post-ICU depression and PTSD symptoms were strongly correlated with post-ICU anxiety symptoms (5 of 5 studies (21,25,35,37,38)). In addition, anxiety was associated with lower quality of life in 2 of 2 studies (23,25) (Table 2).

3.5. Interventions to Reduce Anxiety Symptoms

Four categories of post-discharge interventions were identified: physical rehabilitation, a self-help manual, ICU diaries, and ICU follow-up clinics. No study assessed the effectiveness of post-discharge pharmacological interventions in ICU survivors. Physical rehabilitation after discharge showed a significant benefit in one RCT (20) and one pre-post cohort study (28). However, physical rehabilitation during the post-ICU stay on the hospital ward was not associated with lower anxiety symptoms in one study (19). Use of ICU diaries was associated with lower anxiety symptoms in 1 randomized trial (21), with a trend toward

lower symptoms that did not reach statistical significance in a pre-post study (34). ICU follow-up clinics and self-help manuals, each were reported in 1 RCT, were not associated with a significant difference in anxiety measures (Table 3).

4. DISCUSSION

Our systematic review and meta-analysis of 27 studies with 2,880 general ICU survivors demonstrates a prevalence of anxiety symptoms of 32-40% over 1-year follow-up. Studies with longitudinal assessment of the same population of ICU survivors showed no significant change in HADS-A scores or prevalence during the first year after discharge.

The reported anxiety symptoms across different studies ranged from 5 to 73%. This variability may be due to differences in patient populations, anxiety instruments, cut-off thresholds, and timing of follow up assessments, which complicate comparisons and analyses. However, within studies using the HADS-A instrument, the pooled prevalence of anxiety symptoms among general ICU survivors is similar to normative data using HADS-A in the UK general population (46), but higher than normative data from other European countries (47,48). This finding differs from PTSD and depressive symptoms that appear to have greater prevalence in ICU survivors compared with the general population (5,7) and merits further investigation in future research.

Among the reported risk factors, age and sex were not associated with anxiety symptoms, in contrast with studies in the general population, in which lifetime prevalence of anxiety disorder is 60% higher in women, with the highest prevalence in the 30-44 years age group (44). One reason for this contradictory finding in ICU survivors may be that individual studies are underpowered to show a significant difference based on sex and age. Another possibility may be that the underlying mechanisms by which patients develop anxiety after critical illness might be affecting both sexes and all age groups similarly. We currently do not have adequate evidence to explain this difference, and future research is needed to investigate it.

Many ICU risk factors, including severity of illness, length of ICU and hospital stay, and ICU admission diagnosis, were consistently not associated with anxiety symptoms. Similar findings have been reported previously in studies assessing the association of these factors with post-ICU depressive symptoms and PTSD (5-7).

Notably, we were able to pool data for identical populations of patients at two different time-points to evaluate their change in symptoms over time. We found that there was no significant change in anxiety symptoms over time. This is similar to anxiety disorders in non-ICU populations that show chronicity and a low remission rate (45).

Of the 27 unique studies in this review, all but 5 used the HADS-A instrument to detect anxiety symptoms. This unanimity among studies for assessing anxiety symptoms after critical illness makes pooling of study data feasible. Given this instrument's wide use for detecting anxiety and depressive symptoms (7) in critically ill patients, we believe the HADS is a good candidate for further validation in this specific population of general ICU survivors. HADS psychometric performance has been evaluated in other populations, such

as in ARDS and general medical patients, demonstrating good internal consistency and sensitivity to change (49–51).

Among post-ICU interventions, only physical rehabilitation and ICU diaries showed potential benefit. However, scarcity of high-quality data makes any definitive recommendation premature. Importantly, evaluation of both pharmacological and behavioral interventions (e.g., cognitive behavioral therapy) for anxiety symptoms in this population are warranted to confirm efficacy, as observed in other populations.

There are potential limitations to this meta-analysis. First, because of lack of data on pre-ICU anxiety symptoms, the incidence of post-ICU anxiety symptoms cannot be assessed. Measuring baseline anxiety should be a priority for future studies, when feasible (52). Second, all studies used questionnaires to assess anxiety symptoms. While questionnaires provide quantitative data that can be analyzed, no diagnosis can be made from these patient assessments. HADS-A is a measure of general anxiety symptoms and was not designed to screen for a specific psychiatric diagnosis. Third, most studies in this review, and all studies included in the meta-analysis, were conducted in Europe; thus our findings may not be generalizable to other geographic regions. Lastly, rigorous attempts were made to identify and include every eligible study. However, there is a possibility of studies being inadvertently omitted from our systematic review.

5. CONCLUSION

In this meta-analysis of 27 studies with 2,880 general ICU survivors, we found that at least one-third of ICU survivors experience anxiety symptoms that persist during the first year after critical illness. Many traditional ICU factors, such as severity of illness and length of stay, were not associated with anxiety symptoms. Psychiatric symptoms in the hospital and memories of delusional experiences while critically ill were associated with anxiety at post-ICU follow-up. No post-ICU interventions had strong evidence supporting for treating anxiety symptoms; however, physical rehabilitation and ICU diaries merit further evaluation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Flow chart of number of citations screened.

Table 1

Measurements of anxiety symptoms

Study	Past psychiatric illness (%)	Instrument	Follow-up in months	N at follow-up	Mean (SD) or median (IQR)	Cut-off score	Point prevalence (%)
Eddleston(53)	0%	HADS-A	3	143	-	8; 11	12; 7
Kress(54)	2 ^a ;38 ^b	STAI-S STAI-T	14 ^a ; 12 ^b	13 ^a ; 19 ^b	48.2 (39) ^a ; 59.4 (32.4) ^b 72.1 (33) ^a ; 60.2 (35) ^b	84% 84%	31 ^a ; 21 ^b 46 ^a ; 63 ^b
Jones(55)	20	HADS-A STAI-T	2	30	6.5 (5.2) -	8; 11 -	37; 17 -
Scragg(56)	3	HADS-A	13 (6)	80		8	43
Jones(57)	Excluded	HADS-A	2 6	58 ^a , 45 ^b 53 ^a , 40 ^b	6.7 (5.1) ^a ; 6.1 (4.1) ^b 3.7 (3.6) ^a ; 4.5 (4.1) ^b	8; 11	43; 19 ^a / 40; 13 ^b 45; 25 ^a /40; 23 ^b
Rattray(58)	-	HADS-A	6 12	80 80	6.5 (4.5) 6.6 (4.3)	8; 11	41; 22 45; 18
Samuelson(59)	-	HADS-A	2	226	1 (4)	11	4.9
Sukantarat(25)	-	HADS-A	3 9	51 45	6.4 (4.3) 6.7 (4.8)	8; 11	37; 16 44; 20
McWilliams(60)	-	HADS-A	1 w 2	38 38	8.2 (4.4) 6.2 (3.8)	8; 11	52; 26 18; 13
Cuthbertson(42)	-	HADS-A	6 12	105 ^a , 115 ^b 93 ^a , 100 ^b	6 (4.5) ^a ; 7 (4.6) ^b 5.5 (4.6) ^a ; 6.4 (4.4) ^b	8; 11	32; 17 ^a / 45; 20 ^b 34; 16 ^a / 36; 21 ^b
Knowles(61)	22 ^a ;28 ^b	HADS-A	1 2	18 ^a ; 18 ^b 18 ^a ; 18 ^b	6.6 (3.9) ^a ; 7.2 (4.6) ^b 4.7 (3) ^a ; 6.6 (4.5) ^b	8	44 ^a ; 44 ^b 11 ^a ; 39 ^b
Myhren(43)(62)	-	HADS-A	1 3 12	252 191 192	3.6 (4.5) 5.2 (4.7) 5.8 (4.9)	8; 11	29; 15 28; 15 33; 18
Peek(63)	-	HADS-A	6	57 ^a , 46 ^b	5.8 (0.6) ^a ;	8; 11	19; 8 ^a /24, 11 ^b

Study	Past psychiatric illness (%)	Instrument	Follow-up in months	N at follow-up	Mean (SD) or median (IQR)	Cut-off score	Point prevalence (%)
					7.4 (0.8) ^b		
Treggiari(18)	-	HADS-A	1	52 ^c ; 50 ^d	5.3 (4.2) ^a ; 5 (4.2) ^b	8; 11	42; 12 ^a / 30; 12 ^b
Van der Schaaf(64)	-	HADS-A	12	247	4.6 (4.4)	8; 11	21; 11
Rattray(65)	-	HADS-A	2 6	64 50	7.4 (4.3) 6.8 (4.1)	8; 11	45; 23 50; 16
Strøm(16)	-	STAI- S	24	13 ^a ; 13 ^b	48 (45, 50) ^a ; 50 (45, 53) ^b	-	-
Garrouste-Orgeas(66)	19 ^c 6 ^d 20 ^e	HADS-A	3	21 ^c 19 ^d 12 ^e	6.2 (4.5) 5.0 (3.7) 7.3(2.8)	8; 11	29; 14 11; 11 33; 17
McKinley(67)	Excluded	DASS-A	1 w 2 6.5	156 156 156	8 (4, 14) 4 (0, 8) 4 (2, 10)	10; 15	53; 26 26; 11 26; 11
Schandl(68)	18 ^a ; 15 ^b	HADS -A	3 6 12 14	100 ^a 70 ^a 50 ^a 98 ^a ; 73 ^b	5.3 (4) ^a 4.4 (3.9) ^a 4.0 (3.1) ^a 4.4 (4.2) ^a ; 5.1(4.7) ^b	8; 11	28; 13 ^a 21; 10 ^a 8; 2 ^a 20; 7 ^a /25; 14 ^b
Wade(69)	16 ^f	STAI (short form)	3	100	-	44	44
Kowalczyk(70)	-	HADS-A	34	186	8.7 (4.8)	8; 11	34; 14
Raveau(71)	42 ^f	COVI	3	26	-	>3	73
Risnes(72)	54; 4 ^g	HADS-A	60	27	7.3 (4.4) ^h ; 4.59 (3.1) ⁱ	-	-
Battle(73)	10 ^f	HADS-A	3	63	7.3 (5.7)	8; 11	38; 29
Jones(74) ^m	Excluded	HADS-A	3	14 ^j , 18 ^k , 19 ^l , 16 ^m	5 (4.1) ^j ; 3.1 (3.4) ^k ; 8 (5.7) ^l ; 4.9 (4.2) ^m	8; 11	29; 14 ^j / 10; 5 ^k / 58; 32 ^l / 25; 12 ^m
Walsh(75)	-	HADS-A	3 6 12	98 ^a ; 87 ^b 86 ^a ; 80 ^b 81 ^a ; 77 ^b	7.2 (5.2) ^a ; 6.93 (4.8) ^b	8; 11	16; 31 ^a / 36; 22 ^b 57; 29 ^a / 36; 26 ^b 49; 31 ^a / 35; 19 ^b

Study	Past psychiatric illness (%)	Instrument	Follow-up in months	N at follow-up	Mean (SD) or median (IQR)	Cut-off score	Point prevalence (%)
					7.7 (5) ^a ; 7.31 (5.4) ^b 7.5 (5.4) ^a ; 7.35 (4.5) ^b		

Abbreviations: HADS-A: Hospital Depression and Anxiety Scale-Anxiety Subscale; STAI-T: State-Trait Anxiety Inventory-Trait, STAI-S: State-Trait Anxiety Inventory-State; DASS: Depression Anxiety Stress Scales; COVI: Covi Anxiety Scale

Footnotes:

^a intervention

^b control

^c pre-diary

^d dairy

^e post diary

^f history of depression

^g Number of patients with Generalized Anxiety Disorder at baseline

^h Scores in 11 patients with psychiatric sequelae

ⁱ Scores in 17 patients without psychiatric sequelae

^j Control supplement, no PEPSE (outpatient physiotherapy class)

^k Control supplement, PEPSE

^l EAA (essential amino acid) supplement, no PEPSE

^m EAA supplement, PEPSE

Table 2

Association of Anxiety Symptoms With Pre-ICU, ICU, and Post-ICU Factors, Across Eligible Studies

Risk factors	Total	No Association		Positive Association (more anxiety)	
	N	N	%	N	%
Pre-ICU factors					
Age	5	5	100%	0	0%
Gender	4	4	100%	0	0%
Income and socioeconomic status	2	1	50%	1	50%
Low employment status	2	1	50%	1	50%
Low educational status	2	1	50%	1	50%
Chronic health status	2	2	100%	0	0%
ICU factors					
Sedation minimization ^a	2	2	100%	0	0%
Duration of sedation	2	2	100%	0	0%
Opioids in ICU	2	2	100%	0	0%
Severity of illness ^b	4	4	100%	0	0%
TISS score	2	2	100%	0	0%
ICU LOS, Hospital LOS	4	4	100%	0	0%
Admission diagnosis	4	4	100%	0	0%
Psychiatric symptoms in ICU/ Hospital ^c	3	0	0%	3	100%
Post-ICU factors					
Time since hospital d/c	5	4	80%	1	20%
memories of delusional experiences	3	0	0%	3	100%
No factual memories from ICU stay	3 ^d	1	33%	1	33%
Quality of life	2	0	0%	2	100%
Psychiatric problems after ICU	5	0	0%	5	100%

Abbreviations: SBTs: Spontaneous breathing trials; d/c: discharge; LOS: length of stay; TISS: Therapeutic intervention scoring; MV: mechanical ventilation

Footnote:

^aNo sedation versus interruption of sedation, or interruption of sedation versus control

^bAPACHE II/ SAPS II

^cStress reactions in the ICU, anxiety at hospital discharge, stressful nightmares and extreme fear

^dAmong 3 studies, 1 showed negative association (no factual memory was associated with less anxiety)

Table 3

Association of Post-ICU Interventions with Anxiety Symptoms, Across Eligible Studies

Post-ICU Interventions	Total	No Association		Negative Association (less anxiety)	
	N	N	%	N	%
Rehabilitation during post-ICU hospitalization	1	1	100%	0	0%
Physical rehabilitation after discharge ^a	3	1	33%	2	67%
Self-help manual	1	1	100%	0	0%
ICU diaries	2	1	50%	1	50%
Nurse-led ICU follow-up clinic	1	1	100%	0	0%

Abbreviations: ICU: Intensive Care Unit, No: Number**Footnote:**^aIn one randomized controlled trial, physical rehabilitation plus essential amino acid supplement was effective