



Research Paper

The effects of sedation cessation within the first four hours of intensive care unit admission in mechanically ventilated critically ill patients – a quality improvement study

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ABSTRACT

Background: Early deep sedation in mechanically ventilated patients during the first 48 h of intensive care unit (ICU) admission can be associated with adverse outcomes. We hypothesised that moving the 'daily sedation break' process forwards, might allow earlier titration of sedation to target levels – an 'early sedation cessation' (ESC).

Methods: We commenced a quality improvement project with the primary outcome being to stop sedation completely, within 4 h of ICU admission, in 95% of eligible patients. This was done by small, step-wise tests of change. No ethical approval was required.

Findings: Between 1 February 2014 and 31 January 2018, 1787 intubated patients were included. 1052 received an 'ESC' within 4 h ('Yes'), 545 were excluded ('Excluded'), and 190 were inadvertently omitted from 'ESC' ('No'). The primary aim was achieved for the first time after 12 months. Compared to the 'Yes' group, the 'Excluded' group received 38% more propofol in the first 48 h of admission (IRR 1.38 (1.31–1.47), $p < 0.001$), while the 'No' group received 32% more (IRR 1.32 (1.22–1.43), $p < 0.001$). At four hours, 19.6% (12.9–27.9) of the 'Yes' group had attained a target RASS of -1, 0 or 1, compared to 13.6% (8.0–21.0) of those in the 'No' group. This proportion increased to 55.6% (46.1–64.9) at 24 h compared with 44.9% (35.6–54.4) in the 'No' group.

Interpretation: Ceasing sedative infusions as soon as possible, is safe and feasible, in both medical and surgical patients, and can be implemented into 'real life' with no additional staffing.

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Introduction

Sedative medications, in bolus or infusion form, are used in the intensive care unit (ICU) to facilitate patient comfort, and manage agitation and invasive ventilation. Over-sedation is associated with prolonged periods of mechanical ventilation, longer ICU and hospital stay, increased incidence of delirium, and increased mortality [1–5]. The level of sedation is important even during the first 48 h, a period not commonly studied in randomised controlled trials [3,4,6–10].

The Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS) Guidelines recommend optimising sedative use in ICU by targeting light or no sedation, and paying close attention to

pain [1]. This practice can only be achieved by frequent assessment of the patient.

Implementing change into ICU practice can be challenging [11–13]. With reference to acute respiratory distress syndrome (ARDS), several years following publication of the landmark low tidal volume ventilation paper [14], even critical care units involved in the study, were unable to sustain the same level of reliability over time with baseline staffing levels [15]. The use of quality improvement (QI) principles may help to implement targeted sedation protocols and other practices into real-life [16–18].

In our ICU, a 'daily sedation break' takes place during the morning ward round in all patients, unless they fulfil exclusion criteria. This has been embedded since 2008 as part of the Scottish Patient Safety Programme (SPSP) Ventilator Associated Pneumonia (VAP) protection bundle [19]. We hypothesised that moving this process to an earlier point in admission, with the aim being to cease sedation as soon as practical, would facilitate titration of sedative agents to an optimal target level, well before the first morning ward round.

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Research in Context

Evidence before this study

We carried out a MEDLINE search from 1980 to January 2014 prior to commencing this project, and at six-monthly intervals following this, the last being April 2020. Search terms used were ((critical care) or (ICU)) and ((sedation) or (delirium) or (agitation)). Studies were included if they involved patients aged 18 and over, admitted to an ICU and undergoing mechanical ventilation.

Prior to commencing, two prospective cohort studies suggested an association between early deep sedation and a prolonged time on a ventilator. A further randomised controlled trial investigated a protocol of no sedation versus daily interruption of sedation until awake. The no sedation group spent a shorter time on a ventilator.

During our project, a randomised, parallel group, multi-centre trial in post-abdominal surgery patients, showed that time to successful extubation was reduced in those who had both sedation and opioid infusions discontinued as soon as possible following admission.

Added value of this study

In this study, we have stopped sedation in a greater number of patients, at an earlier point in ICU admission than all but one previous study. We have also included both surgical and medical patients. A greater proportion of patients who had sedation discontinued within four hours of ICU admission, reached a target sedation score, in a shorter time interval, when compared to those who were omitted from an 'early sedation cessation' (ESC).

Implications of all the available evidence

Our results provide evidence that immediate cessation of sedation, allows rapid titration of sedation to target levels in both medical and surgical patients and could be adopted as a recognised technique to reduce sedative use and improve outcomes. Further studies should be done to corroborate the evidence we have reported from a quality improvement initiative.

means of an endo-tracheal tube or tracheostomy were included in data collection. Patients were excluded from an 'ESC' if they required targeted temperature management post-cardiac arrest, infusion of neuro-muscular blocking agents, suffered from active seizures despite treatment, had been anaesthetised due to severe agitation, were difficult to ventilate, required intra-cranial pressure management, had an airway issue whereby inadvertent extubation would have been life-threatening, required imminent transfer, had severe cardiovascular compromise, or multiple trauma. We followed the guidance issued by NHS Greater Glasgow and Clyde in 2008 entitled 'Process for Consideration and Approval of Requests to Conduct Non-research projects within NHS GG&C' which confirmed that this quality improvement work did not require ethical approval.

Procedure

Standard unit sedation practice following endo-tracheal intubation is an infusion of propofol combined with a morphine infusion (or alfentanil if renal impairment is present). Benzodiazepines are reserved for palliative care, treatment of acute alcohol withdrawal, or difficult to control status epilepticus, but never exclusively for sedation. Sedative agents such as dexmedetomidine and clonidine are used infrequently and never at the point of admission to ICU.

Routine 'daily sedation breaks' take place during the consultant-led ward round and are an integral and obligatory part of patient care, embedded within our unit since 2008. The propofol infusion is suspended in appropriate patients, with sedation level targeted to a Richmond Agitation and Sedation Scale (RASS) score of -1, 0 or 1 [20]. Should ongoing sedation still be required following a 'daily sedation break', propofol is recommenced at half the previous infusion rate, with repeated titration to target RASS. Opioid infusions are not stopped at the same time as the sedative infusion, unless a reduced conscious level persists.

The 'ESC' process was carried out in the same way as the 'daily sedation break', except we aimed to perform this within four hours of admission to ICU (or initial intubation if this was at a later time). The absence of residual neuro-muscular block was assessed prior to stopping sedation in any patient who had recently received a bolus of neuro-muscular blocking agent, usually to facilitate intubation or transfer to the unit.

Throughout the four year period of data collection, weekly multi-disciplinary QI meetings allowed presentation of progress, dissemination of information, teaching sessions, and discussion about small changes to practice that might improve compliance with the 'ESC' protocol [16]. Multiple tests of change were initiated over the four year period, and we learned by both our successes and mistakes, as we endeavoured to embed this into standard unit practice.

Outcomes

The primary outcome measure was completion of an 'ESC' within four hours of admission or intubation. This data was collected on a daily basis by one critical care consultant. Patients were assigned to one of three groups – 'Yes' - 'ESC' performed within four hours; 'Excluded' - excluded from 'ESC' with appropriate reason documented; 'No' - 'ESC' inadvertently omitted in a patient who would have been eligible. The 'No' group therefore corresponds closely to our previous standard unit practice, where sedation would first be titrated at a 'daily sedation break' the day following admission. An 'ESC' was deemed to have occurred if the sedative infusion was completely stopped within the first four hours, irrespective of whether it required to be recommenced.

Additional data was collected retrospectively from the electronic care record (Intellispace Critical Care and Anaesthesia, Philips) and WardWatcher, a national ICU database, with the 'Yes' group being compared against the 'No' group. We assessed propofol requirements

Methods

Glasgow Royal Infirmary ICU is a 20-bedded adult, medical and surgical, closed critical care unit in the West of Scotland. Around 1200 patients per year are admitted, of which 40% require mechanical ventilation. A patient to nurse ratio of 1:1 is normal practice for all ventilated patients in the United Kingdom. Two junior doctors are resident on call, with two critical care consultants present during the day, and one available overnight. All patients are assessed twice a day by physiotherapists for mobilisation, and chest physiotherapy if required. Ventilator weaning plans are led by medical staff, following discussion with the nurse looking after each individual patient. Pharmacy, dietician and microbiology input is available daily.

A multi-disciplinary, quality improvement (QI) programme was commenced in February 2014 [16]. Along with improving adherence to a sepsis bundle, medicines reconciliation and early mobilisation, minimising sedative use was a further target. The primary aim was to stop sedative infusions completely in 95% of intubated patients, within four hours of admission to ICU, or four hours of endo-tracheal intubation, if this occurred following ICU admission. This process was called an 'early sedation cessation' (ESC) to differentiate from the already embedded 'daily sedation break'. No additional staff or research nurses were utilised, and no funding was required.

Patients

All patients admitted to ICU between 1 February 2014 and 31 January 2018, who underwent mechanical ventilation at any point, by

in the 48 h following admission (or intubation if this occurred at a later time), corresponding RASS scores with proportion of patients in each group reaching target RASS, and requirement for any further sedative agents at any point during ICU admission. Time spent on a ventilator, length of ICU and hospital stay, and ICU and hospital mortality was also recorded. STROBE Guidelines were adhered to.

Statistical analysis

All analyses were carried out with R statistical software version 3.5.1. A two-sided p value of less than 0.05 was taken as significant. Group medians were compared by Kruskal-Wallis or Pearson Chi-Square tests. Propofol infusion rate with time is illustrated by a multi-level zero inflated Poisson regression model. Change in RASS score with time for each group is a non-linear b-spline to model time across the three groups to enable the modelling of proportions. Numerical data is presented as incidence rate ratio (95% confidence interval). In both models, data from patients dying within the first 48 h, was removed prior to the models being built. Both models were adjusted for the baseline characteristics of age, gender, presence of endotracheal tube, Glasgow Coma Scale and time. Time spent on a ventilator, and ICU and hospital length of stay are unadjusted secondary analyses.

No funding was required for this quality improvement project.

Results

4451 patients were admitted to the ICU between 1 February 2014 and 31 January 2018. 1808 (40.6%) had an endo-tracheal tube or tracheostomy in situ. After excluding some patients repatriated to the hospital with a tracheostomy, and a small number with an endo-tracheal tube in situ who did not require any sedation, primary outcome data was available for 1787 patients. 545 (30.5%) patients were excluded from ‘ESC’. Of those patients eligible, 1052 (84.7%) had sedation stopped within the first four hours (Fig. 1).

Primary outcomes were available for all patients. A small amount of secondary data was unavailable, but all existing data for these patients was analysed. Other than Acute Physiology and Chronic Health Evaluation (APACHE) II score [21], baseline characteristics were not the same (Table 1). We included the 24 patients in the ‘Excluded’ group transferred out of the unit within the first 48 h of admission in our analysis, by extrapolating the propofol infusion rate and RASS score at the time of transfer to the whole 48 hour period.

Primary outcome

Data for the primary outcome measure was available for 1787 patients. Initial baseline data in February 2014 showed that the ‘Yes’ group made up 17.4% of eligible patients. A greater proportion of the ‘No’ group occurred near the beginning of this project, while the practice was becoming embedded. The run chart displaying progress over the four years shows that the 95% aim was achieved for the first time in month twelve (Fig. 2). Stability was achieved following this with a median of 91.2% eligible patients receiving an ‘ESC’ for the subsequent 37 months. The median proportion of patients excluded from an ‘ESC’ in the first four hours varied between 24 and 36%. The most common reason for this was targeted temperature management, and continued neuro-muscular blockade. Fig. 2 also illustrates the tests of change that were implemented during this project, and timings of other educational initiatives.

There was no difference in the rate of inadvertent extubation between the groups (p = 0.5) (Table 2). As is normal practice in the United Kingdom, no mechanical restraint was utilised at any point in admission, and no additional staff were required, although a 1:1 nurse:patient ratio is normal practice.

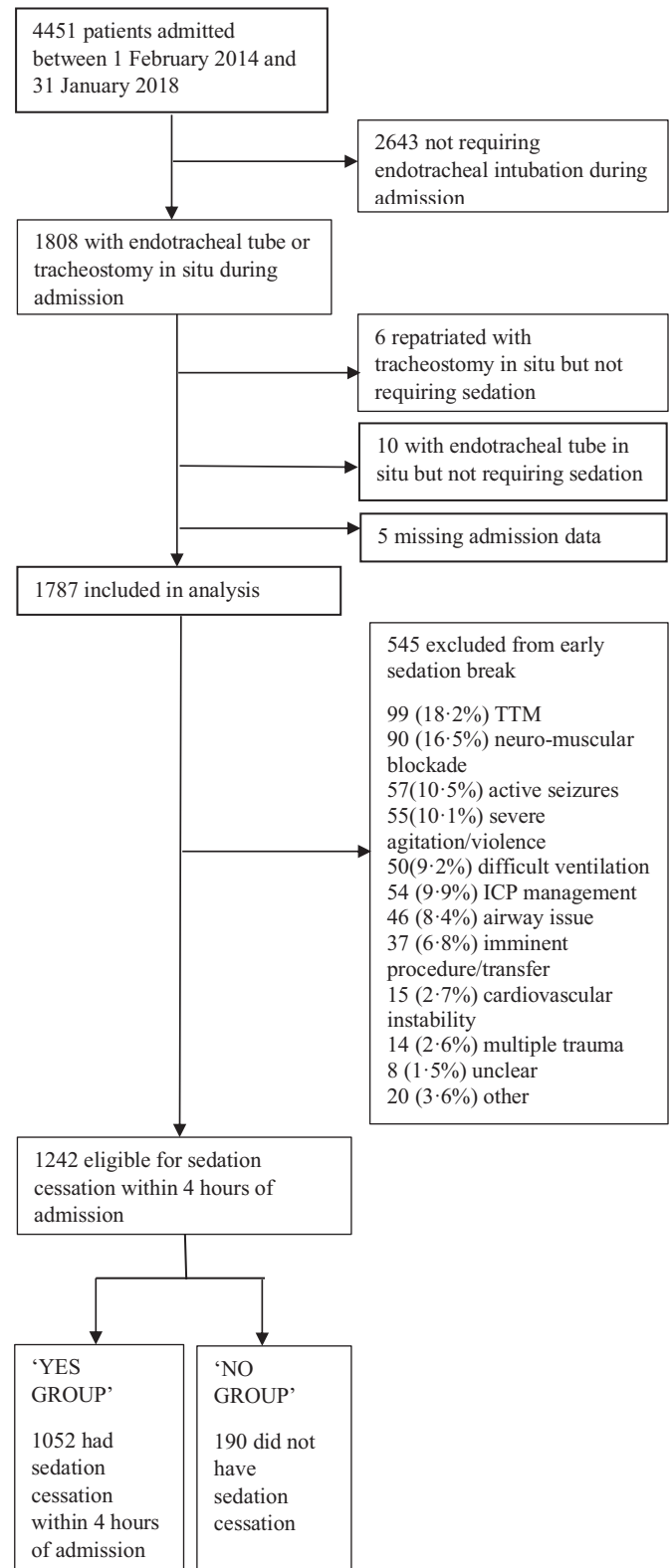


Fig. 1. Consort diagram. A decision to exclude from an early sedation cessation (‘ESC’) was taken by the critical care consultant following discussion with bedside nurse and nurse in charge of the unit. While some patients may have been excluded for several reasons, only the most relevant was recorded. TTM – targeted temperature management post-cardiac arrest; Neuro-muscular blockade – includes all patients requiring continued neuro-muscular blockade for any reason, mostly during treatment for acute respiratory distress syndrome (ARDS); Active seizures – an admission diagnosis of seizures did not preclude ‘ESC’, as long as seizures had been treated and there was no evidence of continued seizure activity; Severe agitation/violence – only excluded if this was the reason for intubation and cause of agitation was unlikely to be resolved within four hours; Difficult ventilation –

Table 1
Baseline characteristics of study group.

	Whole cohort (n = 1787)	'Excluded' (n = 545)	'No' (n = 190)	'Yes' (n = 1052)	P value
Gender, male	1050 (58•8)	343 (62•9)	116 (61•1)	591 (56•2)	0•03 ²
Age, years	56 (43–67)	51 (36–64)	59 (44–69)	57 (44–69)	<0•01 ²
APACHE II	20 (13–26)	20 (13–27)	19 (14–26)	20 (13–27)	0•88 ¹
APACHE II risk prediction	31•6 (8•5–59•7)	28•5 (5•6–61•3)	29•0 (12•1–54•4)	32•3 (9•1–59•7)	0•27 ¹
Admitted from					<0•01 ²
Emergency Department	700 (39•2)	268(49•2)	60(31•6)	372(35•4)	
Operating Theatre	429 (24•0)	86 (15•8)	45 (23•7)	298 (28•3)	
Ward	328 (18•4)	103 (18•9)	45 (23•7)	180 (17•1)	
High Dependency Unit	250 (14•0)	71 (13•0)	34 (17•9)	145 (13•8)	
Other Intensive Care Unit	35 (2•0)	8 (1•5)	3 (1•6)	24 (2•3)	
Obstetrics	5 (0•2)	1 (0•2)	1 (0•5)	3 (0•3)	
Other	40 (2•2)	8 (1•6)	2 (1•0)	30 (2•9)	
Type of Surgery *					<0•01 ²
Emergency/Urgent	337 (18•9)	67 (12•3)	35 (18•4)	235 (22•4)	
Scheduled/Elective	90 (5•0)	18 (3•3)	10 (5•3)	62 (5•9)	
No surgery prior to admission	1358 (76•1)	459 (84•4)	145 (76•3)	754 (71•7)	
Admitting specialty **					<0•01 ²
General Medicine	805 (45•1)	268 (49•3)	72 (37•9)	465 (44•2)	
General Surgery	495 (27•7)	96 (17•7)	57 (30•0)	342 (32•5)	
Orthopaedic Surgery	72 (4•0)	24 (4•4)	11 (5•8)	37 (3•5)	
Gastroenterology	69 (3•9)	19 (3•5)	14 (7•4)	36 (3•4)	
Plastic Surgery	60 (3•4)	23 (4•2)	8 (4•2)	29 (2•8)	
Geriatric Medicine	39 (2•2)	8 (1•5)	5 (2•6)	26 (2•5)	
Obstetrics	37 (2•1)	10 (1•8)	2 (1•1)	25 (2•4)	
Respiratory Medicine	36 (2•0)	11 (2•0)	7 (3•7)	18 (1•7)	
Other	173 (9•7)	85 (15•6)	14 (7•4)	74 (7•0)	
Intubated prior to ICU admission ***	1314 (73•6)	405 (74•3)	118 (62•1)	791 (75•3)	<0•01 ²
Admission Diagnosis ****					<0•01 ²
Cardiovascular	249 (14•3)	108 (20•8)	15 (8•1)	126 (12•2)	
Gastrointestinal	431 (24•8)	64 (12•3)	51 (27•6)	316 (30•5)	
Metabolic / Renal	25 (1•4)	10 (1•9)	3 (1•6)	316 (30•5)	
Neurological	262 (15•1)	106 (20•4)	16 (8•6)	12 (1•2)	
Poisoning/toxic/overdose	136 (7•8)	34 (6•6)	11 (5•9)	140 (13•5)	
Respiratory	251 (14•4)	67 (12•9)	45 (24•3)	91 (8•8)	
Sepsis	207 (11•9)	62 (11•9)	24 (13•0)	139 (13•4)	
Trauma (including head injury)	107 (6•1)	46 (8•9)	10 (5•4)	121 (11•7)	
Other	72 (4•1)	22 (4•2)	10 (5•4)	51 (4•9)	

'Excluded' – no early sedation cessation ('ESC') carried out as patient fulfilled one of the exclusion criteria; 'No' – inadvertently omitted from an 'ESC' when one should have been carried out; 'Yes' – 'ESC' carried out within four hours of admission or intubation.

Data is presented as median (interquartile range) or number (percentage). Any missing data is denoted by an asterisk. * - 2 missing, ** - 1 missing, *** - 1 missing, **** - 47 missing. Kruskal-Wallis test¹, Pearson Chi-Square test². APACHE II – Acute Physiology and Chronic health Evaluation II, ICU – intensive care unit.

Additional data

The histogram in Fig. 3 illustrates the actual propofol infusion rate with time for each individual patient in the first 48 h following ICU admission. By four hours, almost 60% of patients in the 'Yes' group did not require any propofol, although 35.8% did require this to be recommenced, mostly at a lower rate, at some point in the first 48 h.

A model of the change in propofol requirements with time is shown in Fig. 4. There was no difference in the propofol requirements between the 'No' and the 'Yes' group at time zero as shown by an incidence rate ratio (IRR) 1.02 (0.91–1.15) $p < 0.001$. The 'Excluded' group received 25% more propofol at time zero than the 'Yes' group (1.25 (1.15–1.37) $p < 0.001$). During the first 48 h of admission, the 'No' group received 32% more propofol than the 'Yes' group (IRR 1.32 (1.22–1.43) $p < 0.001$) while the 'Excluded' group received 38% more than the 'Yes' group (IRR 1.38 (1.31–1.47) $p < 0.001$).

Over the same time frame, the model in Fig. 5 shows the change in proportion of patients, who attained a target RASS score of –1, 0 or 1. At four hours (the cut-off for determining if an ESC had taken place),

19.6% (12.9–27.9) of the 'Yes' group had attained this target, compared to 13.6% (8.0–21.0) of the 'No' group. This proportion increased to 55.6% (46.1–64.9) by 24 h, compared with 44.9% (35.6–54.4) in the 'No' group.

Unadjusted exploratory secondary analyses show that duration of mechanical ventilation was lower in the 'Yes' group, a median of 31 h versus 53 h in the 'No' group ($p < 0.01$) (Table 2). 7.5% of all patients required reintubation within 48 h of extubation ($p = 0.94$). The 'Yes' group, had a shorter median ICU length of stay of 1.0 day compared to the 'No' group ($p = 0.02$). Median hospital length of stay was almost 3 days shorter in the 'Yes' group compared to the 'No' group ($p < 0.01$). These results have not been adjusted for deaths or other variables and should be interpreted with caution.

Discussion

This was a single-centre QI project aiming to perform an 'ESC' within the first four hours of admission to ICU, in critically unwell, mechanically ventilated patients. The 'ESC' was carried out in the same manner as the 'daily sedation break' [22]. The process was safe and feasible from the outset, with no additional staffing, no increased device removal, no use of restraints, and no alternative sedative use. This has resulted in a decrease in propofol use, with an associated increased proportion of patients reaching target RASS in a faster time. There may also be an indication of improvement in time spent

individual consultant decision, does not include neuromuscular blockade for ARDS; ICP – intracranial pressure; Airway issue – severe airway or facial swelling, mostly secondary to burns; Cardiovascular instability – severe hypovolaemic shock; Other – charge nurse and consultant deemed unit unsafe for 'ESC' due to very high workload, other emergencies or staffing issue.

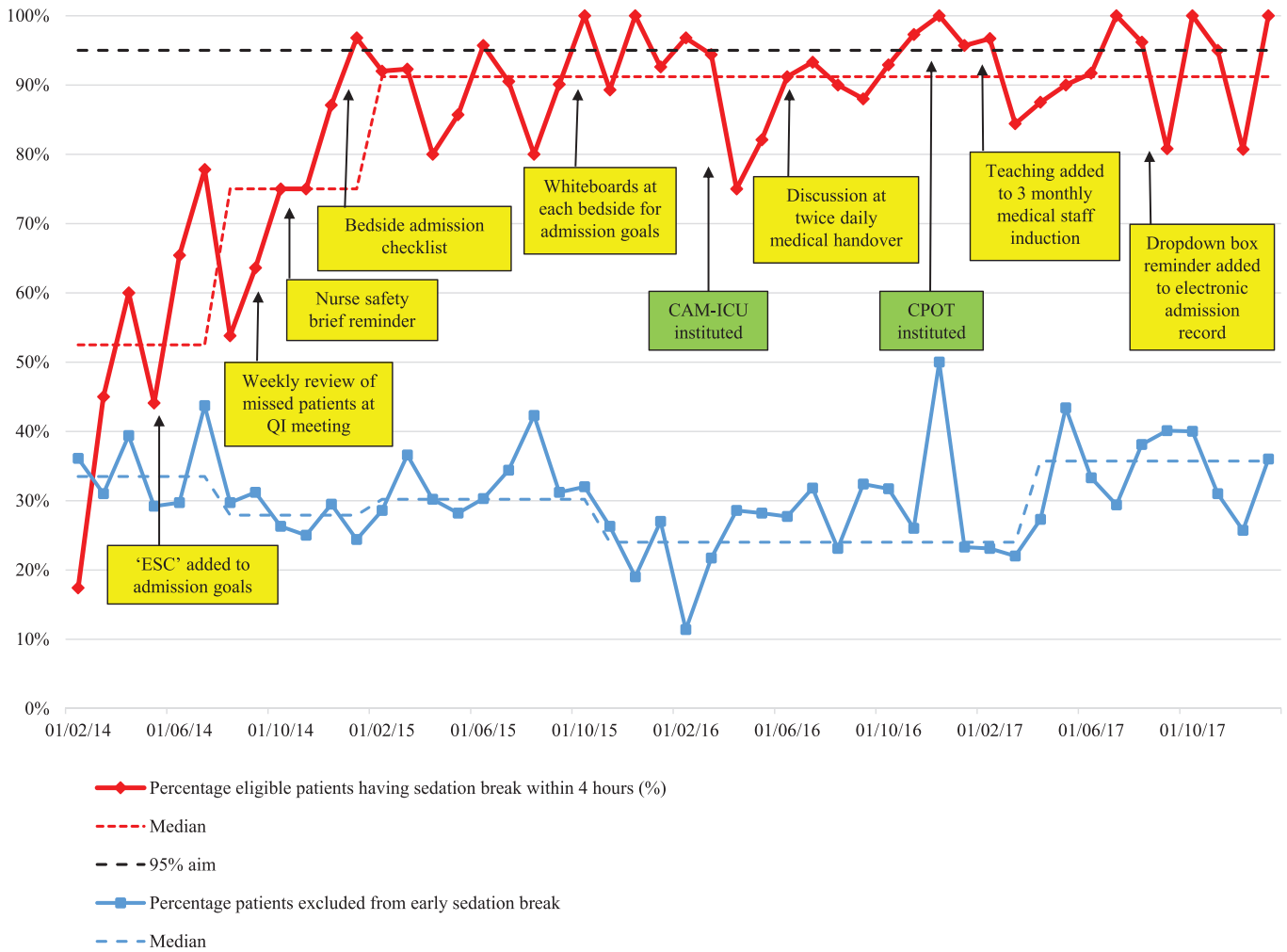


Fig. 2. Run chart illustrating the progress in achieving early sedation cessation ('ESC') in 95% of eligible patients within four hours of admission or intubation (if this occurred at a later time once in ICU). X axis – time (months), Y axis – percentage eligible patients receiving an 'ESC'. The green boxes show when in the process our unit introduced the critical care pain observation tool (CPOT) and confusion assessment method-ICU (CAM-ICU). The yellow boxes illustrate some of the 'tests of change' that were instituted over time in an attempt to embed the process into unit practice.

Table 2
Unadjusted secondary analyses for each group.

	Whole cohort (n = 1787)	'Excluded' (n = 545)	'No' (n = 190)	'Yes' (n = 1052)	P value
Re-intubation within 48 h	134 (7.5)	42 (7.7)	15 (7.9)	77 (7.3)	0.94 ²
Tracheostomy in situ at any point during ICU stay	60 (3.4)	20 (3.7)	11 (5.8)	29 (2.8)	0.09 ²
Duration of mechanical ventilation (hours)	39 (14–118)	53 (18–137)	53 (18–146)	31 (12–99)	<0.01 ¹
Self-extubation in first 48 h	18 (1.01)	4 (0.73)	1 (0.53)	13 (1.23)	0.50 ²
Unit Outcome					<0.01 ²
Improved	1276 (71.4)	351 (64.4)	141 (74.2)	784 (74.5)	
Died	471 (26.4)	175 (32.1)	47 (24.7)	249 (23.7)	
No change	26 (1.5)	13 (2.4)	0 (0.0)	13 (1.2)	
Worse	14 (0.8)	6 (1.1)	2 (1.1)	6 (0.6)	
Unit length of stay (days)	3.8 (1.5–9.3)	3.7 (1.6–8.9)	4.6 (1.9–11.3)	3.6 (1.4–8.9)	0.02 ¹
Hospital Outcome, died *	550 (30.9)	192 (35.2)	52 (27.4)	306 (29.2)	0.03 ²
Hospital length of stay (days)	10.9 (3.6–26.0)	7.7 (2.7–21.0)	14.4 (4.3–33.5)	11.6 (4.3–26.9)	<0.01 ¹
Additional sedative medication at any point during admission					
Atypical anti-psychotics	21 (1.2)	12 (2.2)	2 (1.1)	7 (0.7)	0.03 ²
Benzodiazepines	310 (17.3)	101 (18.5)	44 (23.2)	165 (15.7)	0.03 ²
Clonidine	36 (2.0)	17 (3.1)	2 (1.1)	17 (1.6)	0.08 ²
Dexmedetomidine	5 (0.3)	2 (0.4)	1 (0.5)	2 (0.2)	0.65 ²
Haloperidol	350 (19.6)	97 (17.8)	57 (30.0)	196 (18.6)	<0.01 ²

'Excluded' – no early sedation cessation ('ESC') carried out as patient fulfilled one of the exclusion criteria; 'No' – inadvertently omitted from an 'ESC' when one should have been carried out; 'Yes' – 'ESC' carried out within four hours of admission or intubation. * - 5 missing patients.

Additional sedative medication – patients were included if they received even just one dose of additional sedative medication at any point during their ICU stay. Only exceptionally rarely was this given in the first 48 h following admission/intubation and never to facilitate an 'ESC'. Kruskal-Wallis test¹, Pearson Chi-Square test². Unit and hospital length of stay and duration of mechanical ventilation have not been adjusted for deaths.

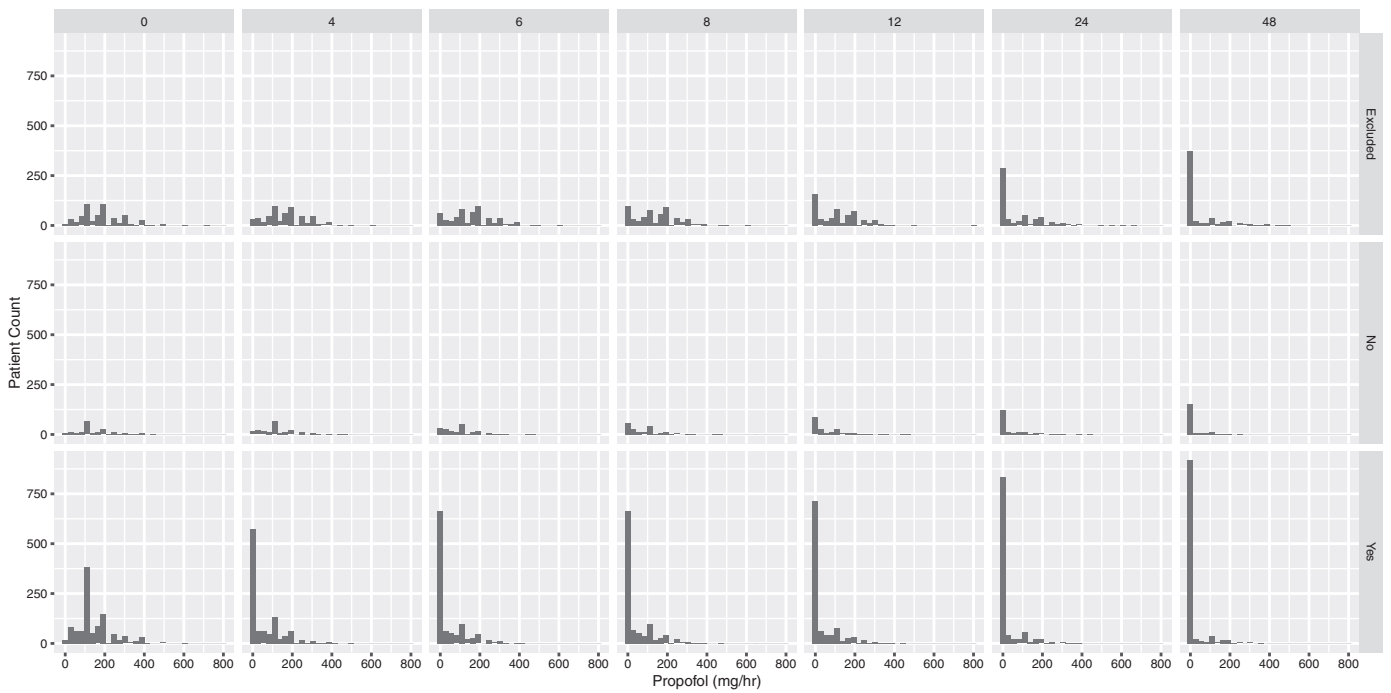


Fig. 3. Histogram illustrating the change in actual propofol infusion rate with time for each individual patient in each of the three groups. X axis (bottom) – propofol infusion rate (mg/hour); X axis (top) – times 0, 4, 6, 8, 12, 24 and 48 h following ICU admission or intubation; Y axis (left) individual patient count; Y axis (right) sedation cessation state (Yes, No, Excluded). 24 patients in the ‘Excluded’ group were transferred to another hospital within the first 48 h of admission. They remain included in analysis, with the propofol infusion rate at the time of transfer, extrapolated onwards to the whole 48 h.

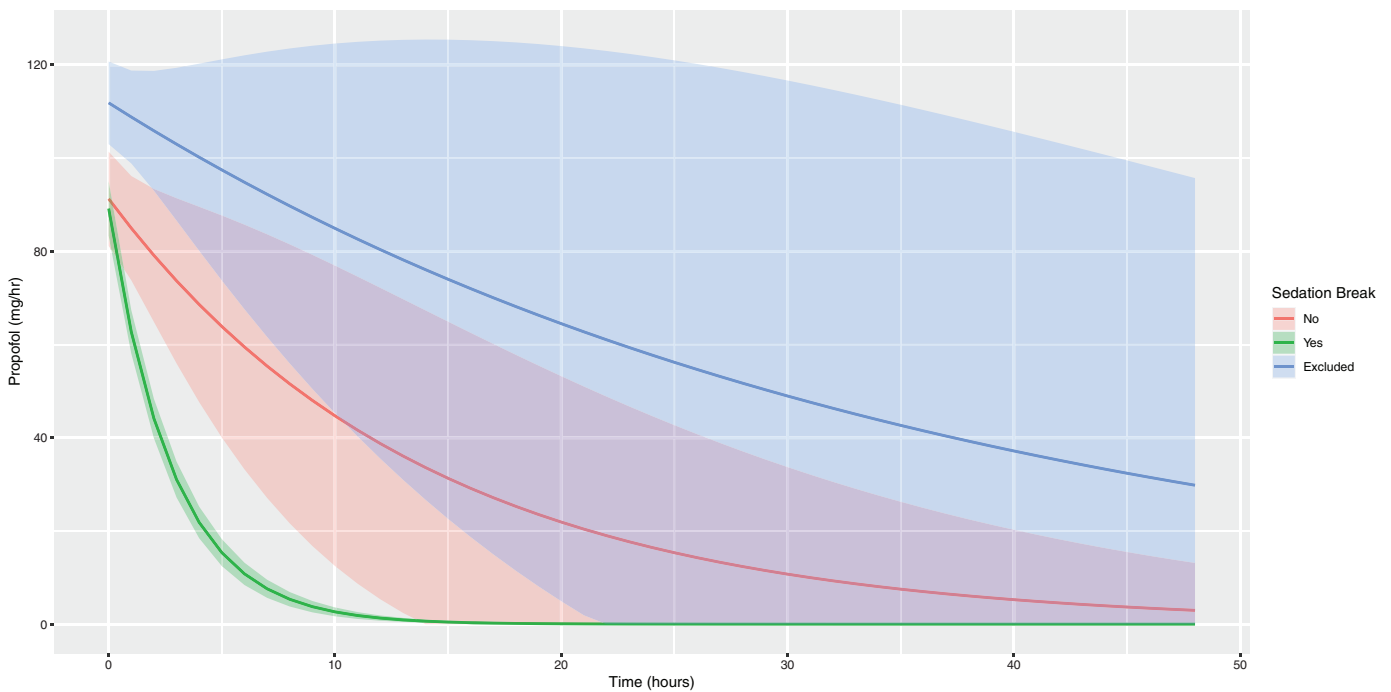


Fig. 4. Model of change in propofol infusion rates with time for each group over the first 48 h. Multi-level zero inflated Poisson regression model adjusted for time, sedation break status, age, gender, and Glasgow Coma Scale (GCS). This accounts for repeated measures in the data and the disproportionate number of patients receiving no propofol at all as time goes on. There is also an interaction between early sedation cessation (‘ESC’) and time to allow for each state to change at different rates. Deaths were removed prior to building this model. X axis – time (hours), Y axis (median propofol infusion rate mg/hour). Solid lines – model estimation for propofol infusion rate; Shaded areas – 95% confidence intervals for each group.

on a ventilator, and ICU and hospital length of stay but this requires further investigation.

The ‘ESC’ process was implemented at the same time as other projects. This was purposeful, to provide more opportunities to learn about QI principles. Unlike other ICU processes, the ‘ESC’ occurs only once, and at any point in a 24 hour period. Embedding the ‘ESC’ into

unit practice lagged behind other projects like medicines reconciliation and mobilisation, as these were carried out daily, for every patient, and at a specific time, therefore were easier to implement.

The weekly QI meetings were crucial in this process. We learned about QI principles from an expert, presented our data by means of a run chart, discussed our difficulties and our failures, and provided all

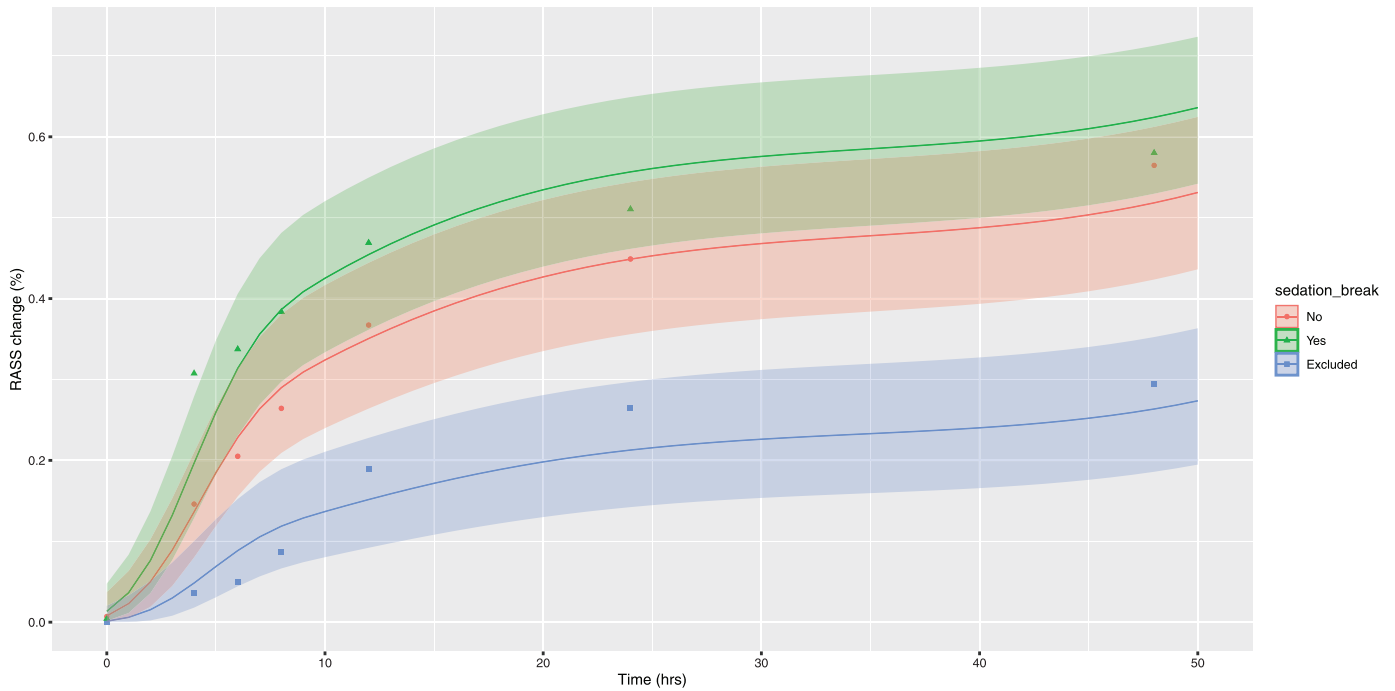


Fig. 5. Beta regression model illustrating the change in proportion of patients in each group who attained a target RASS score of -1, 0 or 1 by time. A nonlinear, b-spline to model time across all three groups has been used. The model is adjusted for time, sedation break status, age, gender and Glasgow Coma Scale (GCS). Deaths were removed prior to building this model. Solid lines – model prediction; Triangles/diamonds/squares – actual data percentage points; Shaded areas – model confidence intervals.

staff with the opportunity to suggest how to improve. While not working clinically, we took the opportunity to observe how the ICU admission process works, and to gain feedback from the team involved.

Education of staff was also important. In addition to our formal QI meetings, nurse educators disseminated new information and discussed tests of change, while providing support to nursing staff building their confidence in a new process. All projects were discussed daily at the morning medical handover and during new medical staff ICU induction sessions. Each admission also acted as an additional educational opportunity. It did not take long for the positive effects of an ‘ESC’ to be detected by all staff, and as confidence in our ability to safely carry out the process was boosted, enthusiasm increased exponentially.

We noticed that patients admitted overnight, especially from the operating theatre, had an ‘ESC’ omitted more than any other group of patients. Choosing to stop sedation, and extubate a post-operative patient overnight was a big change from previous practice. In addition, a very busy unit, or consecutive admissions, made it more likely that an ‘ESC’ would be inadvertently omitted. These issues were resolved over time as the process became embedded within the unit.

Specific changes to our unit admission practice have facilitated the ‘ESC’. We carry out a hands off admission pause, involving all staff looking after the patient. This includes an ‘ESC’ decision. This decision is documented in the electronic patient record, and immediately on a whiteboard at the head of the bed. First tasks are invasive line placement or other procedures, prior to any written documentation. Procedures that can be carried out with local anaesthesia do not delay discontinuation of sedation. Nursing staff organise their working day to ensure that all patients receiving an ‘ESC’ always have one nurse immediately by the bedside. A member of medical staff with airway skills is always present in the unit during an ‘ESC’. These changes worked for us, but may not be directly transferrable to other critical care units.

The four hour maximum time scale for discontinuing sedation was an arbitrary selection, taking into account what we felt we could

realistically achieve, and the point where we felt there might be some benefit. Organisationally, our aim was to stop sedation as soon as practically possible, and not wait until the end of the four hour period. Our RASS target of -1, 0, or 1 was tighter than most previous studies. We felt that this level of consciousness was required to facilitate patient co-operation with early mobilisation.

We have succeeded in stopping sedation at an earlier point in admission than any randomised controlled trial, other than SOS-Ventilation [7]. This French multi-centre study included 137 mechanically ventilated patients following abdominal surgery. The intervention group had both sedative and major opioid infusions discontinued soon after ICU admission, and showed a significant reduction in time spent on a ventilator. We have shown that this immediate approach to sedation titration, can be successfully implemented in the ‘real-world’ and in a much wider patient population of both medical and surgical patients. Our additional results, although unadjusted, also suggest a potential reduction in ventilator time.

Unlike SOS-Ventilation, we chose to continue opioids during our ‘ESC’. This corresponded with our ‘daily sedation break’ practice, which all staff had confidence in carrying out. The trajectory of opioid use pre- and post-‘ESC’ is currently being analysed in our unit. Despite opioids continuing, and irrespective of the need for resumption of a propofol infusion, the rapidity of achieving a target RASS score in our ‘ESC’ group, shows it is possible to rapidly titrate sedation to a calm, conscious and cooperative patient. It may be that the early target RASS score is crucial, rather than the method used to achieve this. 55.6% of patients in our ‘Yes’ group achieved a RASS target of -1, 0 or 1 within 24 h. This corresponds with Shehabi et al., who achieved 60% by 24 h (although this included a RASS of -2) with the use of dexmedetomidine as the primary sedative agent [23].

All ICU survivors in our hospital are invited to attend a multi-disciplinary post-ICU recovery clinic [24]. The staff who run this clinic, report that many of our patients felt that the periods of time during which they had no recollection of events were more distressing. Very few claimed to have felt anxious or in pain when conscious, appreciating being involved and understanding of their care, and being able

to communicate. These testimonies correspond with evidence suggesting that there is no increased incidence of post-traumatic stress disorder (PTSD) or other psychological disorders in ICU patients receiving light or no sedation [25–27].

As this was a quality improvement project, with the aim of improving care using simple, step-wise changes in practice, we took a pragmatic approach to reporting our results. While the propofol and RASS models have been adjusted for deaths and other variables, we accept that other secondary analyses are unadjusted and require further investigation. Despite this, we feel there is an indication of improvement in time spent on a ventilator, and ICU and hospital length of stay, from the current exploratory data analysis. Our reported results may also not be directly due to an 'ESC' alone. More likely, achieving an early target RASS has facilitated early mobilisation, both of which have been reported in the literature as improving outcomes [28].

We did not report incidence of delirium and pain, since an educational intervention to improve frequency and accuracy of documentation was required during the period of data collection, prior to us having confidence in the validity of these values. Confusion Assessment Method for ICU (CAM-ICU) is now recorded three times in a 24 hour period, with RASS scores recorded hourly [29]. Critical Care Pain Observation Tool (CPOT) scoring was implemented in 2016 and is now recorded at the same time as RASS scores [30].

The strengths of this study are the large size compared to other studies assessing early critical care sedation practice [2,7–8,31–32]. Primary outcome data collection was robust, being completed manually, by the same consultant. We analysed our data by intention to treat, irrespective of whether propofol was required to be recommenced following an 'ESC'. In addition, patients who just missed the four hour target for stopping sedation, continued to be analysed in the 'No' group.

It may be that while we have presented our results as an example of what can be achieved in a typical ICU, this may not be generalizable to all units, particularly those who do not have a 1:1 nurse to patient ratio. Smaller units with less staffing flexibility may also struggle. We also accept that within our unit, two colleagues had expertise in QI principles prior to commencing.

By utilising the principles of QI, we have succeeded in embedding this intervention into normal unit practice, with very high reliability, despite significant staff turnover, and maintained these results over time. The main driver for change behind this has been the enthusiasm, hard work and unanimous buy-in from all medical, nursing, and physiotherapy staff.

Further research should focus on attaining a specified target RASS score as soon as possible following admission, although this will be challenging within the constraints of a randomised, controlled trial. The mechanism by which this occurs, be it stopping sedation and/or analgesia completely, targeting light sedation by means of sedative or analgesia boluses or infusions, or a completely different method, may not be as significant as the endpoint, but should be explored. We feel that our results provide evidence that the 'ESC' process could be adopted as a recognised technique to reduce sedative use and improve outcomes.

Contributors

J Cuthill carried out conception and design along with the multi-disciplinary quality improvement project team, primary outcome data collection, secondary outcome data collection, analysis of quality improvement data, interpretation, initial drafting and revision of the manuscript

L Jarvie carried out secondary outcome data collection, interpretation and manuscript revision

C McGovern carried out secondary outcome data collection and manuscript revision

M Shaw carried out all statistical analysis, design, interpretation and manuscript revision

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Datasets

The datasets used in this study can be accessed by contacting the first author. They are not subject to restrictions or embargo.

Declaration of Competing Interests

None declared

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References

- Devlin J, Skrobik Y, Gelinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med* 2018;46(9):e825–73.
- Shehabi Y, Chan L, Kadiman S et al. for the SPICE Study Group investigators. Sedation depth and long-term mortality in mechanically ventilated critically ill adults: a prospective longitudinal multicentre cohort study. *Intens. Care Med.* 2013;39(5):910–8.
- Shehabi Y, Bellomo R, Kadiman S et al. for the SPICE study investigators. Sedation intensity in the first 48 h of mechanical ventilation and 180-day mortality: a multinational prospective longitudinal cohort study. *Crit. Care Med.* 2018;XX 00–00. doi: 10.1097/CCM.0000000000003071.
- Tanaka L, Azevedo L, Park M et al. for the ERICC Study Investigators. Early sedation and clinical outcomes of mechanically ventilated patients: a prospective multicentre cohort study. *Crit. Care* 2014;18:R156.
- Aragon R, Proano A, Mongilardi N, et al. Sedation practices and clinical outcomes in mechanically ventilated patients in a prospective multicentre cohort. *Crit. Care* 2019;23:130.
- Stephens R, Dettmer M, Roberts B, et al. Practice patterns and outcomes associated with early sedation depth in mechanically ventilated patients: a systematic review and meta-analysis. *Crit Care Med* 2018;46:471–9.
- Chanques G, Conseil M, Roger C, et al. Immediate interruption of sedation compared with usual sedation care in critically ill postoperative patients (SOS-Ventilation): a randomised, parallel-group clinical trial. *Lancet Respir. Med.* 2017;5:795–805.
- Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. *Lancet* 2010;375:475–80.
- Balzer F, Weiss B, Kumpf O, et al. Early deep sedation is associated with decreased in-hospital and two-year follow up survival. *Crit. Care* 2015;19:197.
- Shehabi Y, Bellomo R, Reade M, et al. Early intensive care sedation predicts long-term mortality in ventilated critically ill patients. *Am J Respir Crit Care Med* 2012;186(8):724–31.
- Nassar A, Zampieri F, Salluh J, et al. Organizational factors associated with target sedation on the first 48h of mechanical ventilation: an analysis of Checklist-ICU database. *Crit. Care* 2019;23:34.
- Kydonaki K, Hanley J, Huby G, Antonelli J, Walsh T. on behalf of DESIST study investigators. Challenges and barriers to optimising sedation in intensive care: a qualitative study in eight Scottish intensive care units. *BMJ Open* 2019;9:e024549. doi: 10.1136/bmjopen-2018-024549.
- Carrothers K, Barr J, Spurlock B, Ridgely M, Damberg C, Ely W. Contextual issues influencing implementation and outcomes associated with an integrated approach to managing pain, agitation, and delirium in adult ICU's. *Crit. Care Med.* 2013;41:S128–S35.
- Network The Acute Respiratory Distress Syndrome. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *NEJM* 2000;342(28):1301–8.
- Needham D, Colantuoni E, Mendez-Tellez P, et al. Lung protective mechanical ventilation and two year survival in patients with acute lung injury: prospective cohort study. *BMJ* 2012;344:e2124. doi: 10.1136/bmj.e2124.
- Daniel M, Puxty A, Miles B. Making quality improvement happen in the real world: building capability and improving multiple projects at the same time. *BMJ Qual. Improv. Rep.* 2016 u207660.w4159. doi: 10.1136/bmjqualityu207660.w4159.
- Balas M, Burke W, Gannon D, et al. Implementing the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle into

- everyday care: opportunities, challenges and lessons learned for implementing the ICU pain, agitation, and delirium guidelines. *Crit. Care Med.* 2013;41:S116–S27.
- [18] Hager D, Dinglas V, Sunhas S, et al. Reducing deep sedation and delirium in acute lung injury patients: a quality improvement project. *Crit. Care Med.* 2013;41:1435–42.
- [19] Scottish Intensive Care Society Audit Group, NHS National Services Scotland. VAP prevention bundle guidance for implementation. <http://www.sicsag.scot.nhs.uk/hai/VAP-Prevention-Bundle-web.pdf>. Accessed 14 February 2020.
- [20] Sessler C, Gosnell M, Grap M, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002;166:1338–44.
- [21] Knaus W, Draper E, Wagner D, Zimmerman J. APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13(10):818–29.
- [22] Kress J, Pohlman A, O'Connor M, Hall J. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *NEJM* 2000;342:1471–7.
- [23] Shehabi Y, Howe B, Bellomo R, et al. Early sedation with dexmedetomidine in critically ill patients. *N Engl J Med* 2019;380:2506–17.
- [24] Intensive care syndrome: promoting independence and return to employment programme (InS:PIRE) <https://www.nhsggc.org.uk/about-us/professional-support-sites/inspire/> Accessed 14 March 2020.
- [25] Kress J, Gehlbach B, Lacy M. The long-term psychological effects of daily sedative interruption on critically ill patients. *Am J Respir Crit Care Med* 2003;168:1457–61.
- [26] Jones C, Griffiths R, Humphris G. Memory, delusion, and the development of acute posttraumatic stress disorder-related symptoms after intensive care. *Crit Care Med* 2001;29:573–80.
- [27] Strom T, Stylsvig M, Toft P. Long-term psychological effects of a no-sedation protocol in critically ill patients. *Crit. Care* 2011;15:R293.
- [28] Schweickert W, Pohlman M, Pohlman A, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009;373(9678):1874–82.
- [29] Ely E, Inouye S, Bernard G, et al. Delirium in mechanically ventilated patients. Validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA* 2001;286:2703–10.
- [30] Gelinas C, Fillion L, Puntillo K, Viens C, Fortier M. Validation of the critical-care pain observation tool in adult patients. *Am J Crit Care* 2006;15:420–7.
- [31] Olsen H., Nedergaard H., Strom T. et al. Nonsedation or light sedation in critically ill, mechanically ventilated patients. *NEJM*. doi: 10.1056/NEJMoa1906759.
- [32] Trial Group SRLF. Impact of oversedation prevention in ventilated critically ill patients: a randomised trial – the AWARE Study. *Ann. Intens. Care* 2018;8:93.