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FRIGHTENING AND TRAUMATIC MEMORIES EARLY AFTER INTENSIVE CARE DISCHARGE

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RESEARCH LETTER – TRACK CHANGES

FRIGHTENING AND TRAUMATIC MEMORIES EARLY AFTER INTENSIVE CARE DISCHARGE

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Author Contributions

TSW, CK, and CJW conceived the DESIST study, secured funding, and managed the research. All authors conceived the current sub-study, contributed to analysis, wrote the manuscript, and approved the final version. All authors are accountable for the accuracy and integrity of the work.

Grants

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Running title: Early frightening and traumatic memories in ICU survivors

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References: 12~~3~~

Anxiety, depression, and post-traumatic stress are prevalent among intensive care (ICU) survivors, can persist long-term, and are associated with low quality of life[1]. Risk factors include frightening and delusional memories of ICU stay, especially for long-term post-traumatic stress[2,3]. Frightening memories could relate to ICU stress, for example from pain, anxiety, and dreams.~~; and d~~Delusional memories may originate from~~to~~ hallucinations and periods of delirium. These may all be influenced by sedation, analgesia and delirium management[4]. Few studies have described the nature and prevalence of frightening and traumatic memories early after ICU discharge~~,~~. This transition of care is known to be stressful to both patients and family members, and is the time ~~when~~ patients are starting to adjust to critical illness sequelae. Screening and intervention for psychological morbidity at this time might reduce long-term problems, especially if the patients at highest risk could be identified.

In a pre-planned sub-study within a published cluster randomised quality-improvement trial of sedation interventions in eight Scottish ICUs (the 'DESIST' trial[5,6]), we administered two validated questionnaires to ICU survivors during their recovery on general wards early after ICU discharge. These were the Impact of Events Scale-Revised (IES-R) which measures traumatic symptomatology[7], and the Intensive Care Experience Questionnaire (ICE-Q)[8]. The ICE-Q includes 31 items measuring patients' perceptions of their intensive care experience, grouped into four domains including a 'frightening experiences sub-score' (FESS; comprising six questions)[8]. The FESS demonstrates a Cronbach α>0.7 in previous studies, indicating validity, and previous studies have also~~which also~~ found that ICE-Q scores could predict subsequent psychological morbidity[8,9,10].

Participants in the DESIST trial required mechanical ventilation (MV) with anticipated duration >48 hours. When possible, surviving participants were approached after ICU discharge to complete the questionnaires and asked to anchor their responses to ICU memories. All patients provided written consent and the study was approved by the Scottish A Research Ethics Committee. These data were exploratory secondary outcomes, and were not reported in the main trial, but some results have been previously reported in the form of an abstract.[11] We report here a cohort analysis of all survivors who completed questionnaires.

We aimed to describe the frequency and nature of frightening and traumatic memories early after ICU discharge, while patients were still in hospital. ~~A secondary aim was to explore associations between memories and plausible exposures available in our database, with a focus on the detailed sedation/agitation data collected in the trial. Exposure variables comprised age, gender, APACHE II score, duration of MV, and length of ICU stay. We created sedation exposure variables based on a Sedation Quality Assessment Tool (SQAT)[12], which was validated for the study and was the primary~~

~~outcome in the main trial. SQAT data were recorded for sequential 12-hour care periods during ICU stay; this was used to create a patient-level variable describing the number and proportion of care periods with deep sedation and with agitation during MV. Data were complete for 86% of all care periods among patients who answered questionnaires; missing values were imputed from data in adjacent care periods. In addition to agitation, we explored associations with total haloperidol exposure (the most widely used antipsychotic) as a surrogate for agitated delirium. We had two outcome variables.~~ For the ICE-Q questionnaire, we reported responses to each of the six questions comprising the FESS sub-score; the total FESS sub-score; and the proportion of patients with a FESS >18 (a cut-off representing an average score >3 ('neutral' response) across contributing questions). For the IES-R we reported responses to all 22 questions; the IES-R total score; and the proportion of patients with a score >35 (indicating significant traumatic symptomatology[7]).

We also used responses to a separate ICE-Q question: 'I have no memory of intensive care' (five potential responses ~~(~~ranging from~~:~~ strongly agree to strongly disagree) to explore relationships between patients' overall memory of ICU and the ~~sedation variables,~~ FESS sub-score~~,~~ and IES-R score.

There were 1291 ICU survivors in the trial. The ICE-Q and IES-R were completed by 517 survivors (40%). Survivors who completed questionnaires had longer post-ICU hospital stays, and~~,~~ included lower proportions of general medical and higher proportions of ~~more~~general surgical patients than those who did not complete questionnaires (see table 1). There was~~, and there was~~ also some imbalance in admission source ~~(Table 1)~~. The ~~M~~median number of days to questionnaire completion was 7 days (IQR: 4-14 days) post ICU discharge. Responses to the individual questions are shown in figure 1. The ~~M~~median (IQR) sum score for the ICE-Q FESS was 15 (11-21), and for IES-R was 19 (7-36). There were 34.4% (95% Confidence Interval: 30.3 to 38.5%) of the patients with a FESS scores >18 and 25.1% (95% CI: 21.4 to 28.8%) with an IES-R score >35. Patient responses to the two questionnaires correlated strongly indicating that patients who had more frightening memories also reported greater trauma symptomatology (Spearman Rho coefficient =0.62; P<0.001). Post-ICU memories were diverse: among the ICE-Q responses fear, helplessness, and anticipating death were frequent. Among the IES-R responses~~, together with~~ memories of numbness, unreality and sleep disturbance were most common.

~~For the FESS, we found very weak negative correlations with age (rho -0.09; P=0 .040) and APACHE II score (rho -0.12; P=0.009), and very weak positive associations with ICU length of stay (rho 0.10; P=0.035). There was no association with gender, duration of MV, any of the ICU sedation or agitation variables, or haloperidol use. For the IES-R, there were very weak negative correlations with age (rho~~

~~-0.11; P=0.02) and APACHE II score (rho -0.11; P=0.014), and very weak positive associations with duration of MV (rho 0.12; P=0.009), ICU length of stay (rho 0.09; P=0.042), and haloperidol dose (rho 0.12; P=0.009). As for the FESS, there was no association with gender or any sedation or agitation variables.~~

In relation to patients' ~~For~~ overall memory of ICU, we found ~~very weak correlations between having less overall memory and spending more time with deep sedation (rho 0.19, P<0.001). Similarly, patients~~those with less overall memory had fewer frightening memories (correlation with FESS scores: rho -0.18, P<0.001) and traumatic memories (correlation with IES-R scores: rho -0.13, P=0.004), although both associations were very weak.

To our knowledge, this is the largest reported study of frightening and traumatic memories in the early post-ICU discharge period. Our data suggest these occur in 25 to 35% of patients. Although our cohort was large, and from a general ICU population, both inclusion and response bias could have influenced these estimates. Patients who required no or only brief MV were excluded from the DESIST trial, and data were available for only 40% of participants. Missed responses were mainly due to limited trial resource; we found many patients were already discharged from hospital when ward-based follow-up occurred and later contact was not feasible. Missing cases were more likely to have~~be~~ general medical diagnoses~~surgical~~, had shorter hospital stays, and were more often admitted directly from the emergency department. These and other unmeasured confounders could have biased the prevalence estimates. However, our data are consistent with smaller studies describing 'delusional' memories early after ICU discharge and previous studies using the ICE-Q[3,8-10]. ~~Post-ICU memories were diverse: fear, helplessness, and anticipating death were frequent, together with memories of numbness, unreality and sleep disturbance.~~ Although delusion-like memories are known predictors of long-term psychological morbidity[2], controversy exists regarding whether factual memories, even if frightening, are protective[3,12~~3~~]. Our data illustrate the diversity, complexity and personalised nature of early post-ICU memories. ~~The lack of strong associations with sedation-related exposures contradicts previous work, and support a multifactorial etiology that is difficult to predict from ICU variables.~~

In conclusion, our data demonstrate prevalent early traumatic and frightening memories that might contribute to long-term psychological morbidity after ICU. This supports a hypothesis that systematic screening at this time may be useful as part of a strategy for personalised targeted care and interventions to reduce later psychological morbidity.

Table 1. Demographic data of participants who completed or did not complete the questionnaire follow-up. *P* value denotes comparison using Mann-Whitney U test for age, and duration variables; independent sample t test for APACHE II; Chi^2 for gender and case mix (medical or surgical). Unless stated, the variable contains no missing values. APACHE II: Acute Physiology and Chronic Health Evaluation II.

Characteristic		ICE-Q and IES-R Completed	ICE-Q and IES-R Not Completed	*p* value
	Valid (missing)	517 (0)	772 (2)	
Age, years	Median (IQR)	60.0 (48.5-69.0)	61.0 (47.0-71.0)	0.46
Male	n (%)	305/517 (59.0)	463 (59.9)	0.77
APACHE II Score	Valid (missing)	491 (26)	750 (24)	
	Mean (SD)	20.58 (6.93)	21.16 (7.49)	0.17
Length of ICU Stay days	Median (IQR)	6.74 (3.66-12.67)	6.76 (3.70-11.86)	0.43
Duration of Ventilation days	Median (IQR)	3.44 (1.70-8.40)	4.0 (1.86-8.08)	0.25
Length of Hospital Stay days	Valid (missing)	516 (1)	771 (3)	
	Median (IQR)	27.0 (15.0-48.75)	19.0 (10.0-34.0)	<0.001
Case mix: Proportion medical	n (%)	274 (52.9)	482 (62.4)	<0.001
Medical Specialty				
General Medicine		147 (28.9)	299 (38.7)	
Cardiology		33 (6.4)	44 (5.7)	
Gastrointestinal		29 (5.6)	32 (4.1)	
Respiratory		26 (5.0)	35 (4.5)	
Ear/Nose/Throat		11 (2.1)	13 (1.7)	
Neurology		5 (1.0)	18 (2.3)	
Renal		6 (1.2)	13 (1.7)	
Other		17 (3.3)	28 (3.6)	
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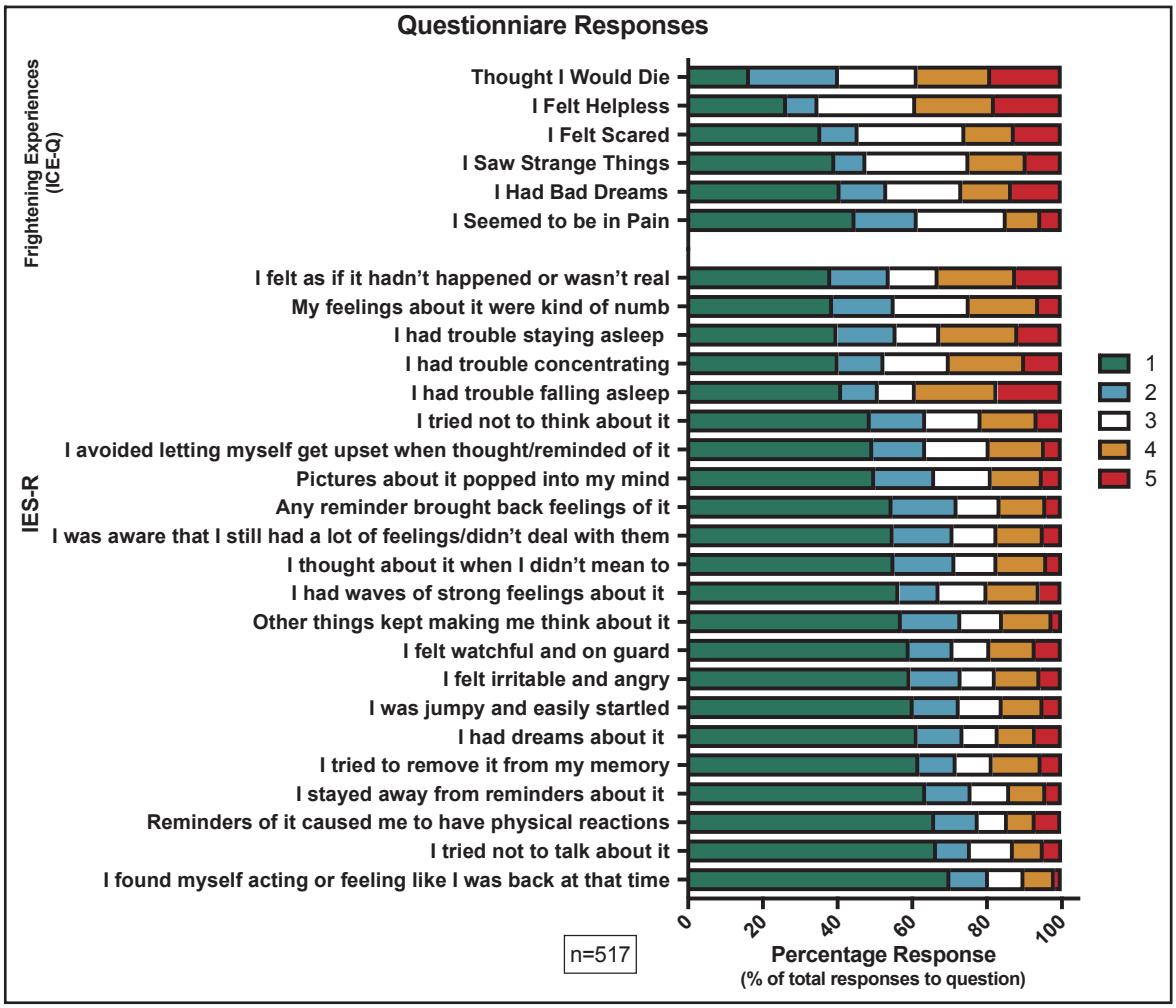
General Surgery		156 (30.2)	188 (24.3)	

Vascular	24 (4.6)	43 (5.6)	
Transplant	30 (5.8)	12 (1.6)	
Orthopaedics	19 (3.7)	27 (3.5)	
Cardiac	5 (1.0)	5 (0.6)	
Neurosurgery	0 (0)	4 (0.5)	
Other	9 (1.7)	11 (1.4)	
Source of Admission			P = 0.02
Operating Room	171 (33.0)	198 (25.6)	
Emergency Department	119 (23.0)	241 (31.2)	
High Dependency Unit	101 (19.5)	129 (16.7)	
Other Ward in hospital	69 (13.3)	100 (12.9)	
Other Hospital	23 (4.4)	41 (5.3)	
Other ICU	16 (3.1)	18 (2.3)	
Other Immediate Care Area	12 (2.3)	18 (2.3)	
Other	6 (1.2)	17 (2.2)	

Figure 1. Individual responses to the questions that comprise the Frightening Experiences Sum Score (FESS) of the Intensive Care Experience Questionnaire (ICE-Q)) and Impact of Event Scale Revised (IES-R) responses. Scores Represent:
ICE-Q: 1 never/strongly disagree; 2 rarely/disagree; 3 sometimes/neither; 4 frequently/agree; 5 all the time
IES-R: 1 not at all; 2 a little bit; 3 moderately; 4 quite a bit; 5 extremely.



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RESEARCH LETTER – CLEAN VERSION

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Running title: Early frightening and traumatic memories in ICU survivors

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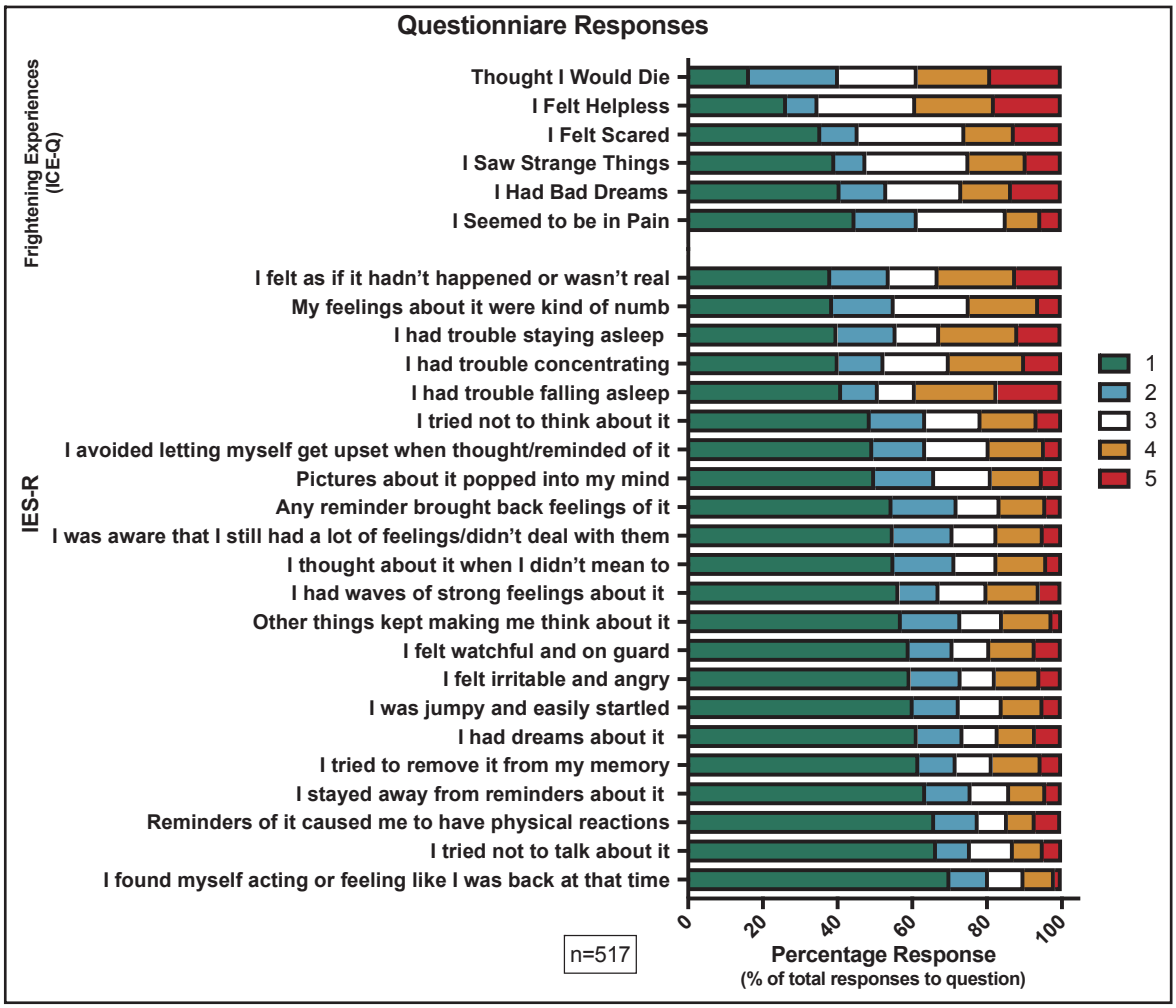

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