Cognitive impairment in ICU patients: A pilot mixed methods feasibility study exploring incidence and experiences for recovering patients

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Abstract

Background

Despite improvements in survival after critical illness and intensive care unit (ICU) treatment, some recovering patients still face ongoing challenges. There are few investigations exploring the incidence, risk factors and trajectory for cognitive impairment (CI) in former ICU patients in Australia.

Objectives

To test the feasibility of a study protocol designed to ascertain the incidence and impact of CI during recovery from a critical illness.

Methods

We conducted a mixed-methods longitudinal single centre pilot study. Participants were adult patients mechanically ventilated for ≥48 hours. Cognitive function was assessed during hospitalisation and at 1 week, 2 and 6 months after hospital discharge, using the Montreal Cognitive Assessment instrument. Factors potentially affecting cognitive function were also collected, including demographic and clinical variables, and fatigue, frailty and muscle strength. Semi-structured interviews were conducted to further explore participants' experiences during recovery.

Results

We screened 2068 patients (10% met the inclusion criteria). Participants (n=20) were mostly male with a mean age 61.9 years and a median of 4 days of mechanical ventilation. Data collection was complete for 14 and 11 participants at 2 and 6 months, respectively. Pre-illness patients were not cognitively impaired; one patient had delirium in ICU. The proportion of patients with CI ranged from 80% (17/18) while in hospital to 35% (5/14) at 6 months. Participants were challenged by fatigue and sleep disruption during recovery, but were not particularly concerned about CI.

Conclusions

Recruitment in ICU was challenging as few patients received prolonged mechanical ventilation. The protocol was feasible but some attrition was noted. A significant proportion of patients had mild CI, largely confined to recall and language cognitive domains; quantitative findings were supported by interview findings. Further investigations are required to ascertain the most appropriate inclusion criteria to enable identification of those at highest risk of CI.

Key words

Cognitive impairment, critical illness, mechanical ventilation

Introduction

Despite improvements in hospital survival after critical illness and intensive care unit (ICU) treatment[1, 2], some patients face physical, psychological and cognitive challenges during their recovery. International reports of cognitive impairment (CI) in this patient cohort are frequent, impacting on recovery and perceived quality of life, and a return to independent living/employment. Cognition relates to an individual's ability to comprehend, reason, plan and make decisions. These mental processes require a working memory, attention/concentration and executive function (EF). Executive function is 'the coordinated operation of various processes to accomplish a particular goal in a flexible manner' [3, pg 150.]

The prevalence of CI presents in varying degrees for most ICU patients until hospital discharge[4, 5], and remains high (78%) beyond six months[6]. Persistent impaired EF is particularly difficult for younger patients who are unable to return to fulltime employment[7], while for older individuals independent living may be impossible[8]. Self-reports from former ICU patients indicate that impaired EF is a common problem during recovery[9] together with frailty, fatigue, sleep disruption and poor appetite[10]. While the risk factors for CI after critical illness are unclear the underlying mechanism is probably multifactorial[6]. Pre-illness CI and sedative medications are known risk factors [11, 12], education level and advanced age are considered contributing factors[13], and there is a strong association between ICU delirium (a temporary confusional state) and CI during recovery[14]. The influence of illness and many treatment related factors on short and long-term cognitive function and the trajectory of CI is however largely unknown, with infection, low oxygen levels and shock states implicated [5].

Most research reflect patient outcomes from North America and Europe, with investigations into the incidence of and risk factors for CI in ICU patients in Australia in their infancy[15, 16]. Studies in related topics with former patients indicate it may be a frequent and serious problem for Australian patients [17, 18]. In light of this we aimed to test the feasibility of a specifically designed protocol to ascertain the

incidence of CI in patients who had received invasive mechanical ventilation for 48 hours or more in ICU.

Materials and methods

The study was approved by the Human Research Ethics Committee (HREC) of the Local Health District (HREC/14/HAMKE221) and ratified by the university HREC (HREC 2014000680). Study participation was voluntary; participants provided written consent and were informed that they could decline further participation at any time without prejudice.

Primary and secondary aims

The primary objective was to test the feasibility of the study protocol including numbers of patients agreeing to participate and completion rates. Secondary objectives included collection of data on cognitive status, fatigue and frailty, and to explore patient experiences of recovering from critical illness.

Design

This was a mixed-methods longitudinal pilot study, using a prospective cohort design with imbedded semi-structured interviews. The study setting was a single-centre tertiary referral facility ICU and the hospital wards that participants were discharged to.

The 58-bed ICU supported all medical and surgical sub-specialties, separated into four distinct areas ('pods'); two general medical-surgical, one cardiothoracic surgery and one neurosurgery unit. The ICU operated as a closed unit, with registered nurse: patient ratios of 1:1 for mechanically ventilated patients, and 1:2-3 for high dependency patients.

Pain and sedative management was targeted to individual patient requirements guided by the Critical Care Pain Observation Tool[19] and Richmond Agitation and Sedation Scale[20] (usual sedation target level for mechanically ventilated patients: 0 = alert and calm).

Sample

All patients treated in the ICU were screened for eligibility; aged ≥ 18 years and mechanically ventilated for ≥ 72 hours. When it was clear that few patients received prolonged mechanical

ventilation we amended the intubated and mechanical ventilated study criterion three months into patient recruitment to ≥ 48 hours. Exclusion criteria were: documented history of drug/alcohol dependence; intellectual disability; diagnosis of dementia; brain/spinal cord injury on imaging; non-English speaking; or documented palliation/treatment limitation orders. Patients were screened daily for potential inclusion. As this was a feasibility study no specific sample size calculation was conducted, with a pre-specified minimum target sample of 20 patients considered appropriate.

Measuring instruments

A specific case report form (CRF) was designed to collect demographic and clinical data (severity of illness on ICU admission (Acute Physiology and Chronic Health Evaluation[21]; APACHE II), admission diagnosis, sedative medications intravenously administered, duration of invasive mechanical ventilation, and length of ICU and hospital stay). To assess cognitive status and a range of potential influencing factors, a battery of instruments was used (see Table 1 for details and study time points) including: delirium in ICU (Confusion Assessment Method in ICU[22] (CAM-ICU) and wards (CAM[23]; both instruments were used routinely in daily practice), quality of sleep in hospital (Richards Campbell Sleep Questionnaire[24] visual analogue scale five; RCSQ VAS 5), CI (Montreal Cognitive Assessment[25]; MoCA), physical function (Chelsea Critical Care Physical Assessment Tool[26]; CPAx), muscle strength (Medical Research Council muscle strength scale[27]; MRC), fatigue (Fatigue Severity Scale[28]; FSS-9) including the Visual Analogue Fatigue Scale (VAFS), frailty (Clinical Frailty Scale[29]; CFS), pre-illness cognitive function (Informant Questionnaire on Cognitive Decline in the Elderly - Short Form[30]; IQCODE), and unwanted symptoms (Symptom Assessment Scale[31]; SAS).

Recorded semi-structured interviews were conducted at two and six months for available and consenting participants. Questions were designed to explore any 'out of range' answers patients reported from the written questionnaires, enabling elaboration of experiences and any specific concerns about cognitive function during their recovery.

At two months questions focused on the nature and impact of unwanted symptoms, and exploring responses to the MoCA, experiences of CI and any coping strategies. At six months, questions again explored cognitive function, experience of CI and coping strategies.

Recruitment and data collection

After first checking with the patient's nurse eligible patients (or their proxies) were invited to participate while they were in the ICU by the investigators. The initial study protocol comprised of collecting relevant data after informed consent at four measurement time points: in ICU, on the hospital ward day two after ICU discharge and 1-2 days prior to hospital discharge, and two months after discharge. Due to missed assessments during the ward admission period, we revised the protocol with HREC approval and collected data once only on the ward 2-4 days prior to hospital discharge, one week, two and six months after hospital discharge (see Table 1).

The MoCA-TV was administered for participants who resided beyond a 50 km radius and did not attend a follow-up appointment at the study hospital for the two month and six month data collection time points. To reduce the likelihood of loss to follow up two or more contact telephone numbers were recorded for each patient. Feasibility issues and screening challenges with the protocol were noted by investigators throughout the study.

Data management and analysis

Quantitative data were entered into Microsoft Excel spreadsheet (Microsoft Corporation, USA). Descriptive statistics were used for continuous data, with means and standard deviations (SD) and medians and interquartile range (IQR) reported depending on the data distribution. Categorical data were described using frequencies and percentages. Data collected from semi-structured interviews were initially transcribed verbatim, and then analysed line by line using content analysis techniques to identify key concerns and associated patterns.

Text was reduced to concepts via open coding[32, 33]. Content analysis was performed independently by two investigators (RE and KC) with trustworthiness of the data interpretation checked by another investigator (DE)[34].

Results

Study screening and participant recruitment occurred from November 2014 to August 2015 with a break mid-December 2014 to January 2015, and final follow-up data collection was completed in February 2016. We screened 2068 patients; 217 met the inclusion criteria and 168 were excluded. The final sample size was 20 (Figure 1). Some loss to follow up was noted, with a number of participants not contactable at follow-up (n = 6 at two months; n = 3 at six months). The final number of patients who completed data collection six months after hospital discharge was 11/14 (Figure 1).

Feasibility

Despite adjustments to the protocol, only 10% (n = 217/2068) of screened patients met the inclusion criteria. While initial enrolment and data collection (in ICU) was successful (n = 20/20) there was loss to follow-up at two months (n = 14/20, 70%). The proportion of participants available at six months improved (n = 11/14, 78%). Participants reported that they did not find the data collection procedure onerous; the reason for declining further involvement was the potential for additional 'mental' burden they perceived associated with on-going medical consultations and rehabilitation treatment (n = 2). Some participants not contactable were later found to be receiving treatment in another facility or were not living in their home at the time of data collection (n = 3).

Patient characteristics and cognitive function

The mean age of the sample was 61.9 (15.6) years with more males than females (13:7). The majority had an operative diagnosis and the mean severity of illness score was high: 21.7 (7.2). Patients received benzodiazepine and opioid medication infusions for a median of 6 days (Table 2). Our sample appeared to reflect the expected characteristics of a cohort of patients treated in the study ICU for >3-4 days. At baseline, cognitive function was not impaired (median IQCODE score 3.05 (3.00-3.20)) and no patient had likely CI (>3.6). Delirium was identified in only one patient in ICU (CAM-ICU: positive) and the same patient was identified to have delirium while recovering on the hospital ward. The mean MoCA score was 21.9 (3.3) for participants on hospital wards (15 scores

exceeded the MoCA cut-off score for CI of 26; 75% incidence). For participants who completed the MoCA-TV one week at home after hospital discharge (n =12) the mean score was 16.7 (3.7) (eight scores exceeded the cut-off score for CI of 19; 67% incidence).

Of note, the majority of patients achieved MoCA / MoCA-TV scores reflective of population norms at two and six month follow-up (Table 3). Of note, 35% and 45% of participants demonstrated cognitive dysfunction at these time points. The most common cognitive domains that participants had difficulty with were memory (specifically delayed recall) and language. Self-reported sleep on the hospital ward varied greatly (RCSQ VAS 5 1-100 mm; the 'worst possible' to 'could not be any better'), with a mean of 53.2 (29.9) mm.

The majority of patients reported mild to moderate severity for unwanted physical symptoms during their recovery (median SAS score <5). Higher scores were noted for 'fatigue' and 'insomnia'. Persistent fatigue was evident for all measures beyond two months. Clinician reports of frailty and muscle strength appeared to improve over time and were within population norms at two months (Supplementary file: table 1).

Patient interviews

Ten patient interviews were recorded at two months and 11 at six months. The average duration of interview recordings was 14 (range: 2 to 35) minutes. There was wide variation in the recovery experiences, but some common key concepts emerged which were congruent with the descriptive quantitative findings; physical fatigue, cognitive fatigue, and delayed recovery. De-identified direct quotes are used to elaborate findings.

At two months the prevalent theme was 'fatigue'; for example:

> '*When you are tired you don't want to blooming, think you just want to go with the flow.*' (#10, two months)
>
> *'Well fatigue is the main thing that is affecting my life in that I do not have the stamina to do what I do in my normal life even simple tasks I would not even thought twice about like walking around the block. I find it exhausting.*' (#7, two months)

Also of note were the number of references to 'muscle weakness' and 'the length of time it was taking to feel stronger/get better':

> *'I just can't, I've got no energy to do anything. I have trouble. I can't walk very far. I've just got no energy. I've got no strength on my arms. I can't even open a bottle of drink without help.'* (#20, two months)

> *'I was stunned at the drop in physical fitness. I am similarly stunned at the time it's taken to get to the point where I am at. I thought I would be here much quicker. I am disappointed to be told that it will take a fairly long time and measured in [several] months not weeks*.' (#7, two months)

'Sleep difficulties' - problems getting to sleep and staying asleep - were noted by several participants; for example:

> '*Ever since I come back from hospital I haven't been able to sleep properly. They given me* [sic] *sleeping tablets but they did not work so I stop taking them. I can go to bed at say 10 o'clock at night and wake up again at say 12 o'clock and then stay awake till maybe 2, 3, or 4 o'clock in the morning just tossing and turning*.' (#18, two months)

Content from the six month interviews was even more varied, although concepts highlighted in the two month interviews remained evident:

> *'I did slow down a bit and lost my fitness physical fitness … which I am now slowly regaining. But it is a bit of an effort. I try to walk every morning and I do gardening*.**'** (#3, six months)

> *'… getting back into my normal old routine is taking much longer than I ever expected. But then I got people saying yes it is only seven months and three operations. [laughter] I am sick of hearing it*.' (#17, six months)

As participants perhaps became less concerned about physical symptoms, they were more aware of their 'cognitive fatigue' and some volunteered strategies to deal with this, such as the use of reminders in calendars, Sudoku and pacing activity levels; for example:

> *'But you know I think that definitely helps … when I play it [Sudoku] and the time it takes for me to do it is all related to the fatigue factor and the concentration factor so if I am fatigued it takes forever to do it and I just have to put it down.'* (#21, six months)

> *'I do have to write on the calendar. So I write everything down so that I am doing something every day this week. Sometimes 2 or 3 like I am going to the taxman, yesterday and the day before I was doing things. But I had the whole week planned in the beginning and I had to write it all down to make sure I knew exactly what I was doing. Tomorrow the car is going in for service, today you were coming and get down to the taxman.'* (#13, six months)

Discussion

This pilot study explored the feasibility of a comprehensive mixed methods protocol to explore the incidence of and contributing factors for CI in recovering critically ill patients. While the study protocol was achievable with low levels of burden reported by patients, screening and recruitment of an adequate sized cohort of patients with a relatively long duration of mechanical ventilation was challenging. We recruited a small heterogeneous sample of participants who were characteristic of ICU patients who had received mechanical ventilation for a prolonged period.

The selection criteria were successful in excluding patients with pre-existing CI and therefore pre-illness cognitive function for our participants was reflective of population norms. While the incidence of delirium was low, this was assessed when patients were suitable for ICU discharge and on the ward. Any floridly delirious patient would not have been transferred and may have had other reasons requiring treatment in critical care.

Despite the known and theoretical increased risk associated with longer duration of mechanical ventilation, the incidence of CI for our cohort during recovery was similar to estimates derived from

systematic reviews[6, 14]. Early in recovery approximately 80% of our cohort had mild impairments in cognitive function; primarily confined to deficits in patients' ability to successfully complete tasks with delayed recall and language, although this had resolved at six months. Our findings contrast with other studies where more difficulties with EF[35, 36] were reported, and was an unexpected finding in our study. Long term (>6 months after discharge from hospital) rates of CI in general differ widely[37]. Higher rates (50-94%[35, 36]) are found at the time of hospital discharge and tend to stabilise (<50%) after a year[36]. A recent Australian study[16] identified an incidence rate of 24% at 6 months in a sample with lower APACHE II (18.1 versus 21.7), mechanical ventilation duration (2.2 versus 4.0 days) and ICU length of stay (4.3 versus 8.5 days) than our cohort. Cognitive function was assessed by a trained psychologist using two validated instruments. With a combined administration time of 30-35 minutes, this approach may not be feasible from a routine practice or screening perspective. Congruent with other studies reporting patient experiences of recovery from critical illness [38, 39], fatigue was a persistent unwanted symptom with our cohort. This may in part be explained by the prevalence of self-reported insomnia. Both symptoms were reported during interviews and appeared to be the predominant concern for several participants. While muscle weakness and the time taken to recover were also concerns, notably CI did not appear to feature highly in patient interviews. Our quantitative measurement of muscle strength and physical function indicated that participants had recovered sufficient gross muscle strength to participate in activities of daily living. The severity of muscle weakness was apparently less troublesome for our cohort compared to reports of other similar cohorts in which physical function was more limited early in recovery[38, 40]. Likewise frailty did not appear to be as prevalent in our cohort; a recent prevalence rate of 30% was estimated based on international reports for patients with moderate to severe critical illness but this rate was predominately based on pre-illness assessments[41].

Our qualitative findings reflected similar themes to a recent grounded theory study from Scotland[42]. Participants' concerns about being in transition, reflecting 'liminality' (experiences of being in-

between and uncertainty), and attempting to move forward by setting goals with specific targets and tasks, within an intitial focus on physical recovery[42], were echoed by our participants.

Strengths and limitations

Our study protocol was comprehensive, and strengthened by the embedded patient interviews. The study inclusion criteria affected enrolment and therefore the feasibility for recruitment was poor. Despite a protocol to optimise patient screening and pre-hospital data collection, we were unable to recruit a sample size sufficient to allow inferential data analyses to determine factors contributing to CI in recovering ICU patients.

The data collection protocol was however feasible, although some attrition was evident. Many functional measures and screening assessments are not sensitive enough to highlight subtleties that may impact patients' abilities to function at levels required for work and complex activities of daily life such as financial planning [43]; inclusion of participant interviews were therefore vital in capturing this information.

We did not however collect data on education level of participants; this may have affected the results for cognitive function. However one participant told us that he had 'trouble finding words' and that he had not completed school beyond age 15 years and we were able to make the necessary adjustment (i.e. add 1 point) for the MoCA score.

Implications for practice

Despite a limited sample size, our pilot study findings suggest that there may be considerable burden associated with reduced physical and cognitive function early in recovery and during this vulnerable time patients are frequently reliant on family and friends[38, 39, 44]. It is imperative that hospital discharge planning is comprehensive and includes assessment of social and living conditions for recovering critically ill patients. No participants reported social isolation with provision of specific support noted. It is therefore essential that families and carers are consulted in relation to the type of support necessary to reduce the burden during this sometimes prolonged recovery period.

Recommendations for further research

Our findings suggest that further research is required using a similar study protocol to explore the effects of sleep quality and fatigue on cognitive and physical recovery after critical illness. In order to achieve an adequate sample size and more accurately identify those at greatest risk of CI (and in need of interventions), different inclusion criteria are required. 'Prolonged mechanical ventilation' (≥ 48 hours) may not be the appropriate criterion to select patients most at risk of CI (and therefore in need of interventional investigation), particularly in a cohort who was treated with a relatively conservative sedative medication regimen (individual ICU sedation levels were titrated to a calm and cooperative level).

Criteria such as duration of systemic inflammatory response or diagnosis of moderate traumatic injury may be more specific for exploring CI[8, 45], as at least one study failed to demonstrate an association between long-term CI and severity of illness[46]. More appropriate inclusion criteria for future studies therefore may be confirmed diagnosis of sepsis on ICU admission[47]; increased problems with cognition after hospitalisation for patients with severe sepsis were confirmed in one study [8] and one case study revealed long term structural brain decline on MRI [48] in North America. Addition of a more comprehensive subjective sleep assessment for each time point would add valuable information about the mediating effects of sleep quality on cognitive aspects of recovery.

Conclusions

Our pilot study findings reveal that CI was evident for a significant proportion of patients and largely confined to memory recall and language cognitive domains. Further investigations are required to ascertain the most appropriate inclusion criteria in order to identify those at greatest risk of CI and need of investigation for effective interventions. Developing a feasible and sustainable study protocol, for exploring CI is challenging.

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Figure legend

Figure 1 Flow diagram showing patient enrolment and follow-up during the study *Changed protocol potential 14 patients

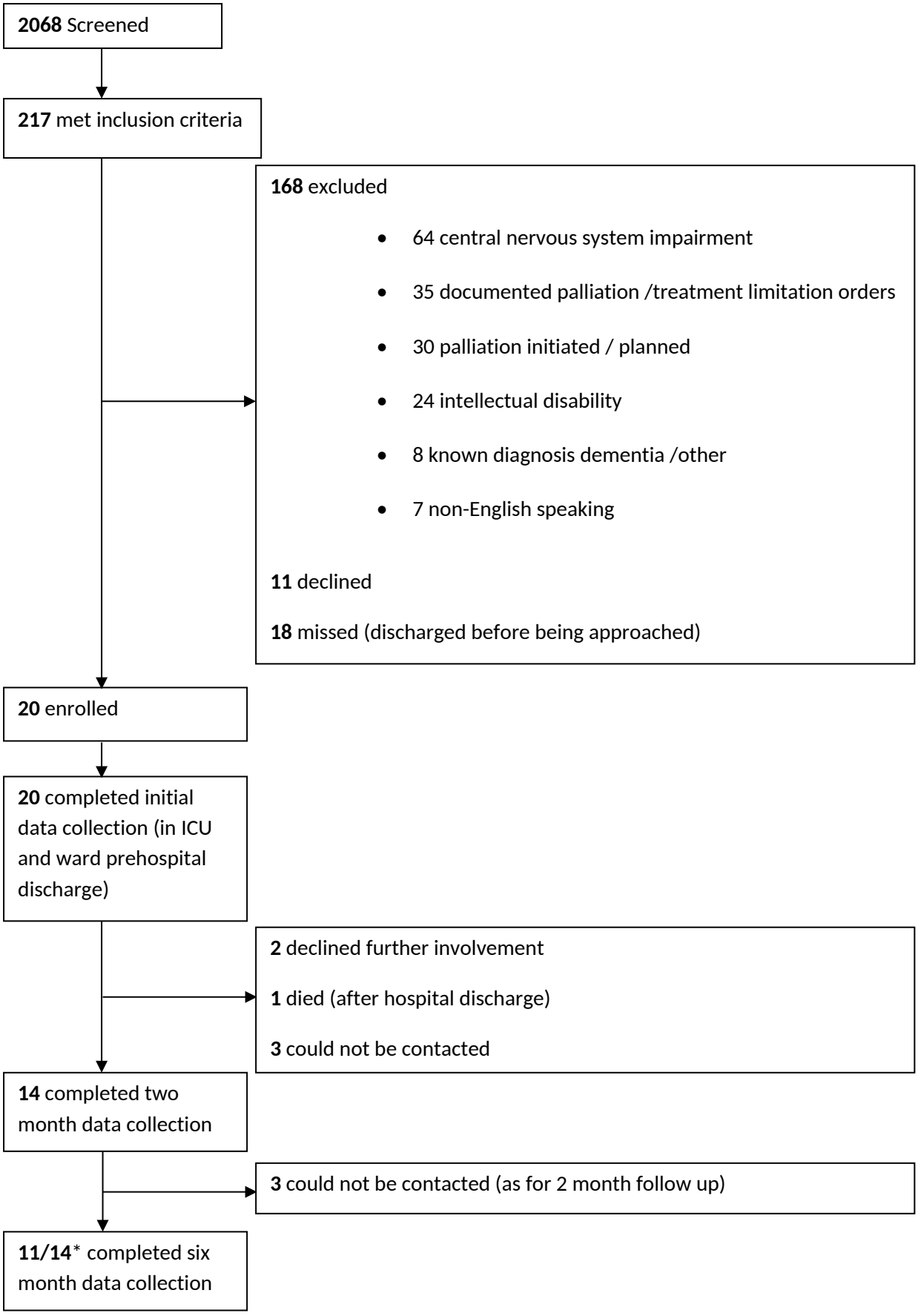

Figure 1 Flow diagram showing patient enrolment and follow-up during the study *Changed protocol potential 14 patients

Tables

Table 1 Description of instruments and administration time points

Instrument	Domain/s	Description /response	Time to administer (minutes)	Study time point				
				ICU day 1	2-4 days post-ICU	Post-hospital discharge	1 week	2 months	6 months
Confusion Assessment Method in ICU (CAM-ICU)[21]	Delirium	Extensive validation in this population [45] and recommended for use in clinical practice guidelines [46] / Categorical negative or positive	5-10	X					
Confusion Assessment Method (CAM)[22]	Delirium	A reliable and valid instrument for distinguishing delirium from permanent types of CI in non-ICU settings [22] / Categorical negative or positive	5-10		X				
Richard Campbell Sleep Questionnaire (RCSQ VAS 5[a])[23]	Quality of sleep	100 mm VAS 5 is the visual analogue scale for quality of sleep in the RCSQ. Sleep quality was assessed, as poor sleep quality and fatigue adversely affect cognitive function [47] / 0 mm = worst, 100 mm = best	1-1.5	X	X				

Montreal Cognitive Assessment (MoCA) / telephone (-TV[b])[24]	Visuospatial / executive, naming, memory, attention, language, abstraction, delayed recall, orientation	A brief method for detecting mild CI, with better sensitivity than the MMSE [48] and compares favourably with more detailed neuropsychological tests [49]. Cognitively intact individuals score 30. For this study the cut-off score for CI of <26 (based on reported population norms[24]). MoCA-TV includes items except visuospatial / executive and naming [50] / Total assessment score = 22 (for this study CI was identified if the MoCA-TV was ≤19)[50].	20-30		X	X	X	X
Chelsea Critical Care Physical Assessment Tool (CPAx[c])[25]	Physical function	Demonstrated construct validity for describing physical function at hospital discharge in ICU survivors [39]. Importantly, cognitive function is inextricability linked with physical function and is known to be affected by critical illness [7, 8] / 0 – 50 points (0 = complete dependence, 50 = complete independence)	3		X[b]		X	
Fatigue Severity Scale (FSS-9)[27]	Fatigue experience, cause and impact	Assesses self-reported participant experience, causes and impact of fatigue on daily life, with moderate to high validity[51] across a range of patient populations [52]. Poor sleep quality and fatigue adversely affect human performance on some tests of cognitive function for example, attention, short-term recall and response time[47] / 7-point (1 = strongly disagree, 7 = strongly agree)	3		X	X	X	
Visual Analogue Fatigue Scale (VAFS) (part of the FSS-9)	Global fatigue	Often used in conjunction with FSS-9. A measure of global fatigue / 11-point (0 = worst fatigue possible, 10 = normal)	2		X			

Medical Research Council Muscle Strength Scale (MRC)[26]	Muscle strength	A reliable and valid measure of muscle strength in quadricep and bicep muscles in ICU patients[53 54] / 6-point scale (0 = no muscle movement, 6 = contracts against full resistance)	5-10	X	X		X	
Clinical Frailty Scale (CFS)[28]	Physical abilities / activities	Used to predict the need for assisted living[28], and to screen for frailty over the telephone[55]. Frailty is a recognised risk factor for poor long-term outcomes, and for recovering ICU patients of all ages [10].9-point scale (1 = very fit, 8 = very severely frail, 9 = terminally ill)	3		X		X	
Informant Questionnaire on Cognitive Decline in the Elderly – Short Form (IQCODE)[29]	Cognitive impairment	A brief, reliable screening instrument for cognitive decline by proxies [56 57] Ratings for the 16 items are averaged to give a 1–5 score, with 3 representing no change on any item / A cut off score of > 3.6 indicates cognitive decline.	5	X[d]	X[d]		X[d]	
Symptom Assessment Scale (SAS)[30]	7 physical symptoms [c]	Assesses unpleasant distracting symptoms such as nausea and poor appetite in oncology patients; tested extensively in palliative care settings in Australia[30]. 11-point scale (0 = no problem, 10 = worst possible problem)	5-10		X	X	X	

Notes: [a]RCSQ VAS 5: Richard Campbell Sleep Questionnaire – visual analogue scale 5; [b]MoCA-TV telephone version (only administered to patients who resided >50km away from hospital); [c]CPAx: aspects of physical functioning using the CPAx were recorded using reports from nurse(s) and physiotherapist caring for the patient after carefully questioning; [d] if not already completed

Table 2 Selected demographic and clinical characteristics for the sample

Characteristic	Statistic
Age, yrs, mean (SD [a])	61.9 (15.6)
Male, n (%)	13 (65)
APACHE II score, mean (SD)	21.7 (7.2)
Diagnosis, operative, n (%)	11 (55)
Duration of mechanical ventilation, days, median (IQR [b])	4.0 (3.0 - 6.0)
Length of ICU[c] stay, days, median (IQR)	8.5 (5.0 - 13.7)
Length of hospital stay, days, median (IQR)	22.0 (13.2 – 33.0)
Continuous benzodiazepine infusion, days, median (IQR)	4.0 (3.0 – 6.5)
Continuous opioid infusion, days, median (IQR)	4.0 (3.0 – 6.0)
ICU mortality, n (%)	0 (0)
Hospital mortality, n (%)	0 (0)

Notes:[a] SD = standard deviation; [b]IQR = interquartile range; [c]ICU = intensive care unit

Table 3: Summary descriptive statistics for cognitive function

Score	Statistic
IQCODE[a] – short form score, mean (SD[b])	2.0 (0.3)
CAM-ICU[c] positive (n)	1
CAM[d] positive (n)	1
MoCA[e] Ward	
Mean (SD)	21.9 (3.3)
<26, n (%)	16 (80)
MoCA-TV[e] 1 week (n = 12)	
Mean (SD)	16.7 (3.7)
<19, n (%)	8 (67)
MoCA (<26) or MoCA-TV (<19) two months (n =14), n (%)	5 (35)
MoCA (<26) or MoCA-TV (<19) six months (n = 11), n (%)	5 (45)

Notes: [a] IQCODE: Informant Questionnaire on Cognitive Decline in the Elderly; [b]SD = standard deviation; [c]CAM-ICU = Confusion Assessment Method in ICU; [d]CAM = Confusion Assessment Method; [e]MoCA = Montreal Cognitive Assessment/MoCA-TV telephone version

Supplementary file table 1: Unwanted physical symptoms, fatigue, frailty and strength and function

Symptom	Statistic
Appetite SAS[a] score, median (IQR[b])	
Ward	5.0 (2.0 – 5.0)
Week 1	2.5 (0.0 – 7.0)
Month 2	0.5 (0.0 -3.8)
Bowel SAS score, median (IQR)	
Ward	2.5 (0.0 – 4.0)
Week 1	0.5 (0.0-3.7)
Month 2	0.5 (0.0 -2.8)
Breathing SAS score, median (IQR)	
Ward	3.0 (0.0 – 6.0)
Week 1	6.0 (2.7 – 7.0)
Month 2	1.5 (0.3 – 3.8)
Fatigue SAS score, median (IQR)	
Ward	6.0 (3.0 -8.0)
Week 1	5.5 (2.0 -7.2)
Month 2	5.3 (1.3 -7.8)
Insomnia score, median (IQR)	
Ward	5.0 (3.0 -7.0)
Week 1	3.5 (0.0 – 6.5)
Month 2	3.0 (0.3 – 6.8)
Nausea SAS score, median (IQR)	
Ward	1.0 (0-4.0)
Week 1	0.0 (0.0 – 2.0)

Month 2	0 (0.0 – 1.0)
Pain SAS score, median (IQR)	
Ward	5.0 (1.0 - 7.0)
Week 1	1.0 (0.0 – 6.0)
Month 2	2.0 (0.0 -5.8)
VAFS[c] score, median (IQR)	
Ward	7.5 (4.7 – 10.0)
Week 1	4.7 (3.3 – 5.1)
Month 2	5.0 (2.0 -7.5)
FSS-9[d] score, median (IQR)	
Week 1	4.7 (3.3 -5.1)
Month 2	4.0 (2.8 – 5.8)
MRC MSS[e] score, median (IQR)	
ICU	5.0 (4.0 -5.0)
Ward	5.0 (5.0)
CPAx[f] score, median (IQR)	
Ward	39.0 (36.2 – 44.8)
Month 2	49.0 (48.0-49.0)
CFS[g] score, median (IQR)	
Ward	6.0 (4.7 – 6.3)
Month 2	2.0 (2.0 – 3.0)

Notes: [a]IQR = interquartile range; [b]SAS = Symptom Assessment Scale; [c]VAFS = Visual Analogue Fatigue Scale, [d]FSS-9= Fatigue Severity Scale; [e]MRC MSS = Medical Research Council Muscle Strength Scale (bicep and quadricep muscle bilateral equal limb strength); [f]CPAx = Chelsea Critical Care Physical Assessment Tool; [g]CFS = Clinical Frailty Scale