Journal of Clinical Anesthesia 97 (2024) 111506

Contents lists available at ScienceDirect

Journal of Clinical Anesthesia

journal homepage: www.elsevier.com/locate/jclinane

Original Contribution

A first assessment of the safe brain initiative care bundle for addressing postoperative delirium in the postanesthesia care unit

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HIGHLIGHTS

- Data was collected for 18,697 adult patients for a quality-improvement initiative implementing 18 care recommendations.
- A significant reduction in postoperative delirium risk was observed for 19 months after initiating the care bundle.
- Patients with postoperative delirium in the postanesthesia unit stayed nearly twice as long in the hospital.
- General anesthesia and surgical duration over one hour were significant risk factors for postoperative delirium.
- Postoperative delirium was observed in all adult age groups, with peak incidence in both younger and older adults.

ARTICLE INFO

Keywords:
Anesthesia
Real-world data
Perioperative care
Postoperative delirium
Patient-reported outcomes
Precision medicine

ABSTRACT

Background: Postoperative delirium (POD) following surgery is a prevalent and distressing condition associated with adverse patient outcomes and an increased healthcare burden.
Objectives: To assess the effectiveness of the Safe Brain Initiative care bundle (SBI-CB) in reducing POD in the postanesthesia care unit (PACU).
Design: A multicenter, quality-improvement initiative with retrospective analysis of collected data.
Setting: The study was conducted in the operating rooms and postanesthesia care units (PACUs) of four hospitals across Denmark and Turkey.

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https://doi.org/10.1016/j.jclinane.2024.111506
Received 26 January 2024; Received in revised form 27 May 2024; Accepted 29 May 2024
Available online 6 July 2024

Patients: The convenience sample of patients were aged ≥18 years, scheduled for surgery, and could communicate verbally. Age, sex, preoperative delirium, and the American Society for Anesthesiology physical status classification were used in statistical methods to control for potential confounding influences.
Intervention: The SBI-CB, 18 delirium-reducing recommendations aligned with international guidelines. The intervention included patient education, staff training, coordination meetings across centers, and a dashboard for the monitoring of outcomes in the PACU.
Main outcome measures: The primary outcome was the POD trend in the PACU during implementation months, assessed through Nu-DESC screening at up to three time points in the PACU. We also examined the length of hospital stay.
Results: Data were collected from 18,697 adult patients across four hospitals. Initial POD incidence in the PACU after the first three months was 16.36% across all sites ($n = 1021$). POD in the PACU was observed across all age groups, with peak incidence in younger (18–35 years) and older (>75 years) patients. General anesthesia and longer surgical duration (>1 h) were identified as significant risk factors for POD in the PACU. Matched patients who experienced POD in the PACU had longer stays in hospital, with a mean increase from 35 to 69 h ($p < 0.001$). Implementation of the SBI-CB was associated with a decreased risk of POD in the PACU for each month of SBI-CB implementation (adjusted odds ratio 0.96, 95% confidence interval: [0.94, 0.97], $p < 0.001$).
Conclusions: The presented pragmatic implementation of a multidisciplinary care bundle, encompassing pre-, intra-, and postoperative measures alongside outcome monitoring, has the potential to significantly reduce the incidence of POD in the PACU. Improved patient outcomes may be achieved for general surgical departments with patient cohorts not typically considered at risk for developing POD.
Trial Registration: Clinicaltrials.gov, identifier NCT05765162.

1. Introduction

Postoperative delirium (POD) is a common and distressing complication following surgery. Its incidence ranges from 15% to 53% in older patients and with an incidence of POD in the PACU between 2% to 32% in adults. [1–6] POD is associated with adverse outcomes and increased healthcare burden. [7–9] Beyond immediate hospitalization, delirium has also been associated with long-term cognitive decline and mortality. [10,11] Preventing POD is crucial to improving perioperative care and overall patient outcomes, encompassing physical and psychological well-being and functional recovery.

In 2018, Evered and colleagues published unifying nomenclature of cognitive changes affecting patients after anesthesia and surgery. They defined POD as when symptoms present immediately after anesthesia until one week post procedure or until discharge, whichever comes first. [12] POD presents as a set of fluctuating disturbances in attention and cognition, with previous data indicating that the majority of patients who developed POD were already identified by screening for delirium in the postanesthesia care unit (PACU). [9,13–15] Although some patients may emerge smoothly from anesthesia and be lucid in the PACU, developing POD at a later stage, it is important to note that a lucid period after anesthesia is no longer required for diagnosing POD and what was previously called “emergence delirium” currently falls under the umbrella term POD. [12] A diagnosis of POD, however, should only be made in the absence of other known contributors and the continued presence of drugs that act on the central nervous system used for anesthesia and sedation should be viewed as a possible contributor to symptoms of delirium immediately after surgery. [16] But since these early symptoms can later transition to POD without a lucid period, all patients should not leave the PACU without being screened for delirium symptoms and starting treatment for those diagnosed with POD. [7,17]

Since the pathogenesis of POD is considered to be multifactorial, it is reasonable to infer that its prevention should consist of a bundle of measures. [11] In recent years, perioperative care bundles have emerged as a promising approach to standardize and optimize perioperative care, resulting in decreased risk and severity of POD. [18–24]. These studies, however, mostly involve a small number of patients; the effects of the POD care bundles in large and generalized patient cohorts are yet to be investigated.

In its 2023 update, the European Society of Anaesthesiology and Intensive Care Medicine guidelines on POD in adults endorsed the implementation of perioperative care bundles. [17] They strongly recommend the clinical use of multimodal, non-pharmacological interventions, including the sharing of POD screening results and discussing preventive measures among the entire care team. [17]

The Safe Brain Initiative (SBI) presents a systematic, department-wide approach, which includes the implementation of a perioperative care bundle (SBI-CB) designed to diligently monitor and enhance patient-reported outcome measures (PROMs) across the entire surgical process. This approach led by anesthesiologists aims to not only address perioperative neurocognitive disorders such as POD in the PACU but also emphasizes the critical role of perioperative care in improving POD. The SBI-CB is comprehensive and integrates education and staff awareness alongside a set of guideline-supported protocols and practices to optimize patients' well-being before, during, and after surgery. Although methods for POD prevention typically focus only on elderly populations, the SBI-CB is a department-wide approach that is applied to all surgical patients in the perioperative period and intends to improve care protocols for all patients.

Given the framework of the SBI-CB as a quality-improvement initiative implemented at department level, the aim of this large, multicenter, retrospective cohort study was to present initial findings of the effect of the SBI-CB on POD incidence in the PACU over time, shedding light on its real-world effectiveness. Risk factors for POD in the PACU across diverse populations and settings and its association with time in hospital were also assessed.

2. Methods

2.1. Study design and setting

This first real-world data cohort study examines the effectiveness of the SBI-CB regarding the development of POD in the PACU in adult patients undergoing elective surgery. The study was conducted across four diverse hospitals in Denmark and Turkey: Næstved Hospital (Site 1) in Denmark; Ringsted Sygehus (Site 2) in Denmark; Hospital of Nykøbing Falster (Site 3) in Denmark and Ankara Ibni Sina University Hospital (Site 4) in Turkey. Data presented in this work was collected between February 1st 2017, and October 14th 2022. The clinical protocol of the study was registered at clinicaltrials.gov NCT05765162. The trial settings closely resemble the usual care settings, as the study is conducted within four diverse hospitals, reflecting the variability and diversity of clinical practice. A general description of each participating hospital is given in the Supplementary Material.

Implementing the SBI-CB at each hospital can be considered a quality-improvement initiative in accordance with the evidence-based

manual for implementing guidelines published online by the Danish Health Authority. [25] Reporting follows Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies. [26]

2.2. Patients

Adult patients presenting to the participating hospitals for elective surgery were included for data collection and analysis. We included those able to communicate verbally, which encompassed patients who could be delirious before surgery if they were verbally responsive. Patients younger than 18 years, those admitted with emergencies, and those who could not participate due to a regional language barrier or who were cognitively unable to give verbal consent were excluded.

2.3. Ethics

Permission for the collection of patients' data was granted by the Danish Data Protection Agency, Region Zealand, with the following approval numbers: REG-041-2017 (Site 1), REG-041-2017 (Site 2), and REG-117-2019 (Site 3). For Site 4, implementing the SBI-CB was accepted as a quality development initiative and approved by the Human Research Ethics Committee of Ankara University Faculty of Medicine (ethical approval number: I2–88-21). As quality-improvement initiatives, no written patient consent was required for data collection at all sites (recorded in the Danish Scientific Ethics Committees in the case file J.No. 17–000048).

2.4. The Safe Brain Initiative care bundle

The SBI provides a patient-centered, anesthesia care bundle to decrease the gap between research and current practice. The care bundle consists of 18 evidence-based recommendations listed in Table 1, indicated in international guidelines and selected based on delineation, reproducibility, and feasibility. [7,17]

The introduction of the SBI-CB enabled tailored implementation at each hospital. The autonomy granted to individual hospitals in how they monitor and promote adherence to the intervention is aligned with their established standards of usual care. Patient monitoring and data collection in the SBI-CB were designed to be integrated into routine clinical practice, allowing for pragmatic implementation.

Each site introduced the SBI-CB through comprehensive staff training with educational materials provided to enhance understanding of the SBI-CB rationale and practical application. Each site designated a senior coordinator who was in regular exchange with the other SBI-CB senior coordinators. The senior coordinator regularly monitored SBI-CB outcomes and progress by using an online digital dashboard of aggregate results that is provided by the SBI.

2.5. Data collection

Data were collected by the anesthesia team (doctors, anesthesia nurses and PACU nurses) on working days (Monday to Friday) during daytime shifts. Data collection evolved gradually from a paper case report form (p-CRF) to a digital case report form (e-CRF), with ongoing adjustment and inclusion of additional parameters. Collected data were stored in accordance with European data protection requirements, and access was limited to authorized persons using the clinical trial management system EasyTrial (https://www.easytrial.net/). Medical staff transferred data collected in p-CRF format to the digital database manually.

PROMs were measured using a simple-to-use numeric rating scale (NRS). [27,28] Delirium POD in the PACU was measured using the Nursing Delirium Screening Scale (Nu-DESC). [29–32]. The Nu-DESC has previously been compared to other systems and recommended as the preferred screening system for POD in the PACU. [2] Nu-DESC

Table 1
The SBI-CB 18 core recommendations and how they were measured.*

Item	Recommendation	Measurement recorded
1	Regular screening for delirium.	Nu-DESC screening at time points T1–T4.
2.	Regular PROM screening for postoperative pain and subsequent adjustment to treatment.	Patient-reported NRS scale at time points T2–T4.
3.	Reduce PONV by regarding patient's risk level, employing antiemetic medications, regular PROM screening for PONV and subsequent treatment adjustment.	Patient-reported NRS scale at time points T2–T4.
4.	Reduce preoperative fluid-fasting time to two hours through patient education, staff training, and decrease dehydration by providing a drink during recovery and regular PROM screening for thirst.	Measure time from last drink (>200 mL) during patient preparation for surgery and whether drink was provided.
5	Ensure patients are properly oriented in space and time. Provide hearing aids, dentures, glasses, wall clocks and verbal orientation.	Measure whether a patient needs and was given hearing aids/dentures/glasses.
6.	Communication: use assistive devices and aids and foster an open dialogue.	NR
7.	Minimize noise levels in the perioperative environment to promote a calmer and more comfortable patient atmosphere.	NR
8.	Consider the patient's circadian rhythm and offer earplugs and eyeshades, reduce noise and light to support the natural sleep-wake cycle during recovery.	NR
9.	Address and treat pain before surgery.	Record whether preemptive analgesia was given.
10.	Patient-centered clinical practice: increase patient engagement and integrate patient preferences, needs, and values in care decisions.	NR
11.	Use nociceptive monitoring and continuous analgesia techniques, such as remifentanil, to effectively manage pain.	Record whether nociception monitoring and continuous analgesia were used.
12.	Reduce anti-cholinergic load by promoting alternatives, minimizing dosages of anticholinergic medication, and creating awareness of associated risks.	NR
13.	Monitor the patient's brain activity using electroencephalography (EEG) to detect and prevent adverse neurological events during medium to deep sedation.	Record whether EEG was used.
14.	Use capnography in sedated patients to ensure adequate ventilation and detect possible complications.	Record whether capnography was used.
15.	Reduce stress through staff training in relaxation measures and regular PROM screening for stress.	Patient-reported NRS scale at time points T1–T4.
16.	Measure and address patient satisfaction with their treatment.	Patient-reported NRS scale before leaving the PACU.
17.	Reduce anxiety through staff training in communication and distraction techniques, regular PROM screening for anxiety, and patient education and/or the offer of counseling services.	Patient-reported NRS scale at time points T1–T4.
18.	Monitor and control temperature to prevent hypothermia or hyperthermia and promote patient comfort.	Record whether intra-operative temperature monitoring was used.

* Sites implementing the recommendation. EEG, electroencephalography; NR, not recorded in the data collection; NRS, numeric rating scale from 0 (no problem) to 10 (extreme problem); Nu-DESC, Nursing Delirium Screening Scale; PONV, postoperative nausea and vomiting; PACU, postanesthesia care unit, PROM, patient-reported outcome; SBI-CB, Safe Brain Initiative care bundle; time points: during patient preparation for surgery (T1), arrival in the recovery room (T2), at discharge from the recovery room (T3), highest value estimated throughout recovery room stay measured at discharge from the recovery room (T4).

assesses five categories: disorientation, inappropriate behavior, inappropriate communication, illusions/hallucinations, and psychomotor retardation, where symptoms in each category are scored from 0 (absent) to 2 (severe). [29,31] A patient was considered positive for delirium if the total score was greater or equal to two. [29,31].

We collected Nu-DESC and PROMs at four pre-defined time points: baseline during patient preparation for surgery (T1), PACU arrival (T2), and PACU discharge. At PACU discharge, the patient was assessed for the current state (T3), and worst value during their entire PACU stay (T4).

Patient characteristics collected were age, sex, ASA category (American Society of Anesthesiology physical status classification system, ranging from I to V). Procedure characteristics included surgical time (hours) and whether the patient received general anesthesia.

2.6. Outcomes

The primary outcome was the presence of POD during a patient's stay in the PACU. It is important to note that no formal DSM-5 diagnosis of POD was recorded; a patient was assumed to have POD in the PACU if their Nu-DESC score was equal to or greater than two at any measurement time point (T2–T4). It is important to note, however, that this estimate of POD does include patients that are experiencing symptoms of delirium due to the persistent effects of the drugs used for anesthesia and sedation. In addition, Nu-DESC evaluations were not consistently performed at all time points T2–T4. If data were unavailable for all measurements at T2–T4, POD in the PACU was classified as "NA". POD incidence in the PACU was measured per month since the SBI was initiated per site to analyze POD in the PACU trends over the implementation period. The pragmatic study approach that utilizes the Nu-DESC screening technique instead of applying formal POD diagnosis criteria ensures that the primary outcome closely mirrors what would occur in typical clinical situations when screening all patients for POD in the PACU, enhancing the study's relevance to real-world healthcare. [33] The secondary outcome was the hospital length of stay (LOS), in hours.

2.7. Statistics

All analyses and data visualizations were created using R Statistical Software (v4.3; R Core Team 2023). A comprehensive descriptive statistical analysis summarized patient and procedural characteristics. The proportion of missing data was reported for all data. Categorical variables were expressed as patient counts and proportions. Continuous variables were reported as means and standard deviations and hospital LOS was also reported as medians with interquartile ranges (IQRs). Independent of the statistical test, $p < 0.05$ was considered statistically significant.

Multivariable logistic and linear regressions were used to assess the determinants of POD risk and monthly incidence. The logistic regression outcome was whether a patient developed POD in the PACU, and the linear regression outcome was the monthly POD incidence for patients treated within one calendar month. Patients with missing data in more than one predictor variable were excluded, and the percentage of

Table 2
Characteristics and outcomes used in analyses.

Data item	Site 1		Site 2		Site 3		Site 4	
	Value	% NA	Value	% NA	Value	% NA	Value	% NA
Number of patients, N	12,783	–	2121	–	1458	–	2335	–
Data collection, start–end dates	01.02.17–31.05.21	–	09.01.18–23.03.20	–	14.01.21–10.10.22	–	04.03.21–14.10.22	–
Month count*, N	52	–	25	–	19	–	20	–
Patient characteristics								
Sex, % female	50.00	0.03	99.15	0.00	60.56	0.00	47.81	0.04
Age, mean [SD]	62.59 [15.79]	0.00	60.64 [12.91]	0.00	57.72 [17.58]	0.00	50.94 [15.91]	0.00
18–35, N (%)	1058 (8.28)	–	69 (3.25)	–	199 (13.64)	–	439 (18.80)	–
36–55, N (%)	2478 (19.39)	–	702 (33.10)	–	410 (28.12)	–	922 (39.49)	–
56–75, N (%)	6660 (52.10)	–	1073 (50.59)	–	607 (41.63)	–	844 (36.15)	–
>75, N (%)	2587 (20.24)	–	277 (13.06)	–	242 (16.60)	–	130 (5.57)	–
ASA category	–	3.16	–	1.79	–	12.14	–	2.83
ASA I, N (%)	2416 (19.52)	–	185 (8.88)	–	267 (20.84)	–	881 (38.83)	–
ASA II, N (%)	7103 (57.38)	–	1257 (60.35)	–	761 (59.41)	–	1218 (53.68)	–
ASA III, N (%)	2806 (22.67)	–	640 (30.73)	–	240 (18.74)	–	169 (7.45)	–
ASA IV, N (%)	39 (0.32)	–	1 (0.05)	–	13 (1.01)	–	1 (0.04)	–
ASA V, N (%)	15 (0.00)	–	0 (0.00)	–	0 (0.00)	–	0 (0.00)	–
Preoperative delirium %	1.46	4.52	0.19	0.94	1.71	6.17	1.67	0.60
Procedure characteristics								
Surgical time, h, mean [SD]	0.84 [0.56]	3.29	1.43 [0.80]	8.44	0.96 [0.60]	42.11	2.45 [1.69]	7.15
[0–1] h, N	9102 (73.63)	–	728 (37.49)	–	509 (60.31)	–	388 (17.90)	–
(1–2] h, N	2896 (23.43)	–	836 (43.05)	–	290 (34.36)	–	633 (29.20)	–
>2 h, N	364 (2.94)	–	378 (19.46)	–	45 (5.33)	–	1147 (52.20)	–
Anesthesia type, % general	54.88	2.42	87.74	2.22	69.75	13.72	87.02	2.53
Outcomes								
POD, %	6.13	3.81	1.29	1.04	5.19	7.54	11.26	0.34
Hospital stay, h, mean [SD]	31.39 [106.95]	13.96	21.82 [29.96]	1.70	33.59 [84.11]	0.21	78.47 [107.93]	2.32
Hospital stay, h, median [IQR]	28.28 [25.60]		12.03 [20.77]		7.12 [22.41]		48.06 [72.01]	

* Please note that the month count is less than the total number of months between start and end dates for Sites 2 and 3 because for some months in between, no data was collected. ASA, American Society of Anesthesiologists Physical Classification System; EEG, electroencephalogram; h, hours; IQR, interquartile range; N, number of patients; NA, not available (missing data); POD, postoperative delirium; SD, standard deviation.

missing values across sites was evaluated (patients with missing values in surgery time from Site 3 were excluded due to 34.0% of missing data). The remaining missing values, accounting for 1.12% of the dataset, were imputed on a per-site basis using predictive mean matching imputation, logistic regression imputation or proportional odds logistic regression imputation, as appropriate to the variable type, pooling over 100 imputations and ten iterations as implemented in R's mice package. [34] Predictor variables were binned as shown in Table 2, and the models were expressed as POD event (logistic regression) or POD monthly incidence (linear regression) with age, sex, ASA category, preoperative delirium, surgical time, anesthesia, SBI month (since the SBI-CB was initiated) used as parametric, confounding variables. We used binomial generalized linear model (glm) and linear model (lm) functions from the R stats package for the logistic and linear regressions, respectively (included in R base 4.3). ASA categories as predictor variables (ASA I–II and III–V) were chosen to have enough patients in each category (see patient numbers in Table 2). Patients were grouped by calendar month (by date of surgery), starting the month count immediately after the SBI-CB was initiated until data collection ended for each site independently; full months where no data were collected in between start and end dates were excluded. Given the varied data-collection periods across sites, multisite analyses were aligned to the shortest collection period available (first 19 months) to ensure consistency and avoid site over-representation. Model evaluations, including areas under the receiver operating curves and likelihood-ratio tests, are presented in the Supplementary Material.

Summaries of delirium (positive Nu-DESC scores) were calculated for the different time points separately (T1, T2, and T3) and combined time points (T1–T4 and T2–T4), stratified by age groups. Their uncertainty was estimated using the normal approximation method of the binomial 95% confidence intervals.

Patients with missing or zero-hour hospital LOS and those positive for preoperative delirium were excluded from the hospital LOS analyses, the latter due to the possibility that these patients may have pre-existing cognitive decline, e.g., dementia. Patients were then matched by age, sex, ASA, surgery duration, and use of general anesthesia to address their confounding effects using the R MatchIT package that implements methods from Ho and colleagues. [35] Mean and median hospital LOS, stratified by patients with and without POD in the PACU, were compared across matched groups. Differences in means were tested using the Wilcoxon rank-sum test. Age and site stratifications for hospital LOS looking at differences in POD incidence in the PACU were also performed, using the same age categorization as for the regression analyses.

3. Results

3.1. Patient demographics and differences between hospital sites

Patients were extracted from the original combined database, resulting in a total of 18,697 patients at four sites. After excluding patients with missing data, there remained 17,129 patients for analyzing POD trends in the PACU and 15,895 patients for analyzing hospital LOS. The numbers of patients with reasons for exclusion are given in a flow chart in the Supplementary material.

To estimate the baseline POD, we report the POD incidence in the PACU after only the first three months of SBI-CB data collection. The average initial incidence of POD in the PACU across all sites was 16.36% ($N = 1021$). On a per-site basis, Site 1 and 4 had higher a incidence at 18.56% ($N = 361$) and 18.70% ($N = 508$), respectively. Site 2 and 3 had much lower rates of 3.03% ($N = 33$) and 3.36% ($N = 119$), respectively. In the final three months of data collection, Site 1 had an incidence of 10.46% ($N = 258$), Site 2 had 1.12% ($N = 89$), Site 3 had 3.08% ($N = 65$), and Site 4 had 9.01% ($N = 111$). The demographics at each site were substantially different (Table 2), with Site 2 predominantly including females with ASA II, which does not represent a patient group that is considered at risk for developing POD and, therefore, the incidences should not be compared between presented sites but any intra-site reduction is of value. [6,7,17]

For the entire respective data-collection periods, the mean hospital LOS ranged from 21 to 34 h in Denmark (Site 1–3) and was 78.47 h in Turkey (Site 4) with the longer hospital stay in Turkey reflecting their differing healthcare system. The median hospital LOS over the entire time period is also reported in Table 2. Total hospital LOS was approximately only 1–2 days on average, with medians lower than means signaling that most patients had short hospital LOS with long stays of individuals increasing the overall mean. Many surgeries were performed without general anesthesia and a large proportion of surgeries were shorter than an hour. The data reflects that a substantial proportion of surgeries were of lower complexity, especially for Site 1, with almost 74% of surgeries in the short category (up to one hour). Since the SBI-CB is a department-wide approach integrated into routine care, it is applied to all patients scheduled for surgery, including low-complexity and ambulatory procedures.

3.2. Risk factors for POD in the PACU

Logistic regression was performed to estimate risk factors for POD in the PACU. The model used a combined dataset including sites 1, 3, and 4. 6603 patients were included from the first 19 months after SBI-CB initiation (ensuring the same number of months overall to decrease site bias). Data from Site 2 were not included in further analyses due to a non-converging site-specific logistic regression model (see detailed results and model metrics per site in the Supplementary Material), however, the data were retained for analysis of hospital LOS.

After controlling for confounders (site, age, sex, ASA, preoperative delirium, surgery duration, and use of general anesthesia), our analysis underscored the SBI's pronounced protective role against POD in the PACU, with the duration of SBI-CB implementation consistently emerging as a pivotal factor. Specifically, the adjusted odds ratio (aOR) for each month of implementation was aOR 0.96 (95% confidence interval (CI): [0.94, 0.97], p-value <0.001) and the aOR for the cumulated 19 months from SBI-CB initiation for the combined sites was 0.44 (95% CI: [0.42, 0.47], p-value <0.001), see Table 3.

Table 3
Logistic regression model results including patients from combined*** sites to estimate risk factors for developing POD.

Predictor variable	aOR	95% CI		P-value*
		Lower	Upper	
Month count [1–19], per-month effect	0.96	0.94	0.97	<0.001
Cumulative effect after 19 months	0.44	0.42	0.47	<0.001
Age [reference: 18–35 years]				
Age 36–55 years	0.76	0.58	0.98	0.035
Age 56–75 years	0.90	0.70	1.16	0.41 (NS)
Age > 75 years	1.39	1.00	1.92	0.048
ASA III–V vs ASA I–II	1.26	0.99	1.61	0.058 (NS)
General anesthesia	6.69	4.85	9.21	<0.001
Preoperative delirium	12.38	8.31	18.43	<0.001
Site [reference: Site 1]				
Site 3	0.39	0.28	0.54	<0.001
Site 4	0.45	0.34	0.60	<0.001
Sex (male vs female)	0.84	0.71	1.01	0.06 (NS)
Surgical time [reference: 0–1 h]				
(1–2] h	1.48	1.16	1.88	0.001
>2 h	3.01	2.22	4.07	<0.001

* N = 6603 patients were included in the logistic regression model; Sites 1, 3, and 4 were combined, whereas Site 2 was excluded because the logistic model failed to fit this data due to an extremely low reported incidence of POD (Supplementary Material).

** A p-value < 0.05 is considered significant and reported as < 0.001 if too small. ASA, American Society for Anesthesiology physical status classification system; CI, confidence interval; h, hours; NS, not significant (p ≥ 0.05); aOR, odds ratio adjusted for confounders stated in the methods.

In Table 4, we split the incidence of measured delirium by timepoint and by age. Only 1.41% of patients had preoperative delirium in total, which reduced to only 0.61% of patients who were measured positively for delirium both pre- and postoperatively. The latter are patients who likely included those with dementia but this was not confirmed. Given that not all patients with preoperative delirium had delirium post-operatively, these patients were not excluded but preoperative delirium was added to the regressions to adjust for its confounding effect on delirium in the PACU, which is technically not POD for patients with dementia or other previously existing cognitive difficulties. We also identified a significant increase in the incidence of POD associated with general anesthesia (aOR 6.69, 95% CI: [4.85, 9.21], $p < 0.001$). Other anticipated determinants of POD in the PACU may include age, surgeries exceeding one hour, and preoperative delirium (Table 3).

When stratifying the incidence of POD in the PACU across age groups, we identified a U-shaped distribution, where the incidence for 18–35 and > 75 year-old patients were higher than for those between 36 and 75 (Table 4). Across all age categories, POD in the PACU was still prevalent, with incidence ranging between 5 and 9% over the whole time period that the SBI-CB was implemented.

3.3. Analysis of monthly POD incidence in the PACU

To further assess the influence of the SBI-CB protocol on monthly POD incidence in the PACU, we implemented a multivariate linear regression using the same confounding factors (month count after SBI initiation, age, ASA category, general anesthesia used, presence of pre-operative delirium, site, sex, and surgical time) as in the logistic regression detailed in Table 3. Analyzing the combined dataset from sites 1, 3, and 4, we identified a significant reduction in POD incidence in the PACU over 19 months (−0.50, 95% CI: [−0.51, −0.49], $p < 0.001$). Site 1 exhibited a pronounced decline in POD incidence in the PACU with a coefficient for the SBI-CB month count of −0.19 (95% CI: [−0.19, −0.19], $p < 0.001$). Notably, at Site 1, where data spanned a longer 50-month period, monthly POD incidence in the PACU continued to decrease to below 5% beyond the 19 months reported in the combined analysis. Site 3 showed a less pronounced reduction with a coefficient of −0.07 (95% CI: [−0.12, −0.02], $p = 0.006$), having a lower initial POD incidence in the PACU. Site 4 demonstrated the most substantial decrease, with a coefficient of −0.68 (95% CI: [−0.70, −0.65], $p < 0.001$). For Site 2, characterized by female patients undergoing low-risk surgeries, the model's performance was subpar (see Supplementary material), reinforcing its earlier exclusion from combined analyses (see Supplementary Material). Fig. 1 plots the coefficient for the months-since-SBI-CB-initiated parameter and the respective monthly incidence of POD in the PACU: here, the trend of POD incidence is visualized over time while adjusting for the confounding factors (age, sex, ASA category, presence of preoperative delirium, surgical time, and use of general anesthesia). All regression model results can be found in the Supplementary Materials.

3.4. Length of stay in hospital

We further explored the association between POD in the PACU and the duration of total hospital LOS. To control for confounding factors (age, sex, ASA, surgery duration, and use of general anesthesia), results are reported for matched patient cohorts, including matching details, patient numbers, and a comparison to unmatched outcomes in the Supplementary material. When comparing matched patients with and without POD in the PACU (Fig. 2), hospital LOS decreased on average across all sites: from 45.43 to 30.45 h for Site 1 ($p = 0.0025$), from 22.84 to 21.82 h for Site 2 (not significant), from 47.53 to 31.10 for Site 3 ($p = 0.0051$), and from 134.23 to 79.85 h for Site 4 ($p < 0.0001$). When combining data for all sites, patients with POD in the PACU had an average of 33.63 h longer stay relative to those without POD in the PACU (68.90 vs. 35.27 h, $p < 0.0001$), which corresponds to a 48.8% reduction overall. Site 1 presented incongruence between the mean and median hospital stay. Specifically, those without POD in the PACU had a median stay of 28.37 (interquartile range: 25.62) hours, whereas the group with POD in the PACU had a median stay of 25.37 (26.58) days. A breakdown by age is provided in the Supplementary Material. When combining data from all sites and after patient matching (Supplementary Fig. 9), the difference in hospital LOS was consistently significantly longer in patients with POD in the PACU across all age groups. For three of the four sites, hospital LOS was significantly different across all age groups and the difference was more pronounced for patients 18–55 years in comparison to older patients at Site 1. Site 2 showed the same trend without reaching statistical significance due to limited data. Since patient demographics, procedures, and underlying healthcare systems differ between sites, only the relative increase in hospital LOS is of interest and not the absolute number of hours.

4. Discussion

In this large, multicenter retrospective study, we present evidence of the clinical value of the SBI-CB in effectively reducing the incidence of POD in the PACU in real-world, clinical-practice settings in the framework of a quality-improvement initiative. Our study took a pragmatic approach, integrating with the complexities and challenges of routine clinical care. Results show a compelling inverse correlation between the duration of SBI-CB implementation and the incidence of positive screening results for POD in the PACU. After 19 months since SBI-CB initiation, the observed reduction in the cumulative adjusted odds ratio was 0.44 (95% CI [0.42, 0.47], p-value <0.001) in the combined data of three hospital sites. Although it is important to note here that the observed reduction is unlikely to be linear with the greatest effect expected after SBI-CB initiation that diminishes over time.

In line with previous studies, patients who did experience POD in the

Table 4
Incidence of delirium at different timepoints stratified by age in all sites.

Age	Preoperative delirium, % [95% CI]	Delirium at PACU arrival, % [95% CI]	Delirium at PACU discharge, % [95% CI]	Delirium in the PACU*, % [95% CI]	Pre- and postoperative delirium, % [95% CI]
All ages	1.41 [1.24–1.58]	6.00 [5.65–6.35]	1.00 [0.86–1.15]	6.16 [5.81–6.51]	0.61 [0.49–0.72]
18–35 years	1.19 [0.67–1.71]	8.64 [7.29–9.98]	0.97 [0.50–1.44]	8.76 [7.42–10.10]	0.55 [0.19–0.90]
36–55 years	0.76 [0.50–1.02]	5.85 [5.15–6.55]	0.75 [0.49–1.01]	6.07 [5.37–6.78]	0.47 [0.26–0.67]
56–75 years	1.37 [1.12–1.61]	5.01 [4.56–5.47]	0.88 [0.68–1.08]	5.17 [4.71–5.63]	0.51 [0.36–0.66]
>75 years	2.57 [2.01–3.12]	7.62 [6.67–8.58]	1.76 [1.28–2.24]	7.72 [6.77–8.67]	1.12 [0.74–1.50]

* This is the POD in the PACU used throughout this work unless specified differently; it is positive if any T2, T3, or T4 are positive. The uncertainty is estimated by using the normal approximation method for the binomial 95% confidence interval. Please find numbers of patients and the proportion of missing data per category in the Supplementary material. CI, confidence interval, PACU, postanesthesia care unit.

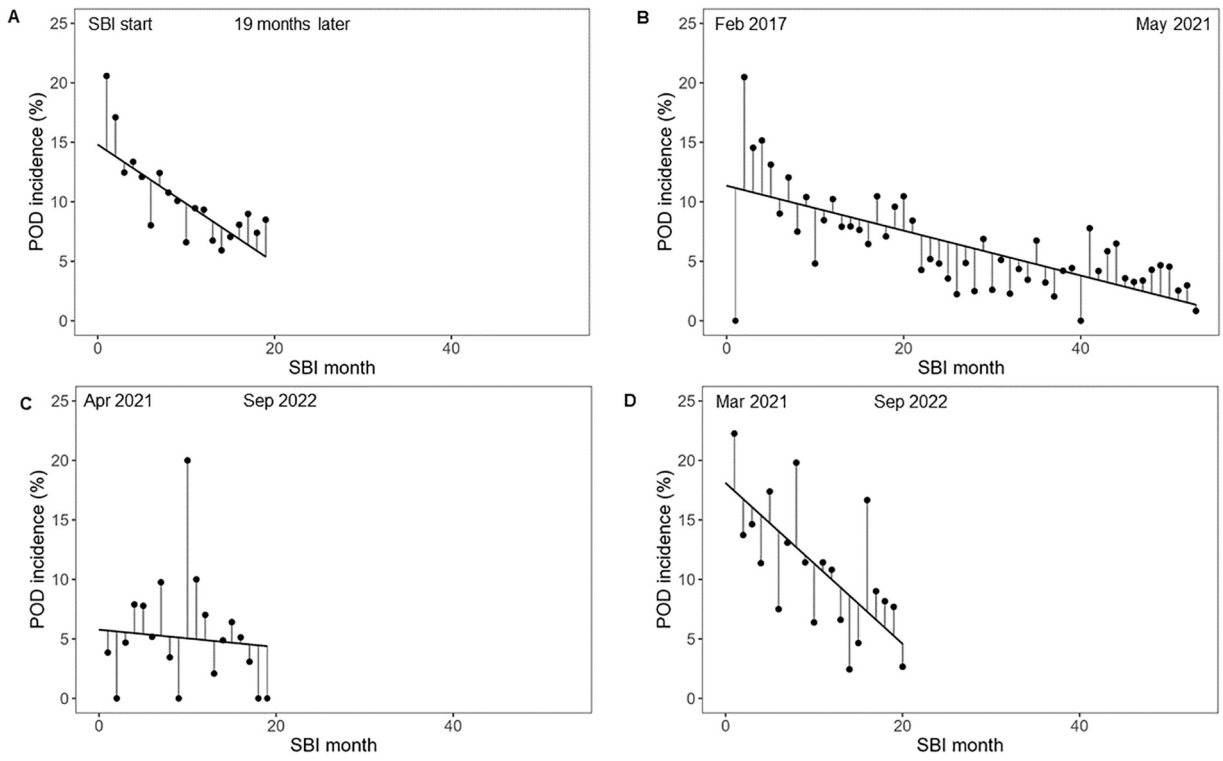

Fig. 1. Trend of monthly POD incidence since the SBI care bundle was initiated. Actual POD incidence (black dots) and the coefficient gradient for the month count variable with model residuals indicating the model fit to the data per month are shown separately for (A) combined patients from Sites 1, 3, and 4; (B) patients from Site 1; (C) patients from Site 3; (D) patients from Site 4. The month-count coefficient effect size was: (A) -0.50 [95% confidence interval − 0.51, −0.49], *p*-value <0.001; (B) -0.19 [−0.19, −0.19], p-value <0.001); (C) -0.07 [−0.12, −0.02], p-value = 0.006); and (D) -0.68 [−0.70, −0.65], p-value <0.001).

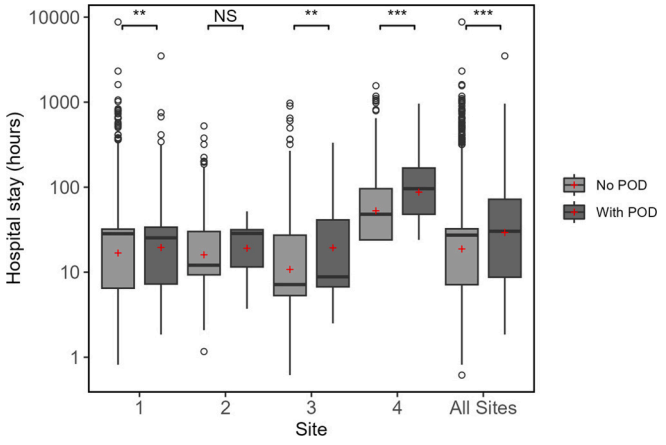

Fig. 2. Boxplot depicting the duration of hospital stay stratified by POD across different sites. Patient matching was performed to control for patient and procedure confounders (site, age, sex, ASA surgery duration, and use of general anesthesia); patients with preoperative delirium were excluded from the analysis. Each box delineates the interquartile range, median (horizontal black line) and mean (red cross). Whiskers extend to data points that fall within 1.5 times the interquartile range. Circles depict outliers. Significance: NS ($p > 0.05$), * ($p < 0.05$), ** ($p < 0.01$), *** ($p < 0.001$); Wilcoxon rank-sum test. All Sites includes patients from all four hospital sites combined. Mean results and total number of patients for each group are given in the Supplementary Material. The combined results assessed 13,492 patients without and 732 patients with POD in the PACU after patient matching. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

PACU had consistently longer hospital stays. [9,36] This was demonstrated across all participating sites and age groups; an observation still measurable after adjusting for age, sex, ASA category, surgery duration, and the use of general anesthesia as confounding factors. It is important to note that these results were achieved on average over all adult ages (≥18 years) with varying patient demographics, for a diverse collection of surgery types, and including a substantial number of low-complexity surgeries. An incongruence between mean and median hospital LOS was observed for Site 1 only where the median was in fact lower for patients with POD in the PACU in contrast to the mean, pointing to a subpopulation that had shorter hospital stays with delirium. This incongruence could not be resolved given the study data but Site 1 did have the shortest surgery times with the lowest percentage of general anesthesia.

Overall, our findings support the effectiveness of comprehensive care-bundle strategies in preventing POD from developing in the PACU, aligning with previously published care-bundle interventions. [18–24]. Results emphasize the importance of evidence-based, multidisciplinary interventions to enhance patient care and safety, while also contributing valuable, real-world evidence to further cement existing perioperative care guidelines and recommendations. [17]

The department-wide integration of the SBI-CB into routine care may foster an ongoing culture of safety and awareness for continuous improvement. Healthcare providers and institutions likely underwent a learning curve. Over time, healthcare teams may have refined their protocols and staff training, resulting in improved adherence to the various components of the SBI-CB. Regular data collection and review may have played a pivotal role in driving improvement, which would be interesting to evaluate in future studies. Healthcare teams may have used this data to identify areas for enhancement and target interventions more effectively. We also acknowledge that changes in staff composition, turnover, or leadership within healthcare institutions could affect care delivery consistency and future adherence to the SBI-CB. Additionally, external factors, such as shifts in patient demographics or

changes in surgical practices, may influence rates of POD. Therefore, ongoing monitoring and adaptation to internal and external influences, and regular education and training are essential to ensure all staff members are well-versed in the SBI-CB's protocols.

Contrary to evidence identified in previous guidelines, our real-world dataset revealed a clear and significant association between general anesthesia and increased risk of developing POD in the PACU while adjusting for the confounding effects of surgical duration, ASA category, age, and sex. [7,17] Although this is possibly an effect of including what was previously considered “emergence delirium”. [12] Most of the patients with a positive POD screening result were experiencing symptoms of delirium at PACU arrival when the persistent effects of drugs used during anesthesia and sedation are likely a contributing factor. [16] This finding merits further investigation in a multicenter, randomized controlled trial including a follow-up including formal diagnoses of POD in the week after surgery.

Our analysis also reaffirms the purported link between surgical duration and POD risk. [7,37–40] The development of POD is multifactorial, with predisposing and precipitating factors with surgical duration acting as a precipitating factor. Surgical duration represents an approximation for both the complexity or magnitude of surgery and the amount of time a patient is exposed to anesthesia/sedation, blood loss, pain, and inflammation; the exact duration of anesthesia was not recorded.

Our data also show that both younger (18–35 years) and older (>75 years) patients had the highest incidence of delirium in the PACU and that for all age groups, delirium was similarly higher at PACU arrival than at discharge. In previous work, younger and older patients were also identified as at risk for inadequate emergence after anesthesia. [9,36] Indeed, younger patients had a higher risk for a hypoactive emergence that was associated with an increased hospital LOS. [36] In another study, abnormal Nu-DESC scores at PACU arrival were associated with POD observed in the ward. [15] Therefore, because SBI-CB is integrated into routine perioperative care and thus applied to all patients—not just the elderly as is typical for most interventions for POD prevention—it allows for potentially improving cognitive function in the PACU for all surgical patients.

Patients who experienced POD in the PACU had longer mean hospital stays across all sites, aligning with existing research that emphasizes the diverse consequences of POD, including increased resource utilization and delayed recovery. [38,39,41,42] The hospital cost of POD was not a focus of our study but has been reported in systematic literature reviews to be USD 806 to USD 24,509. [43,44] Taking the lowest value (USD 806, original study EUR 532.80), a hospital performing 1000 surgeries a month would be expected to prevent 442 cases of POD in the PACU over 19 months; a cost saving of EUR 235,498 (if they performed as per the aggregated data reported here). As a nursing hour in Denmark has been reported to cost EUR 33, [45] the cost saving from POD would be expected to cover the cost of having a nurse manage the SBI, which is estimated to take 20 h per week, giving a total cost over 19 months of EUR 54,340. It is possible that additional costs to initiate the SBI are required, for example purchase of monitors or for staff training. The exact economic implications regarding hospital resources both used in running the SBI and saved through process optimization and improved patient outcomes are planned and remain to be quantified in future studies.

Our study has several strengths. The multicentric approach involving hospitals in Denmark and Turkey contributes to the generalizability of the findings by encompassing diverse patient populations and clinical practices. This diversity minimizes the risk of selection bias, enhancing the study's external validity. Furthermore, the longitudinal data collection allows for an evaluation of trends and the long-term impact of the SBI-CB. Additionally, the study's real-world pragmatic design closely emulates routine clinical care settings, strengthening its findings' relevance and practical significance for everyday healthcare practices. Lastly, the study's large sample size empowers it with substantial statistical power, enabling the detection of meaningful differences in outcomes and strengthening the overall validity of the outcomes. It may be confusing that the presented retrospective analyses were applied to a varying number of patients and/or sites, depending on the analysis. In general, we always maximized the number of patients that could be used for a given analysis and excluded only those patients that could not be assessed for statistical reasons. For example, patients may have been excluded due to missing data in required data categories or Site 2 was excluded from combined regression analyses because the regression model on this data failed to converge. Patients from Site 2 could be used for the hospital LOS analysis, however. We also would like to note that excluding sites or patient populations based on their demographics could have skewed results to a more positive outcome, therefore, this was avoided.

There are also critical limitations to consider. Given that the SBI-CB is an intervention primarily focused on the perioperative period, we did not have data available about a patient experiencing delirium after PACU discharge or whether the patient experienced a lucid interval. We acknowledge that the investigation of delirium in the PACU does not fully capture the entire spectrum of POD. In particular, critically ill patients transferred directly to intensive care (at high risk for POD) or patients developing POD for the first time in the ward will have remained undetected in this analysis. This work involved a large quality-improvement undertaking that integrated into routine, daily care with the assessment of thousands of patients in the surgical department. It was not feasible to include a follow-up of one week after surgery and to ensure that a formal diagnosis of POD was made for all patients in this context. In addition, the Nu-DESC screening was not always performed at the same time point for all patients, which may limit comparability between them. A patient was considered positive for POD if they experienced symptoms of delirium at any time point during their PACU stay. Therefore, presented risk factors when using this POD estimate measure should be confirmed by studies using formal DSM or ICD criteria for diagnosis. The decrease in measured incidence over time and their association with longer hospital stays, however, should be unaffected by this limitation. The presented patient cohort was generally of lower risk, including a substantial proportion of patients with short operations and outpatient treatments, such that reported POD incidence may be lower than in other clinical settings.

The absence of a control group and specifically the lack of randomization and blinding in our study could have introduced potential biases, including bias stemming from personnel motivation and inter-site competition, a factor that is inherent to any quality-improvement undertaking. In the context of this work, the SBI-CB involved the standardized assessment of perioperative changes in patients' neurocognition, fluid-fasting times, anxiety, thirst, etc. None of the participating sites had this in place beforehand, which is why the SBI-CB was introduced. In this context, exclusively monitoring POD before SBI-CB implementation was not easily performed, but availability of POD incidence as a control before SBI-CB implementation would have improved the statistical evaluation of the data. This study took place over multiple years and was likely impacted by the COVID-19 pandemic. Changes in standard of care over time and changes to resources or medication use during the COVID-19 pandemic were not accounted for when considering reductions of POD in the PACU over time. These effects were partly mitigated by the fact that data collection occurred at different, partially non-overlapping times between 2017 and 2022 (Table 2) and sites were therefore not impacted by time effects uniformly. Data collection in real-world clinical settings is error-prone, with missing data for many variables and the transition from paper-based to digital data collection may have introduced further inconsistencies or errors. Finally, we acknowledge the risk of selection, recall, and observer bias inherent in retrospective studies. To mitigate these, we included a large, diverse cohort from multiple centers, used standardized protocols, objective measures like Nu-DESC, and trained staff.

5. Conclusion

This multicenter, retrospective observational study demonstrates that implementing the SBI-CB, a perioperative care bundle, may significantly reduce POD incidence in the PACU. In the combined data, mean hospital stays were twice as long for patients with POD in the PACU than those without. These findings highlight the potential of structured care-bundle implementation for better patient outcomes. Future research should focus on implementation strategies and the broader impact of the SBI-CB on outcomes, resource use, and cost-effectiveness.

Assistance

Thank you to Fabian Distler for feedback and a quality review of the data analysis and for re-running the code for data analysis.

Financial support

SS, MC, and FP are Coreva Scientific GmbH & Co. KG employees that received consultancy fees for performing, analyzing, and communicating the work from the Hospital of Nykøbing Falster. FMR received an unrestricted research grant from Medtronic Inc. Medtronic had no scientific input, and no benefits to their products are presented in this work.

Presentation

Parts of this work were presented at the ASA annual meeting 2023 in San Francisco and the ESAIC annual meeting 2023 in Glasgow.

Author contributions

FMR, KJ, BCM, LAE, PRK, and WB were involved in the conception or design of the SBI-CB. SS and MC were involved in the conception or design of the statistical analyses. BCM, KJ, FMR, BCM, and DHP acquired the data. KJ and FMR were involved in data analysis during SBI-CB monitoring. MC, FP, and SS performed the data analyses presented in the manuscript. JBE, FB, FMR, WB, KJ, BCM, SS, and MC were involved in interpretation of data. SS, MC, JBE, WB, EDR, FMR, KJ, BCM, LAE, and SK were involved in writing. All authors revised and approved the manuscript. BCM and KJ would like to be recognized as joint first authors and JBE and FMR as joint last authors, as equal contributors to this work.

CRediT authorship contribution statement

Basak Ceyda Meco: Writing – review & editing, Writing – original draft, Project administration, Data curation, Conceptualization. **Karina Jakobsen:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Data curation. **Edoardo De Robertis:** Writing – review & editing, Visualization, Validation, Supervision. **Wolfgang Buhre:** Writing – review & editing, Supervision, Methodology, Investigation. **Neslihan Alkış:** Supervision, Resources, Project administration, Data curation. **Peter Roy Kirkegaard:** Resources, Project administration, Methodology, Data curation. **Daniel Hägi-Pedersen:** Project administration, Investigation, Formal analysis, Data curation, Conceptualization. **Florian Bubser:** Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Susanne Koch:** Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Lisbeth A. Evered:** Writing – review & editing, Visualization, Supervision, Formal analysis. **Sita J. Saunders:** Software, Project administration, Investigation, Formal analysis. **Marco Caterino:** Software, Resources, Methodology, Investigation, Formal analysis. **Francesca Paolini:** Writing – review & editing, Validation, Resources. **Joana Berger-Estilita:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology. **Finn M. Radtke:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

SS, MC, and FP are employed at Coreva Scientific GmbH & Co. KG that received compensation for their work. JBE is a member of the ESAIC eLearning and Examinations Committee. She also has received support for travel expenses from Medtronic. WB is the President Elect of the European Society of Anaesthesiology and Intensive Care Medicine (ESAIC) and received fees for a lecture from BD Diagnostics. WB is also the coordinating investigator of the PHOENICS/THEHYS study Fresenius Kabi and ESAIC. EDR received honoraria from Baxter, Fresenius Kabi, MSD, Fisher & Paykel, Drager, and GE health. FMR received unrestricted research and educational grants from Medtronic and is active on the advisory board of GE health. DHP, BCM, FB, KJ, LAE, PRK, NA, and SK claim no competing interests.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Finn M Radtke reports financial support was provided by Medtronic Inc. Finn M Radtke reports a relationship with Coreva Scientific GmbH und Co KG that includes: non-financial support. SS, MC, and FP are Coreva Scientific GmbH & Co. KG employees that received consultancy fees for performing, analyzing, and communicating the work from the Hospital of Nykøbing Falster. FMR received an unrestricted research grant from Medtronic Inc. Medtronic had no scientific input, and no benefits to their products are presented in this work. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinane.2024.111506.

References

[1] Bilotta F, Russo G, Verrengia M, Sportelli A, Foti L, Villa G, et al. Systematic review of clinical evidence on postoperative delirium: literature search of original studies based on validated diagnostic scales. J Anesth Anal Critic Care 2021;1. https://doi.org/10.1186/s44158-021-00021-8.

[2] Hernandez BA, Lindroth H, Rowley P, Boncyk C, Raz A, Gaskell A, et al. Post-anaesthesia care unit delirium: incidence, risk factors and associated adverse outcomes. Br J Anaesth 2017;119:288–90. https://doi.org/10.1093/bja/aex197.

[3] Hesse S, Kreuzer M, Hight D, Gaskell A, Devari P, Singh D, et al. Association of electroencephalogram trajectories during emergence from anaesthesia with delirium in the postanaesthesia care unit: an early sign of postoperative complications. Br J Anaesth 2019;122:622–34. https://doi.org/10.1016/j.bja.2018.09.016.

[4] Marcantonio ER. Postoperative delirium: a 76-year-old woman with delirium following surgery. JAMA 2012;308:73–81. https://doi.org/10.1001/jama.2012.6857.

[5] Swarbrick CJ, Partridge JSL. Evidence-based strategies to reduce the incidence of postoperative delirium: a narrative review. Anaesthesia 2022;77(Suppl. 1):92–101. https://doi.org/10.1111/anae.15607.

[6] He M, Zhu Z, Jiang M, Liu X, Wu R, Zhou J, et al. Risk factors for postanesthetic emergence delirium in adults: a systematic review and meta-analysis. J Neurosurg Anesthesiol 2023. https://doi.org/10.1097/ANA.0000000000000942.

[7] Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Audisio R, Borozdina A, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. Eur J Anaesthesiol 2017;34:192–214. https://doi.org/10.1097/EJA.0000000000000594.

[8] Gou RY, Hshieh TT, Marcantonio ER, Cooper Z, Jones RN, Travison TG, et al. One-year medicare costs associated with delirium in older patients undergoing major elective surgery. JAMA Surg 2021;156:430–42. https://doi.org/10.1001/jamasurg.2020.7260.

[9] Zhang Y, He S-T, Nie B, Li X-Y, Wang D-X. Emergence delirium is associated with increased postoperative delirium in elderly: a prospective observational study. J Anesth 2020;34:675–87. https://doi.org/10.1007/s00540-020-02805-8.

[10] Goldberg TE, Chen C, Wang Y, Jung E, Swanson A, Ing C, et al. Association of delirium with long-term cognitive decline: a meta-analysis. JAMA Neurol 2020;77:1373–81. https://doi.org/10.1001/jamaneurol.2020.2273.
[11] Inouye SK, Westendorp RGJ, Saczynski JS. Delirium in elderly people. Lancet 2014;383:911–22. https://doi.org/10.1016/S0140-6736(13)60688-1.
[12] Evered L, Silbert B, Knopman DS, Scott DA, DeKosky ST, Rasmussen LS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery-2018. Anesth Analg 2018;127:1189–95. https://doi.org/10.1213/ANE.0000000000003634.
[13] Radtke FM, Franck M, Schust S, Boehme L, Pascher A, Bail HJ, et al. A comparison of three scores to screen for delirium on the surgical ward. World J Surg 2010;34:487–94. https://doi.org/10.1007/s00268-009-0376-9.
[14] Radtke FM, Franck M, MacGuill M, Seeling M, Lütz A, Westhoff S, et al. Duration of fluid fasting and choice of analgesic are modifiable factors for early postoperative delirium. Eur J Anaesthesiol 2010;27:411–6. https://doi.org/10.1097/EJA.0b013e3283335cee.
[15] Stukenberg S, Franck M, Spies CD, Neuner B, Myers I, Radtke FM. How can postoperative delirium be predicted in advance? A secondary analysis comparing three methods of early assessment in elderly patients. Minerva Anestesiol 2016;82:751–9.
[16] Almuzayyen HA, Chowdhury T, Alghamdi AS. Postoperative cognitive recovery and prevention of postoperative cognitive complications in the elderly patient. Saudi J Anaesth 2023;17:550–6. https://doi.org/10.4103/sja.sja_529_23.
[17] Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Spies CD, Aceto P, et al. Update of the European Society of Anaesthesiology and Intensive Care Medicine evidence-based and consensus-based guideline on postoperative delirium in adult patients. Eur J Anaesthesiol 2023. https://doi.org/10.1097/EJA.0000000000001876.
[18] Kratz T, Heinrich M, Schlauß E, Diefenbacher A. Preventing postoperative delirium. Dtsch Arztebl Int 2015;112:289–96. https://doi.org/10.3238/arztebl.2015.0289.
[19] Milisen K, Foreman MD, Abraham IL, de Geest S, Godderis J, Vandermeulen E, et al. A nurse-led interdisciplinary intervention program for delirium in elderly hip-fracture patients. J Am Geriatr Soc 2001;49:523–32. https://doi.org/10.1046/j.1532-5415.2001.49109.x.
[20] Mudge AM, Maussen C, Duncan J, Denaro CP. Improving quality of delirium care in a general medical service with established interdisciplinary care: a controlled trial. Intern Med J 2013;43:270–7. https://doi.org/10.1111/j.1445-5994.2012.02840.x.
[21] Chuan A, Zhao L, Tillekeratne N, Alani S, Middleton PM, Harris IA, et al. The effect of a multidisciplinary care bundle on the incidence of delirium after hip fracture surgery: a quality improvement study. Anaesthesia 2020;75:63–71. https://doi.org/10.1111/anae.14840.
[22] Peden CJ, Miller TR, Deiner SG, Eckenhoff RG, Fleisher LA. Improving perioperative brain health: an expert consensus review of key actions for the perioperative care team. Br J Anaesth 2021;126:423–32. https://doi.org/10.1016/j.bja.2020.10.037.
[23] Inouye SK, Bogardus ST, Charpentier PA, Leo-Summers L, Acampora D, Holford TR, et al. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med 1999;340:669–76. https://doi.org/10.1056/NEJM199903043400901.
[24] Inouye SK, Robinson T, Blaum C, Busby-Whitehead J, Boustani M, Chalian A, et al. Postoperative delirium in older adults: best practice statement from the American Geriatrics Society. J Am Coll Surg 2015;220. https://doi.org/10.1016/j.jamcollsurg.2014.10.019. 136–48.e1.
[25] Danish Health Authority. Implementation manual for national clinical guidelines. 2023. https://sundhedsstyrelsen.dk/da/viden/Sundhedsvaesen/NKR-og-NKA/Implementeringshaandbog (accessed 28 April 2023).
[26] Cuschieri S. The STROBE guidelines. Saudi J Anaesth 2019;13:S31–4. https://doi.org/10.4103/sja.SJA_543_18.
[27] Lee MK, Schalet BD, Cella D, Yost KJ, Dueck AC, Novotny PJ, et al. Establishing a common metric for patient-reported outcomes in cancer patients: linking patient reported outcomes measurement information system (PROMIS), numerical rating scale, and patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). J Patient Rep Outcomes 2020;4:106. https://doi.org/10.1186/s41687-020-00271-0.
[28] Renskers L, van Uden RJJC, Huis AMP, Rongen SAA, Teerenstra S, van Riel PLCM. Comparison of the construct validity and reproducibility of four different types of patient-reported outcome measures (PROMs) in patients with rheumatoid arthritis. Clin Rheumatol 2018;37:3191–9. https://doi.org/10.1007/s10067-018-4285-x.
[29] Gaudreau J-D, Gagnon P, Harel F, Tremblay A, Roy M-A. Fast, systematic, and continuous delirium assessment in hospitalized patients: the nursing delirium screening scale. J Pain Symptom Manage 2005;29:368–75. https://doi.org/10.1016/j.jpainsymman.2004.07.009.
[30] Hägi-Pedersen D, Thybo KH, Holgersen TH, Jensen JJ, Gaudreau J-D, Radtke FM. Nu-DESC DK: the Danish version of the nursing delirium screening scale (nu-DESC). BMC Nurs 2017;16:75. https://doi.org/10.1186/s12912-017-0271-x.
[31] Heinrich TW, Kato H, Emanuel C, Denson S. Improving the validity of nurse-based delirium screening: a head-to-head comparison of nursing delirium-screening scale and short confusion assessment method. Psychosomatics 2019;60:172–8. https://doi.org/10.1016/j.psym.2018.09.002.
[32] Winter A, Steurer MP, Dullenkopf A. Postoperative delirium assessed by post anesthesia care unit staff utilizing the nursing delirium screening scale: a prospective observational study of 1000 patients in a single Swiss institution. BMC Anesthesiol 2015;15:184. https://doi.org/10.1186/s12871-015-0168-8.
[33] Ford I, Norrie J. Pragmatic trials. N Engl J Med 2016;375:454–63. https://doi.org/10.1056/NEJMra1510059.
[34] van Buuren S, Groothuis-Oudshoorn K. Mice multivariate imputation by chained equations in R. J Stat Softw 2011;45. https://doi.org/10.18637/jss.v045.i03.
[35] Ho DE, Imai K, King G, Stuart EA. Matching as nonparametric preprocessing for reducing model dependence in parametric causal inference. Polit Anal 2007;15:199–236. https://doi.org/10.1093/pan/mpl013.
[36] Radtke FM, Franck M, Hagemann L, Seeling M, Wernecke KD, Spies CD. Risk factors for inadequate emergence after anesthesia: emergence delirium and hypoactive emergence. Minerva Anestesiol 2010;76:394–403.
[37] Eschweiler GW, Czornik M, Herrmann ML, Knauer YP, Forkavets O, von Arnim CAF, et al. Presurgical screening improves risk prediction for delirium in elective surgery of older patients: the PAWEL RISK study. Front Aging Neurosci 2021;13:679933. https://doi.org/10.3389/fnagi.2021.679933.
[38] Kirfel A, Guttenthaler V, Mayr A, Coburn M, Menzenbach J, Wittmann M. Postoperative delirium is an independent factor influencing the length of stay of elderly patients in the intensive care unit and in hospital. J Anesth 2022;36:341–8. https://doi.org/10.1007/s00540-022-03049-4.
[39] Bramley P, McArthur K, Blayney A, McCullagh I. Risk factors for postoperative delirium: an umbrella review of systematic reviews. Int J Surg 2021;93:106063. https://doi.org/10.1016/j.ijsu.2021.106063.
[40] Wittmann M, Kirfel A, Jossen D, Mayr A, Menzenbach J. The impact of perioperative and predisposing risk factors on the development of postoperative delirium and a possible gender difference. Geriatrics (Basel) 2022;7. https://doi.org/10.3390/geriatrics7030065.
[41] Wiinholdt D, Eriksen SAN, Harms LB, Dahl JB, Meyhoff CS. Inadequate emergence after non-cardiac surgery-a prospective observational study in 1000 patients. Acta Anaesthesiol Scand 2019;63:1137–42. https://doi.org/10.1111/aas.13420.
[42] Austin CA, O'Gorman T, Stern E, Emmett D, Stürmer T, Carson S, et al. Association between postoperative delirium and long-term cognitive function after major nonemergent surgery. JAMA Surg 2019;154:328–34. https://doi.org/10.1001/jamasurg.2018.5093.
[43] Kinchin I, Mitchell E, Agar M, Trépel D. The economic cost of delirium: a systematic review and quality assessment. Alzheimers Dement 2021;17:1026–41. https://doi.org/10.1002/alz.12262.
[44] Mosharaf MP, Alam K, Ralph N, Gow J. Hospital costs of post-operative delirium: a systematic review. J Perioperat Nursing 2022;35. https://doi.org/10.26550/2209-1092.1165.
[45] Bring C, Kruse M, Ankarfeldt MZ, Brünés N, Pedersen M, Petersen J, et al. Post-hospital medical respite care for homeless people in Denmark: a randomized controlled trial and cost-utility analysis. BMC Health Serv Res 2020;20:508. https://doi.org/10.1186/s12913-020-05358-4.