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Original Article

Psychological symptoms and health-related quality of life in intubated and non-intubated intensive care survivors: A multicentre, prospective observational cohort study

Sumeet Rai, FCICM ^{a, b, *}, Teresa Neeman, PhD ^c, Rhonda Brown, PhD ^{d, e}, Krishnaswamy Sundararajan, FCICM ^{f, g}, Arvind Rajamani, FCICM ^{h, i}, Michelle Miu, B.Med, MD ^j, Rakshit Panwar, PhD ^k, Mary Nourse, GradCertIntCareN ^b, Frank M.P. van Haren, PhD ^{a, l}, Imogen Mitchell, PhD ^{a, b, **}, Dale M. Needham, MD, PhD ^{m, n}, for the PRICE study investigators

^a School of Medicine and Psychology, Australian National University, Canberra, Australia; ^b Intensive Care Unit, Canberra Hospital, Canberra, Australia; ^c Biological Data Science Institute, College of Science, Australian National University, Canberra, Australia; ^d Research School of Psychology, Australian National University, Canberra, Australia; ^e School of Psychology, University of New England, Armidale, NSW, Australia; ^f Intensive Care Unit, Royal Adelaide Hospital, Adelaide, Australia; ^g Faculty of Health and Medical Sciences, The University of Adelaide, Adelaide, Australia; ^h Nepean Clinical School, University of Sydney, Kingswood, Sydney, Australia; ⁱ Intensive Care Unit, Nepean Hospital, Kingswood, Sydney, Australia; ^j Nepean Hospital, Kingswood, Sydney, Australia; ^k Intensive Care Unit, John Hunter Hospital, New Lambton, Australia; ^l Intensive Care Unit, St. George Hospital, Kogarah, Sydney, Australia; ^m Critical Care Physical Medicine and Rehabilitation Program, Johns Hopkins Hospital, Baltimore, MD, USA; ⁿ Johns Hopkins University School of Medicine and School of Nursing, Baltimore, MD, USA

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ABSTRACT

Objective: To compare long-term psychological symptoms and health-related quality of life (HRQOL) in intubated versus non-intubated ICU survivors.

Design: Prospective, multicentre observational cohort study.

Setting: Four tertiary medical-surgical ICUs in Australia.

Participants: Intubated and non-intubated adult ICU survivors.

Main outcome measures: Primary outcomes: clinically significant psychological symptoms at 3- and 12-month follow-up using Post-Traumatic Stress Syndrome-14 for post-traumatic stress disorder; Depression, Anxiety Stress Scales-21 for depression, anxiety, and stress. Secondary outcomes: HRQOL, using EuroQol-5D-5L questionnaire.

Results: Of the 133 ICU survivors, 54/116 (47 %) had at least one clinically significant psychological symptom (i.e., post-traumatic stress disorder, anxiety, depression, stress) at follow-up. Clinically significant scores for psychological symptoms were observed in 26 (39 %) versus 16 (32 %) at 3-months [odds ratio 1.4, 95 % confidence interval (0.66–3.13), $p = 0.38$]; 23 (37 %) versus 10 (31 %) at 12-months [odds ratio 1.3, 95 % confidence interval (0.53–3.31), $p = 0.57$] of intubated versus non-intubated survivors, respectively. Usual activities and mobility were the most commonly affected HRQOL dimension, with >30 % at 3 versus months and >20 % at 12-months of overall survivors reporting \geq moderate problems. There was no difference between the groups in any of the EQ5D dimensions.

Conclusions: Nearly one-in-two (47 %) of the intubated and non-intubated ICU survivors reported clinically significant psychological symptoms at 3 and 12-month follow-ups. Overall, more than 30 % at 3-months and over 20 % at 12-months of the survivors in both groups had moderate or worse problems with their usual activities and mobility. The presence of psychological symptoms and HRQOL impairments was similar between the groups.

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* Corresponding author. School of Medicine and Psychology, Australian National University, Canberra, Australia.

** Corresponding author. School of Medicine and Psychology, Australian National University, Canberra, Australia.

E-mail addresses: Sumeet.Rai@act.gov.au (S. Rai), Imogen.Mitchell@act.gov.au (I. Mitchell).

1. Introduction

Survivors of critical illness frequently have long-lasting physical and cognitive impairment, clinically important psychological symptoms, and reduced health-related quality of life (HRQOL).^{1–6} Such problems have been collectively termed, post intensive care syndrome (PICS).⁷

There is robust literature of longitudinal follow-up studies demonstrating persistent psychological symptom burden (e.g., post-traumatic stress disorder (PTSD), anxiety, and depression) and impaired HRQOL after mechanical ventilation in the intensive care unit (ICU),^{8–11} although few studies have evaluated these outcomes and compared results, with non-intubated patients. A small number of European studies indicate that anxiety, stress, and traumatic experiences occur in patients receiving non-invasive ventilation.^{12,13} Perhaps commonalities in the ICU environment (e.g., noise, poor sleep, unfamiliar clinical teams, loss of personal control, and isolation from family)^{14,15} and critical illness may produce similar psychological and HRQOL outcomes in ICU patients regardless of the use of invasive ventilation.

Thus, the psychological stress in intensive care survivors study aimed to describe and compare 3- and 12-month psychological symptoms and HRQOL in ICU survivors in patients managed with invasive ventilation (*intubated*) and without invasive ventilation (*non-intubated*).

2. Methods

Psychological stress in Intensive Care survivors (PRICE) was a multicentre prospective cohort study conducted in four tertiary ICUs across four hospitals in Australia from July 2015 until July 2019. The trial was registered (ACTRN12615000880549) and approved by the relevant human research ethics committees and a protocol, eligibility criteria, and statistical analysis plan were published.¹⁶ The study recruited intubated (invasive ventilation >24 h) and non-intubated (inotropic/vasopressor support and/or non-invasive ventilation) ICU survivors. Given the interest in new psychological symptoms occurring after the ICU, patients with pre-existing psychiatric disorders were excluded (detailed inclusion and exclusion criteria provided in [Supplementary file 1](#)). A consecutive sample of patients who met the study inclusion criteria was recruited contingent on research staff availability. Longitudinal follow-up (3- and 12-month) was initially conducted via post (mail), and if there was no response to two study letters, a telephone call was made by trained research staff.

The Strengthening the Reporting of Observational Studies in Epidemiology guidelines were followed in the reporting of the study results.¹⁷

2.1. Study objectives

The *primary objective* of the study was to compare psychological symptoms in intubated versus non-intubated ICU survivors at 3- and 12-month follow-up. The *secondary objective* was to compare HRQOL at 3- and 12-month follow-up.

Measurement instruments: Participants were asked to complete study questionnaires to assess psychological symptoms after discharge from ICU, but before hospital discharge (i.e. *baseline*) and at 3- and 12-month follow-up. These questionnaires included the Post-Traumatic Stress Syndrome-14 (PTSS-14); Depression, Anxiety Stress Scales-21 (DASS21).

PTSS-14 is a validated 14-item measure of post-traumatic symptoms. Scores range from 14 (*least symptoms*) to 98 (*worst symptoms*) with higher scores indicating worse symptoms. A published clinically relevant cut-off score of 45 is suggested for the measure.¹⁸

DASS21 is a 21-item scale that examines the presence and severity of depression, anxiety, and stress symptoms over the past month, with seven items examining each symptom state.¹⁹ Participants were asked to complete the items using 4-point frequency and impact scales (0–3), with higher scores indicating worse symptoms. Published cut-off scores are provided for the subscales to indicate the severity of each state from normal/mild, moderate, severe and extremely severe symptoms.²⁰

HRQOL was assessed at 3- and 12-month follow-ups using the 5-level EuroQoL-5D version (EQ-5D-5L), in which survivors described their health across five dimensions: mobility, self-care, usual activities, pain, and anxiety/depression. Each dimension is scored from 1 to 5 (1 = no problems and 5 = extreme problem). Individual EQ5D-5L dimension scores were converted to a utility score using Australian normative data.²¹ Survivors were also asked to rate their overall health on a visual analog scale (VAS) ranging from 0 to 100, with a score of 100 indicating the best possible health.

2.2. Statistical analysis

A detailed statistical analysis plan was previously published.¹⁶ Patient demographics and baseline characteristics were summarised using means with standard deviations (S.D), medians, and 25%–75% quartiles (interquartile range) on continuous measures and frequencies (percentages) on categorical measures. An *a priori* sample size calculation indicated that 62 patients in each group would provide 80% power to detect a 20% difference between the groups for the presence of any psychological symptoms on follow-up at a significance level of 5%. The study planned to recruit 75 patients in each group to account for a potential attrition rate of 20% on longitudinal follow-up.

Clinically significant PTSD symptoms were indicated by a score of ≥ 45 on the PTSS-14. Individual DASS scores were dichotomized to normal/mild and at least moderate severity scores on each domain: depression (≥ 14), anxiety (≥ 10), and stress (≥ 19) and presented as a percentage of patients with clinically significant symptoms. EQ5D-5L dimensions were dichotomized as normal/mild problems and moderate or worse (extreme) problems and presented as the percentage of patients with \geq moderate problems in HRQOL dimensions. Means with standard errors were used when reporting primary and secondary outcomes. Mean psychological symptom scores, EQ5D VAS, and utility scores were compared between groups at 3- and 12-months.

Patients who died at the time of hospital discharge (before any follow-up) were excluded from the analysis. Data for survivors were included and analysed as long as one of the follow-up assessments was completed. No imputation was conducted for incomplete or missing data (from incident mortality, dropout, or non-response), under the assumption of data being missing at random. A loss to follow-up analysis, including comparisons of baseline characteristics of participants with versus without follow-up data, was conducted. A linear mixed model, with follow-up time (3 and 12 months) and group (intubated vs non-intubated) and their interaction as fixed effects and patient as a random effect, was used to compare assessment scores between intubated and non-intubated survivors at both follow-up periods. Logistic regression analysis was used to compare the presence (prevalence) of individual clinically significant symptoms at each follow-up (3 or 12 months) between the groups, with the patient as a random effect. Measures of association were reported as odds ratio (OR) with 95% confidence interval (CI). Pearson's chi-square test was used for categorical data, and the Wilcoxon rank sum test was used for continuous variables. All data analyses were performed using R statistical software (version 4.0.5) and R studio (version 1.4.1106) for

Windows. P values of <0.05 were considered to be significant in the analyses, without adjustment for multiple comparisons.

3. Results

Of the 172 patients initially recruited, 21 (12 %) patients died at hospital discharge or withdrew consent before follow-up and 18 (12 %) survivors were lost to all follow-up (Fig. 1). Overall, 133 patients with a median age of 66 [57–73] years were included in the analyses. Most patients were males (61 %) and predominantly with medical admissions (62 %). The non-intubated patients had more medical comorbidities (55 % vs 30 %) and active malignancy/metastases (34 % vs 13 %). The intubated group had more patients with trauma (20 % vs 4 %), a higher prevalence of delirium in the ICU (32 % vs 4 %), and increased ICU and hospital length of stay (LOS) (Table 1).

At 3-months, 116 out of 127 survivors (91 %) and at 12-months, 94 out of 119 survivors (79 %) completed follow-up assessments.

3.1. Psychological symptoms at follow-up

Overall, 54/116 (47 %) survivors had clinically significant scores for one or more psychological symptoms (i.e., PTSD, anxiety, depression, and/or stress) at 3- or 12-month follow-up. In intubated vs. non-intubated survivors, a clinically significant score for one of the four psychological symptoms was observed in 26 (39 %) vs 16 (32 %) at 3-months [OR 1.4, 95 % CI (0.66–3.13), $p = 0.38$]; 23 (37 %) vs 10 (31 %) at 12-months [O.R. 1.3, 95 % CI (0.53–3.31), $p = 0.57$], respectively. Psychological assessment scores and the presence of clinically significant psychological symptoms in the two groups are described below.

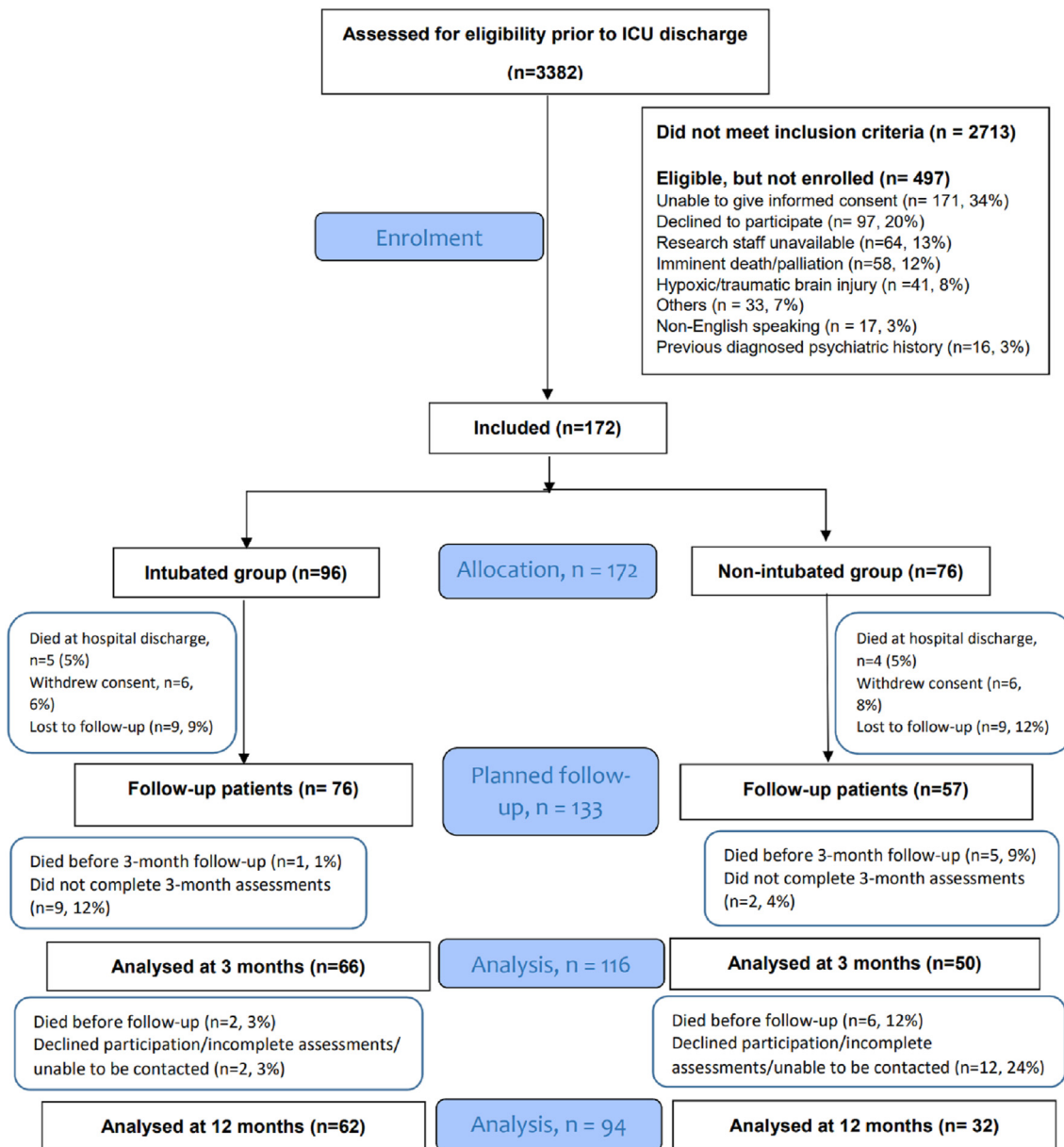


Fig. 1. Consort diagram. ICU: Intensive Care Unit.

Table 1
Baseline patient characteristics stratified by intubation status.

Characteristic	Intubated (n = 76)	Non-intubated (n = 57)
Age (years)	65 [55–71]	68 [60–75]
Male	52 (68 %)	29 (52 %)
Indigenous	6 (8 %)	7 (12 %)
Medical admission	50 (66 %)	33 (58 %)
Major admission category^b		
Respiratory	24 (32 %)	13 (23 %)
Cardiovascular	17 (22 %)	2 (4 %)
Trauma	15 (20 %)	2 (4 %)
Gastrointestinal	8 (11 %)	11 (19 %)
Neurological	4 (5 %)	2 (4 %)
Renal	2 (3 %)	8 (14 %)
Others	6 (8 %)	19 (33 %)
Major admission sub-category		
Sepsis	14 (18 %)	19 (33 %)
Malignancy (active/metastases)	10 (13 %)	20 (35 %)
Any comorbidity ^c	23 (30 %)	32 (56 %)
Comorbidity count ≥ 2	5 (7 %)	7 (12 %)
Delirium ^a in ICU	24 (32 %)	2 (4 %)
Non-Invasive Ventilation in ICU	6 (8 %)	18 (32 %)
Any inotrope/vasopressor use	64 (84 %)	37 (66 %)
Inotrope/vasopressor ≥ 2 (concurrent)	10 (13 %)	1 (2 %)
APACHE II score	19 (7.8)	15 (5.5)
APACHE III score	68 (31.2)	57 (17.3)
Hospital LOS (days)	25 [12.6–53.4]	15 [8.3–24.7]
ICU LOS (days)	7 [4.7–12]	2 [1.6–2.7]
Hospital discharge destination		
Home	53 (70 %)	52 (91 %)
Other hospital	14 (18 %)	4 (7 %)
Rehab	9 (12 %)	0 (0 %)
Nursing Home	0 (0 %)	1 (2 %)

Data presented as number (%), mean (standard deviation) or median [interquartile range].

APACHE: Acute Physiology and Chronic Health Evaluation; LOS: length of stay.

^a Measured by Confusion Assessment Method for the ICU (CAM-ICU).

^b Admission ICU Diagnosis, based on APACHE III-J diagnostic codes.

^c Chronic co-morbidity: based on APACHE II (organ insufficiency prior to hospital admission).

PTSD: There was no difference in the PTSS-14 scores between the intubated and non-intubated survivors at either follow-up time point (Table 2) (Supplementary Figure 1). Clinically significant PTSD symptoms were evident in 11 % and 13 % of the overall survivors at 3- and 12-months, respectively. There was no difference in the presence of PTSD symptoms between the groups at 3 ($p = 0.70$) or 12 months ($p = 0.23$) (Fig. 2) (Supplementary Table 1).

Depression, Anxiety, and Stress: There were no significant differences between the groups at either time point for DASS-depression, DASS-anxiety, and DASS-stress scores (Table 2) (Supplementary Figure 1). The presence of clinically significant symptoms among the overall survivors was as follows: depression (22 % and 24 %), anxiety (24 % and 19 %), and stress (15 % and 12 %) at 3- and 12-months, respectively. There was no difference between the groups on the presence of symptoms at either 3 months

(depression, $p = 0.39$; anxiety, $p = 0.20$; stress, $p = 0.24$) or 12 months (depression, $p = 0.68$; anxiety, $p = 0.94$; stress, $p = 0.62$) (Fig. 2) (Supplementary Table 1).

3.2. Health-related quality of life (HRQOL)

At 3- and 12-month follow-ups, respectively, 94 (81 %) and 90 (96 %) of overall survivors completed the EQ5D-5L assessments. Usual activities and mobility were the most commonly affected HRQOL dimensions in both groups, with $>30\%$ at 3-months and $>20\%$ at 12-months of overall survivors reporting \geq moderate problems in the above HRQOL dimensions (Fig. 3). There was no difference between the groups on \geq moderate problems in the EQ5D dimensions or mean EQ5D VAS scores at either follow-up point (Supplementary table 2) (Table 2). EQ5D utility score was worse in the intubated versus non-intubated patients at 3-months, but not at 12-months (Table 2).

3.3. Lost to follow-up analysis

Eighteen patients (12 %), nine from each group, were lost to all follow-up. Overall, they had similar demographics, baseline PTSS14 and DASS21 scores to participant responses at follow-up (Supplementary table 3 shows survivors stratified by loss to all follow-up). All surviving participants completed at least one psychological follow-up assessment. Of the 11 survivors who did not complete their 3-month assessment, all (except one from the non-intubated group, who did not survive until 12 months) later completed assessments at 12-months. All 25 survivors (12 intubated and 13 non-intubated) who did not complete their 12-month assessments had previously completed them at 3-months. These survivors (without 12-month assessments) had shorter ICU LOS, lower PTSS14, and depression and anxiety scores at baseline, but otherwise did not differ either at baseline or at 3-months relative to those who completed the 12-month assessments (Supplementary table 4 shows survivors stratified by 12-month follow-up completion).

4. Discussion

In this prospective multicentre follow-up study across 4 Australian ICUs, nearly one-in-two (47 %) of the ICU survivors experienced persistent clinically significant psychological symptoms at 3- and 12-months follow-up. Although there was a trend towards worse PTSD and stress symptoms in the intubated versus non-intubated survivors at 3-months, the overall severity of PTSD, anxiety, depression, and stress did not differ at follow-up. Further, at 3-months, $>30\%$, and at 12-months, $>20\%$ of the overall survivors reported at least moderate HRQOL impairment with their usual activities and mobility. Although the self-rating of HRQOL

Table 2
Patient outcomes, stratified by intubation status.

Follow-up screening	3-months			12-months		
	Intubated (n = 66)	Non-intubated (n = 50)	P value	Intubated (n = 62)	Non-intubated (n = 32)	P value
PTSS14 score	30 (1.9)	24 (2.3)	0.07	30 (2.0)	27 (2.5)	0.29
Depression score	9 (1.3)	7 (1.5)	0.46	9 (1.3)	8 (1.7)	0.47
Anxiety score	8 (1.0)	6 (1.2)	0.21	6 (1.0)	6 (1.3)	0.74
Stress score	10 (1.1)	7 (1.3)	0.07	9 (1.1)	7 (1.4)	0.13
EQ 5D 5L VAS	63 (2.8)	69 (3)	0.13	70 (3)	71 (3.5)	0.71
EQ 5D 5L utility score	0.52 (0.04)	0.67 (0.05)	0.02*	0.62 (0.04)	0.68 (0.05)	0.31

Scores provided as mean with standard errors.

PTSS14, Post Traumatic Stress Scale (14 items); EQ5D5L, EuroQOL 5 dimension, 5 level; VAS, Visual Analogue Scale.

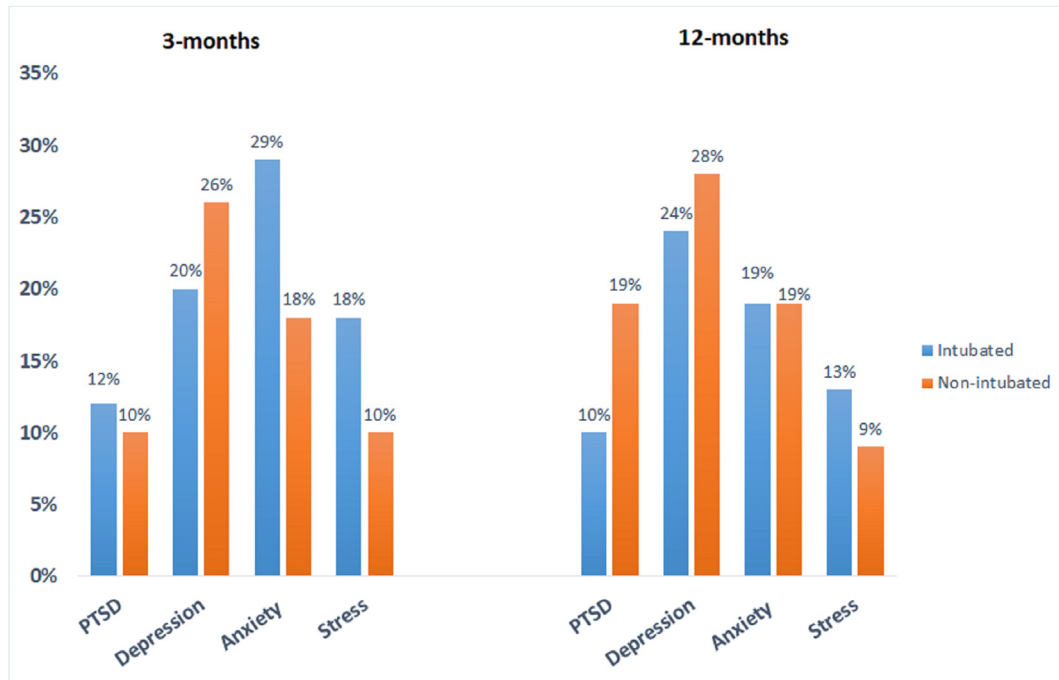


Fig. 2. Clinically significant psychological symptoms at follow-up. PTSD: clinically significant symptoms as defined as PTSS14 \geq 45. Depression/Anxiety/Stress: moderate to worse symptoms on DASS screening.

was similar between groups, the intubated survivors had worse EQ-5D-5L utility scores at 3-months, but this difference did not persist at 12-months. Thus, we found that psychological symptoms were similar in intubated and non-intubated survivors, and although there was a tendency for intubated survivors to report worse HRQOL at 3-months, this difference had resolved by 12-months.

Our study results are consistent with prior findings of psychological outcomes in intubated ICU survivors. Our finding that 10% of intubated ventilated survivors had symptoms of PTSD at 12 months

is similar to recent Australian data showing possible PTSD symptoms in 8% of intubated survivors at 6-months using the Impact of Events-revised Scale.²² Although few studies have evaluated non-intubated patients specifically, our results fit into the broader prevalence rates for PTSD symptoms in ICU survivors at long-term follow-up (5–64%).^{11,23–26} However, no prior studies have directly compared psychological symptoms in intubated versus non-intubated ICU patients over time. In our study, we found that 10% and 19% of non-intubated ICU survivors reported PTSD

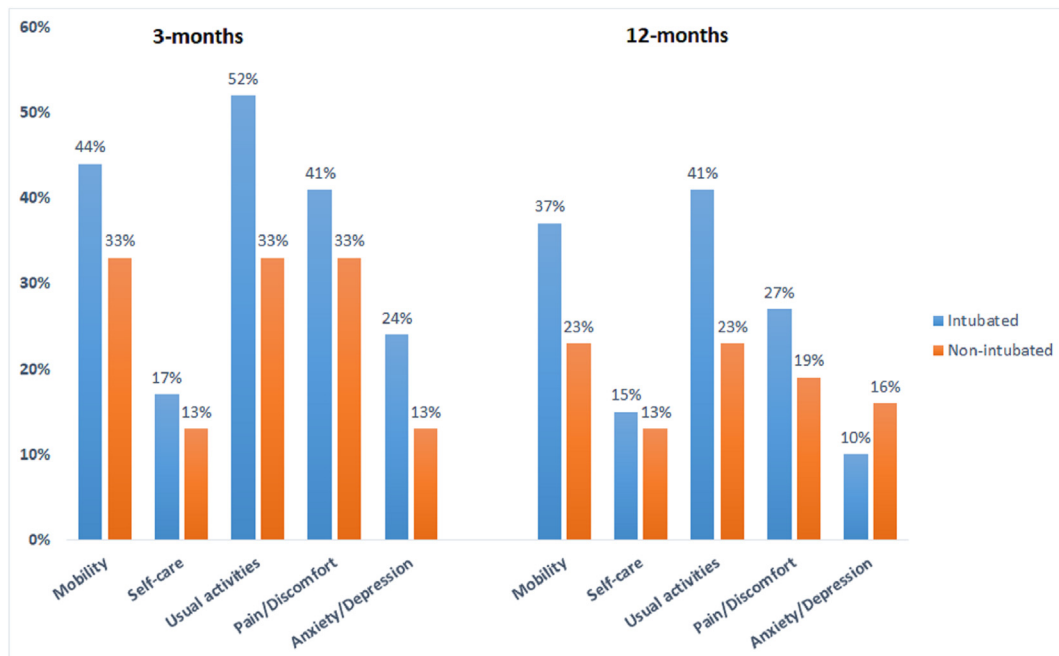


Fig. 3. EQ-5D-5L dimensions with \geq moderate problems at follow-up.

symptoms at 3- and 12-months, respectively. Further, no robust differences were detected in the severity of psychological symptoms in intubated versus non-intubated ICU patients at 3- or 12-months. With reference to normed values, both survivor groups reported a higher prevalence of PTSD symptoms at 12-months, relative to Australian population norms (5.7 %).²⁷

Furthermore, clinically significant symptoms (moderate or severe symptoms of depression, anxiety or stress) were similar between the intubated and non-intubated survivors. In our study, clinically significant depression was present in 24 % of the intubated versus 28 % of non-intubated survivors at 12-months, which is similar to published values in ICU survivors (8–57 %).^{9,23} In addition, 19 % of patients reported clinically significant anxiety at 12-months in our study, which is lower than Australian and international clinical data and published values (21–44 %).^{10,22,23} Although, at 12-months, psychological symptoms in the survivors in our study were much higher than the Australian population normed values for depression (4.8 %) and anxiety (16.8 %).²⁷ Thus, the patient sample was comparable to values obtained in other ICU studies but much worse than in the Australian population. Any differences in our results and those of other ICU studies may be due to inherent differences in the timing of assessments, screening populations, and/or use of different screening tools. In addition, few studies have previously examined stress levels in ICU patients in the long-term ICU outcomes literature. We found that moderate to extremely severe symptoms of stress were present in 13 % of intubated and 9 % of non-intubated survivors at 12-months follow-up, demonstrating the persistence of psychological stress in some patients long after ICU discharge. It is unclear what contributed to their persistent feelings of stress, although our results add to the existing literature on acute stress in ICU survivors.

We advance several possible reasons to explain the similar psychological symptom severity in intubated versus non-intubated survivors.¹ ICUs are stressful environments for patients, with even healthy volunteers reporting symptoms of depression symptoms when admitted to ICU.^{2,28} There were a higher proportion of females in the non-intubated group in our study. A previous systematic review of risk factors for PICS has identified a three-fold higher risk of mental health issues in female sex.²⁹ Also, the non-intubated group in our study had a higher comorbid disease burden and a higher proportion of underlying malignancy. Pre-ICU health status, including severe comorbidities, may have a non-modifiable impact on the long-term outcomes of ICU survivors.³⁰ In cancer patients, prevalence rates for PTSD, depression, and anxiety vary on the type of malignancy and methodology of follow-up, but they are similar to those reported in the ICU literature.^{3,31–34} One-third of non-intubated patients in our study required non-invasive ventilation that may have been potentially distressing for them. Specifically, non-invasive ventilation can induce a psychological stress response, fear of dying, pain, and suffering;³⁵ in part caused by mask discomfort, feelings of claustrophobia, and impaired awareness may contribute to psychological distress.^{36,37} Thus, psychological symptoms in ICU survivors are likely due to similarities in the ICU experience and may be based on their medical condition, although aspects of invasive ventilation may be uniquely stressful for some ICU patients.

Regarding HRQOL, >30 % at 3-months and at 12-months, >20 % of the overall survivors reported \geq moderate and persistent HRQOL impairment with their usual activities, and mobility. Our results are similar to those observed in other intensive care survivors who were more likely to have persistent impairment in physical and mental domains of HRQOL, long after discharge from ICU.^{38–40} A 6-month follow-up study evaluating EQ5D scores in ICU survivors showed that ICU variables were not related to impairments in HRQOL suggesting that other determinants (e.g. pre-existing

health) may be more important than the presence or absence of invasive ventilation.⁴¹ In particular, pre-existing co-morbidities and frailty can influence HRQOL outcomes in ICU survivors,^{42–44} although we did not evaluate pre-existing frailty in our study. We did find that the EQ-5D utility score was significantly worse in intubated versus non-intubated survivors in the short-term (3-months), although any difference had disappeared by 12-months. The reasons underpinning the worse HRQOL in intubated patients at 3-months were not clear from the data available in this study.

There were several limitations in our study. First, due to a higher-than-expected mortality in the non-intubated group, the study may have been underpowered to detect differences between the groups. Second, although the overall loss to follow-up in this study was 12 %, almost all survivors completed at least one of the follow-up assessments. The higher mortality in the non-intubated group reflects the severity of illness of these patients. A poor response to multiple follow-up assessments in the non-intubated group may be reflective of survey fatigue in survivors with multiple co-morbidities. In addition, our results may be influenced by survivorship or selection bias. While a loss to follow-up is a challenge in long-term follow-up studies in ICU survivors,⁴⁵ our rate compares favourably with other ICU survivor studies (e.g. 20–25 %).⁴⁶ Further, we did not find any differences in the characteristics of patients lost/not lost to follow-up, suggesting that the loss of patients was not systematic (e.g. related to symptom severity). Third, the different baseline characteristics of the groups, in addition to the presence or absence of invasive ventilation (e.g., a higher proportion of females, co-morbidities, and malignancy in the non-invasive group versus a higher proportion of trauma patients, higher rates of ICU delirium and an increased ICU and hospital LOS in the intubated group) may have influenced the results. Fourth, we did not collect details on pre-ICU health status, which may have influenced long-term outcomes.^{41,47} And although we excluded patients with diagnosed pre-existing psychiatric disorders, undiagnosed pre-existing mental health disorders may have influenced the results. Finally, the patient sample was derived from Australian metropolitan teaching ICUs and the study results should be considered within this context.

Our study has numerous strengths. The multicentre, prospective design using validated screening tools and a mixed population of general ICU survivors allows wider generalisability. In addition, the study used two follow-up time points (3 and 12 months) allowing comparison with literature with varying follow-up time points and assessment for change over time. Furthermore, almost all the survivors completed at least one of their long-term psychological follow-up assessments. More importantly, due to the inclusion of non-intubated patients, the study creates insight into the long-term psychological and HRQOL outcomes of an increasing group of ICU survivors.

4.1. Implications

The complex myriad of psychological and HRQOL issues leaves a lasting legacy in some ICU survivors. The psychological and HRQOL outcomes of critically ill non-intubated ICU survivors are similar to those of intubated survivors, except that the short-term HRQOL of intubated patients may be worse than for non-intubated patients. Further long-term follow-up research with an emphasis on risk factors for PICS in critically ill non-intubated ICU survivors is required.

5. Conclusions

In this 4-site Australian study, nearly one-in-two of the ICU survivors reported clinically significant psychological symptoms at

3- and 12-month follow-ups. Over a third of the survivors at 3-months and over a fifth of the survivors at 12-months had moderate or worse impairments in their usual activities and mobility. There was no statistically significant difference in the presence of psychological symptoms and HRQOL impairments between the intubated and non-intubated survivors.

Conflict of interest

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

Ethics approval and consent to participate

The study was approved by the relevant local human research ethics committees (HREC) of the Australian Capital Territory (ETH.11.14.315), New South Wales (HREC/16/HNE/64), South Australia (HREC/15/RAH/346). Written, informed consent was obtained from patients.

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CRedit authorship contribution statement

SR conceptualised and was the chief investigator for the PRICE study. SR, RB, FVH, IM, DMN contributed to the study design. SR, KS, AR, MM, RP, MN supervised the conduct of the study and assisted with data collection and follow-up. SR and MN managed the data. TN provided statistical advice on study design and SR and TN conducted the data analysis. SR drafted the manuscript, and all authors contributed substantially to its revision. All authors have contributed substantially to the study and have approved the manuscript for submission.

Consent for publication

Not applicable.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ccrj.2023.10.011>.

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