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Implementation of a multiprofessional, multicomponent delirium management guideline in two intensive care units, and its effect on patient outcomes and nurse workload: a pre-post design retrospective cohort study

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Summary

AIM OF THE STUDY: Delirium is a frequent intensive care unit (ICU) complication, affecting 26% to 80% of ICU patients, often with serious consequences. This study aimed to evaluate the effectiveness, costs and benefits of following a standardised multiprofessional, multicomponent delirium guideline on eight outcomes: delirium prevalence and duration, lengths of stay in ICU and hospital, in-hospital mortality, duration of mechanical ventilation, and cost and nursing hours per case. It also aimed to explore the associations of delirium with length of ICU stay, length of hospital stay and duration of mechanical ventilation.

METHODS: This retrospective cohort study used a pre-post design. ICU patients in an historical control group (n = 1608) who received standard ICU care were compared with a postintervention group (n = 1684) who received standardised delirium management – delirium risk identification, preventive measures, screening and treatment – with regard to eight outcomes. The delirium management guideline was developed and implemented in 2012 by a group of experts from the study hospital. As appropriate, descriptive statistics and multivariate, multilevel models were used to compare the two groups and to explore the association between delirium occurrence and the selected outcomes.

RESULTS: Twelve percent of the 1608 historical controls and 20% of the 1684 postintervention patients were diagnosed with delirium according to the ICD-10 delirium diagnosis codes. Patients being treated for heart disease, and those with septic shock, ARDS, renal insufficiency (acute or chronic), older age and higher numbers of comorbidities were significantly more likely to develop delirium during their stay. Multivariate models comparing the historical controls with the post intervention group indicated significant differences in delirium period prevalence (odds ratio 1.68, 95% confidence interval [CI] 1.38–2.06; p <0.001), length of stay in the ICU (time ratio [TR] 0.94, CI 0.89–1.00; p = 0.048), cost per case (median difference 3.83, CI 0.54–7.11; p = 0.023) and duration of mechanical ventilation (TR 0.84, CI 0.77–0.92; p <0.001). The observed differences in the other four outcomes – in-hospital mortality, delirium duration, length of stay in the hospital, and nursing hours per case – were not significant. Delirium was a significant predictor for prolonged duration of mechanical ventilation and for both ICU and hospital stay.

CONCLUSION: Standardised delirium management, specifically delirium screening, supports timely detection of delirium in ICU patients. Increased awareness of delirium after the implementation of standardised multiprofessional, multicomponent management leads to increased therapeutic attention, a prolongation of ICU stay and increased costs, but with no influence on mortality.

Introduction

Delirium – a sudden, acute deterioration of mental status – is a frequent complication in intensive care unit (ICU) patients. Its reported prevalence and incidence rates in ICU patients vary between 26% and 80% [1–3]. Delirium is linked with negative patient and economic outcomes. Compared with non-delirious ICU patients, the delirious are six times more likely to develop further complications, especially acute respiratory distress syndrome (ARDS), pneumonia, pulmonary oedema or cardiac arrhythmias [4, 5] and to need skilled care, i.e., rehabilitation, after discharge [4, 5]. Further, they are two to three times as likely to die [4–8], stay on average seven to eight days longer in the ICU [4, 5, 8], and require an average of seven more days of mechanical ventilation [4, 5]. The reported additional cost attributable to delirium ranges from EUR ~1,200 (USD ~1300) in a German study [8] to USD 9014 in a USA study [9]. Assuming that 721,600 to 2,263,200 ICU patients develop delirium each year in the US, this corresponds to additional annual healthcare costs ranging from USD 6.6 billion to 20.4 billion [9]. A recent Swiss study calculated that the cost in cases involving delirium was twice as high as in those that did not (respectively CHF 40,000 vs 16,662) [10].

Delirium can result from a multitude of factors. Predisposing and precipitating factors such as age (≥65 years), previous delirium, male gender, dementia, comorbidities such as heart failure, visual and/or auditory impairment, psychoactive medication, and regular consumption of tobacco or alcohol. In ICU patients, these factors commonly converge with intraoperative events and serious conditions such as polytrauma, sepsis, shock, infection, stroke, requirement for mechanical support or transcutaneous pacing, antiarrhythmic agents or use of therapeutic hypothermia, for example after a cardiac arrest [1–3, 11, 12]. The resulting accumulation of predisposing risk factors and precipitators greatly increases the risk of delirium.

For appropriate delirium management, early identification of relevant risk factors is crucial. With this in mind, standardised delirium management routines can increase recognition of at-risk patients [13]. In recent years, several single and multicomponent delirium management guidelines have been developed. Of these, multiprofessional, multicomponent delirium practice guidelines focusing on the prevention, screening, diagnosis and treatment of delirium offer the most effective strategy to minimise delirium rates, related symptoms, associated prolonged length of stay (LOS) and overall in-patient costs [13–16]. However, evidence supporting the benefits and efficiency of such multicomponent guidelines is rare. To date, research has focused predominantly on techniques to improve delirium screening – to help identify delirium onset or delirium-risk patient, and / or to measure the benefits of pharmacological treatments [13] [17]. Some researchers have simultaneously applied multiple guidelines dealing, for example, with pain, agitation and delirium, and studied the effects on selected outcomes [14, 18].

Noting the high frequency of delirium in ICU patients in the study hospital (a Swiss tertiary teaching hospital), a multiprofessional quality improvement and practice development project was launched in 2011 to improve the prevention, early recognition and appropriate treatment of delirium in hospitalised patients. In the context of this project, an interprofessional project team developed, implemented and evaluated an evidence-based multiprofessional, multicomponent delirium management guideline [10, 19–21].

This study is part of a larger delirium health service programme Delir-Path. The aim of this study was to evaluate the effectiveness, costs and benefits of the implemented standardised delirium management guidelines by comparing ICU patients in an historical control (preintervention) group with those in a postintervention group, with regard to eight outcomes: LOS in the ICU and hospital, in-hospital mortality, delirium prevalence and duration, duration of mechanical ventilation, cost and nursing hours per case. We hypothesised that (1) the postintervention group's LOS in the ICU and (2) in hospital would be shorter, (3) in-hospital mortality and (4) delirium prevalence rates would be lower, (5) delirium duration in those who developed a delirium would be shorter, (6) the duration of mechanical ventilation would be shorter and (7) the cost and (8) nursing hours per case would be lower; further, we hypothesised that delirium in surgical ICU patients would be significantly associated with (9) longer ICU LOS, (10) hospital LOS and (11) mechanical ventilation duration.

Materials and methods

Study design, setting and sampling

In this single centre cohort study, which used a pre-post design to allow evaluation of the effects efficiency and costs of the implemented standardised delirium management guideline, an historical group of 1608 patients treated in two surgical ICUs (before implementation of this guideline) were compared with a postintervention group of 1684 ICU patients treated in the same ICUs after the introduction of the guideline, with reference to the selected outcomes. All eligible patients consecutively admitted to a cardio-surgical ICU (ICU 1) and a thoracic-visceral-surgical ICU (ICU 2) from 1 January 1 to 31 December 2013 were assigned to the postintervention group. Those admit-

ABBREVIATIONS:

ARDS	acute respiratory distress syndrome
CHOP	CH (Swiss) Operation Classification
FSO	Federal Statistical Office
LEP	Leistungserfassung in der Pflege, (care performance and process documentation)
LOS	length of stay
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10th Revision
ICDSC	Intensive Care Delirium Screening Checklist
ICU	intensive care unit
MDSi	minimal data set ICU
OR	odds ratio
RASS	Richmond Agitation Sedation Scale
SAPS II	Simplified Acute Physiology Score II
TR	time ratio

ted to the same ICUs between January and December 2011 were assigned to the historical control group. To be included, patients had to fulfil the following criteria: (1) adult (age ≥18 years) ICU patient and (2) no history of abuse of medication or other substances, except possibly alcohol.

Intervention and standard care

In addition to standard ICU care, patients in the postintervention group received standardised multiprofessional delirium management following the chosen guideline. This guideline includes four main components:

1. **Delirium prevention** – by identifying the patients at risk based on defined precipitating or predisposing causes and risk factors, and then, as far as possible, treating the causes and risk factors with appropriate non-pharmacological and pharmacological interventions. This might include the prevention of nosocomial infections in patients with central venous or urinary catheters, communication and orientation support for patients with functional, visual and/or hearing impairment, and amelioration of stress and/or disturbed sleep-wake cycles.

2. **Delirium screening** via instruments specifically designed either for patients in emergency/ICU contexts (e.g., the Richmond Agitation Sedation Scale [RASS] or Intensive Care Delirium Screening Checklist [ICDSC]), or for patients in regular hospital care (e.g., the Confusion Assessment Method [CAM]). ICU patients with RASS scores of −2 to +4 are screened once per shift with the ICDSC [22].

3. **Defined delirium diagnostics**, including laboratory tests, and neurological and/or psychiatric consultations.

4. For patients with delirium, **defined counter-measures** including non-pharmacological and pharmacological interventions to treat the causes of delirium. These are comparable to those used to prevent delirium and its accompanying symptoms.

The professional and interprofessional responsibilities for each component are colour-coded for quick access.

As a first step, the delirium management guideline was implemented in nine units (seven non-ICUs, two ICUs) using practice development and quality improvement strategies including specific interprofessional clinic/unit teams. In addition to implementing the guideline, this team supported the nurses and physicians, answered related questions, and delivered a delirium education programme of professional and interprofessional lectures and eLearning components. Using techniques including feedback loops, they also monitored delirium prevalence rates, numbers of patients screened for delirium and numbers gauged at risk for a delirium. The benefits and efficiency of the guideline were evaluated after 6 months. Because of the indicated benefits, the standardised delirium management system was implemented in all in-patient units using the same implementation strategies [10, 19–21].

Patients in the control group (hospitalised in the study hospital before the implementation of the standardised delirium management) received standard care. This included all necessary standard intensive care therapy (e.g., ventilation, pharmacological treatment to stabilise cardiac and/or cir-

culatory disturbances and, if necessary, sedation management), with any non-standardised delirium prevention, diagnosis and treatment in use at that time.

Primary and secondary outcomes

The three primary outcomes were: (1) LOS (in days) in the ICU: the number of days the patient was hospitalised in the ICU; (2) LOS in hospital: the number of days the patient was hospitalised in the hospital, including the ICU stay; (3) in-hospital mortality: the percentage of patients who died at any time during hospitalisation, either in the ICU or elsewhere.

The five secondary outcomes were: (1) ICU period prevalence of delirium: the percentage of patients who, at any time during their ICU stay, were delirious, based on an ICD-10 delirium diagnosis (F050, F051, F058, F059, F104) and additionally (in the postintervention group) on one or more ICDSC assessment scores (ICDSC ≥4; (2) delirium duration: the number of days a postintervention group patient, who was screened with the ICDSC, spent in a delirium (ICDSC Score ≥4); (3) duration of mechanical ventilation: the number of days the patient spent on a ventilator; (4) costs: the sum of all individual health care costs and overheads per case; and (5) nursing workload: the number of hours spent per case on direct patient care.

Primary and secondary outcomes were adjusted for the following confounders (delirium risk factors, delirium causes): gender (male/female), age, septic shock, ARDS, acute renal insufficiency, chronic renal insufficiency, hepatic insufficiency (based on ICD-10 classification), sedation (based on RASS data [23]), Simplified Acute Physiology Score II (SAPS II) [24] and Charlson comorbidity index [25]. Further variables used were medical diagnosis (ICD-10), treatment/interventions: heart intervention such as cardiovascular surgery, heart valves, heart septum surgeries, neurological intervention such as computed tomography, fluoroscopy or sonography, injection of anaesthetic and analgesic into the spinal canal for pain therapy) codes of Swiss Operation (CHOP) classification [26], alcohol dependency (ICD-10; yes/no) and type of admission. The relevant data (on primary and secondary outcomes) were extracted from the following databases: Minimal Data Set ICU (MDSi) [27], Swiss Federal Statistical Office (FSO) data set [28], ICDSC Assessment data [22], Care Performance and Process Documentation (Leistungserfassung in der Pflege; LEP) [29].

Data analysis

Descriptive statistics (mean and ± standard deviation, median with 25% and 75% quartiles, or counts and percentage rates) were used to describe characteristics of the patients in the postintervention and control groups based on ten baseline values. ICD-10 diagnoses [30] and interventions were categorised into five groups (see table 1 below). Missing values were replaced with the normal value where appropriate (e.g., a patient with no alcohol abuse diagnosis was assumed not to abuse alcohol). We conducted a multivariate, multilevel analysis to explore the effect, efficiency and costs of the implemented standardised delirium management guideline with respect to the selected primary and secondary outcomes. In the crude and multivariate analysis, patients who stayed longer than 7 days in the ICU or 60

days in the hospital, who died in the ICU or were mechanically ventilated for longer than 48 hours were censored. Censoring was chosen for mechanical ventilation because the majority of patients were ventilated for less than 48 hours. The restricted mean LOS (95% CI) presented was also restricted with respect to 7- and 60-day boundaries. To compare the LOS duration of delirium and mechanical ventilation between the postintervention group and the historical control group, we used parametric survival models with accelerated failure time metrics. In-hospital mortality was compared using binomial generalised linear models, with delirium as a predictor. Delirium ICU and hospitalisation period prevalences were compared with logistic regression based on ICD-10 diagnoses [30] and ICDSC scores [19]. In the case of ICDSC scores the analysis was restricted to ICU 1, as only this unit had scores for both 2011 and 2013. We used quantile regression methods to analyse the highly skewed data regarding distributed costs and nursing hours per case, and binomial generalised linear models (logistic regressions) to analyse the association between delirium and in-hospital mortality. For these we present both parametrically modelled and Kaplan-Meier time-to-event curves. ICU LOS and mechanical ventilation duration were modelled using a gamma distribution. Hos-

pital LOS was modelled using log-logistic distribution, and delirium duration was modelled using a log-normal distribution. Distributions for these time-to-event models were selected based on the Akaike Information Criterion [31]. Statistical analyses were performed in Stata 13.0 and R 3.1.1. Figures were created in R 3.1.1 [32]. All tests presented use a two-tailed $\alpha = 0.05$.

Ethical considerations
This study (PB_2016-01264) was approved by the responsible ethics board of the Kantonale Ethikkommission des Kanton Zurich and carried out in accordance with the Declaration of Helsinki, taking into consideration local regulations and standards.

Results

Description of the postintervention and historical control groups
A total of 3496 patients (1620 in 2011, 1876 in 2013) were hospitalised following cardiac or thoracic visceral surgery in the two selected ICUs during the study periods. Based

Table 1: Baseline characteristics of the historical control group and postintervention group.

		Total (2011, 2013)	Historical control (2011)	After intervention (2013)	p-value
N/n		3292	1608	1684	
Gender female, n (%)		1025 (31%)	499 (31%)	526 (31%)	0.91
Age at admission (years), mean ± SD		61.8 ± 14.5	61.8 ± 14.4	61.8 ± 14.6	0.905
Admission planned, n (%)		2011 (61%)	976 (61%)	1035 (61%)	0.668
Alcohol abuse (ICD-10 codes), n (%)		94 (3%)	49 (3%)	45 (3%)	0.532
RASS at baseline, mean ± SD		−2.6 ± 1.9	−2.6 ± 1.9	−2.5 ± 1.9	0.440
SAPS II, mean ± SD		33.0 ± 17.0	31.1 ± 16.3	34.8 ± 17.4	<0.001
Charlson comorbidity index score, mean ± SD		2.5 ± 1.5	2.5 ± 1.5	2.4 ± 1.5	0.281
Interventions (MDSi), n (%)	Heart interventions	2038 (62%)	1004 (62%)	1034 (61%)	0.542
	Neurological interventions	12 (0%)	0 (0%)	12 (1%)	<0.001
Septic shock, n (%)		245 (7%)	109 (7%)	136 (8%)	0.163
ARDS, n (%)		87 (3%)	41 (3%)	46 (3%)	0.828
Acute renal insufficiency, n (%)		557 (17%)	261 (16%)	296 (18%)	0.307
Chronic renal insufficiency, n (%)		364 (11%)	179 (11%)	185 (11%)	0.912
Hepatic insufficiency, n (%)		64 (2%)	27 (2%)	37 (2%)	0.313
ICD-10 chapter N/n		3226	1601	1625	0.093
	Diseases of circulatory system, n (%)	1922 (60%)	916 (57%)	1006 (62%)	
	Neoplasms, n (%)	440 (14%)	233 (15%)	207 (13%)	
	Diseases of the digestive system, n (%)	200 (6%)	109 (7%)	91 (6%)	
	Diseases of respiratory system, n (%)	157 (5%)	80 (5%)	77(5%)	
	Other, n (%)	507 (16%)	263 (16%)	244 (15%)	
CHOP Main intervention N/n		3219	1600	1619	<0.001
	Heart (non-aorta), n (%)	1801 (56%)	892 (56%)	909 (56%)	
	Gastrointestinal tract, n (%)	407 (13%)	226 (14%)	181 (11%)	
	Respiratory system, n (%)	233 (7%)	130 (8%)	103 (6%)	
	Transplantation, n (%)	202 (6%)	112 (7%)	90 (6%)	
	Other, n (%)	576 (18%)	240 (15%)	336 (21%)	
CHOP Secondary intervention N/n		3205	1582	1623	<0.001
	Heart (non-aorta), n (%)	1391 (43%)	788 (50%)	603 (37%)	
	Gastrointestinal tract, n (%)	277 (9%)	175 (11%)	102 (6%)	
	Respiratory system, n (%)	175 (5%)	108 (7%)	67 (4%)	
	No intervention, n (%)	143 (4%)	4 (0%)	139 (9%)	
	Other, n (%)	1219 (38%)	507 (32%)	712 (44%)	

ARDS = acute respiratory distress syndrome; CHOP = Swiss Operation Classification; ICD-10 = International Statistical Classification of Diseases and Related Health Problems 10th Revision; MDSi = Minimal Data Set ICU; RASS = Richmond Agitation Sedation Scale; SAPS II = Simplified Acute Physiology Score II; SD = standard deviation

on the inclusion criteria listed above, 204 patients were excluded. Of the 3292 patients included, 1608 hospitalised in 2011 were assigned to the (historical) control group and 1684 hospitalised in 2013 were assigned to the postintervention group. Besides considerable differences in the SAPS II there were no notable differences between the two groups in terms of baseline characteristics (table 1).

Effectiveness, costs, benefits of the delirium management guideline

Delirium prevalence

Of the 3292 included patients, 534, 200 (12%) in the control group and 334 (21%) in the postintervention group received a delirium diagnosis based on their ICD-10 code. Based on the ICDSC scores ≥4, 816 patients, 214 in the control group and 602 in the postintervention group patients, were diagnosed as delirious. When interpreting these results, it should be borne in mind that in 2011 the ICDSC assessment was implemented in only one of the ICUs, in the context of a nursing thesis. However, in both the crude and the adjusted model, the changes in the delirium rate over time were significant (table 2).

In the crude model using ICD-10-based delirium diagnoses, compared with the overall sample, patients treated for heart disease, and those with septic shock, ARDS, acute kidney injury, chronic kidney disease, older age and higher numbers of comorbidities were significantly more likely to develop delirium during their stay. Neither female gender, neurological disease nor hepatic failure increased the probability of developing delirium. However, the crude model

using ICDSC-diagnosed delirium indicated that all the tested factors increased the probability of developing a delirious state (table 2). In both crude models, baseline RASS scores were significantly linked with delirium (table 2).

Delirium duration

Five hundred and seventy-two ICU patients identified as delirious (ICDSC ≥4) spent a mean of 3 days (3.56 in 2013, 3.29 in 2011) delirious. Changes in the time ratio for delirium duration before versus after introduction of the delirium management guideline were not significant in either the adjusted or the crude models (table 2). Compared with the other patients, those with septic shock, ARDS, acute kidney injury, chronic kidney disease or hepatic failure remained significantly longer in delirium, whereas those with heart disease had a significantly shorter mean duration. Gender, age, neurological or other interventions, baseline RASS level and number of comorbidities had no significant effect on delirium duration (table 2).

LOS in ICU and hospital

Patients typically stayed roughly 2.5 days in the ICU (2011: 2.48, 2013: 2.56) with overall stays of 17 days (in 2011) and 18 days (in 2013) in the hospital (table 3). The crude model indicated that postintervention patients stayed on average significantly longer in the ICU, but not significantly longer in the hospital than the historical controls (table 3). Adjusting for potential confounders confirmed these findings and their significance (fig. 1).

Table 2: Crude odds ratios for delirium incidence based on ICD-10 or ICDSC, and delirium duration.

Variable		Delirium incidence ICD-10			Delirium incidence ICDSC			Delirium duration ICDSC			
		n/N	OR (95% CI)	p-value	n/N	OR (95% CI)	p-value	n	Mean (95% CI)	TR (95% CI)	p-value
Overall		534/3292			816/3292			816	3.7 (3.5–4.0)		
Year 2011		200/1608			214/1608			214	3.2 (2.9–3.6)		
Year 2013		334/1684	1.8 (1.4–2.1)	<0.001	602/1684	3.6 (3.0–4.3)	<0.001	602	3.9 (3.7–4.2)	1.2 (1.1–1.4)	0.006
Gender	Male	375/2267			538/2267			538	3.9 (3.6–4.1)		
	Female	159/1025	0.9 (0.8–1.1)	0.463	278/1025	1.2 (1.0–1.4)	0.037	278	3.5 (3.2–3.9)	0.9 (0.8–1.1)	0.324
Heart intervention	No	173/1254			258/1254			258	4.5 (4.0–4.9)		
	Yes	361/2038	1.3 (1.1–1.6)	0.004	558/2038	1.5 (1.2–1.7)	<0.001	558	3.43 (3.20–3.7)	0.8 (0.7–0.9)	0.003
Neurological intervention	No	532/3280			809/3280			809	3.8 (3.5–4.0)		
	Yes	2/12	1.0 (0.2–4.7)	0.968	7/12	4.3 (1.4–13.5)	0.013	7	3.9 (1.0–6.8)	0.8 (0.4–1.7)	0.618
Septic shock	No	448/3047			700/3047			700	3.24 (3.04–3.44)		
	Yes	86/245	3.2 (2.4–4.2)	< 0.001	116/245	3.0 (2.3–3.9)	<0.001	116	7.02 (6.37–7.66)	2.9 (2.4–3.5)	<0.001
ARDS	No	506/3205			775/3205			775	3.59 (3.38–3.80)		
	Yes	28/87	2.5 (1.6–4.0)	<0.001	41/87	2.8 (1.8–4.2)	<0.001	41	6.8 (5.7–7.8)	2.6 (1.9–3.5)	<0.001
AKI	No	367/2735			555/2735			775	3.6 (3.4–3.8)		
	Yes	167/557	2.8 (2.2, 3.4)	<0.001	261/557	3.5 (2.9–4.2)	<0.001	41	6.8 (5.7–7.8)	2.6 (1.9–3.5)	<0.001
CKD	No	440/2928			674/2928			674	3.51 (3.28–3.73)		
	Yes	94/364	2.0 (1.5–2.6)	<0.001	142/364	2.1 (1.7–2.7)	<0.001	142	4.85 (4.30–5.40)	1.5 (1.3–1.8)	<0.001
Hepatic failure	No	522/3228			788/3228			788	3.62 (3.41–3.83)		
	Yes	2/64	1.1 (0.6–2.3)	0.584	28/64	2.4 (1.5–4.0)	<0.001	28	7.86 (6.61–9.11)	3.8 (2.5–5.8)	<0.001

AKI = acute kidney injury; ARDS = acute respiratory distress syndrome; CI = confidence interval; CKD = chronic kidney disease; ICD-10 = International Statistical Classification of Diseases and Related Health Problems 10th Revision; ICDSC = Intensive Care Delirium Screening Checklist; OR = odds ratio; TR = time ratio

Figure 1: (a) intensive care unit (ICU) and **(b)** hospital length of stay modelled parametrically with a gamma and a log-logistic distribution, respectively. The non-parametric Kaplan-Meier (KM) curves show the cumulative proportions of patients still in the ICU on day 7 and /or in hospital on day 60. Because survival curves from 2011 and 2013 are very similar, we show only the overall KM curve (black line) and parametric fit (red line).
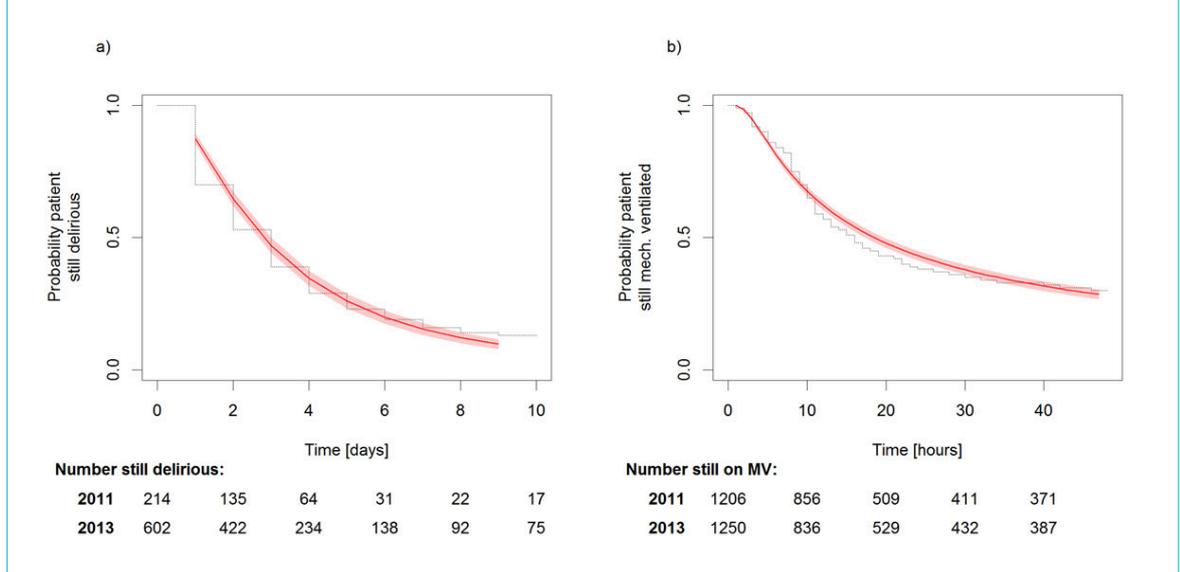
Duration of mechanical ventilation

In both years, patients spent on average just under one day (2011: 23.75 hours, 2013: 23.55 hours) on mechanical ventilation. The crude model indicated that the difference was non-significant, whereas the confounder-adjusted model indicated that the mean duration of mechanical ventilation was significantly shorter in the postintervention group (table 3).

In-hospital mortality

In 2011, 96 and in 2013, 84 patients died during their hospital stay. Neither the crude nor the adjusted model indicated any significant mortality rate difference between the historical-control and postintervention group (table 3).

Cost

The total cost per case increased from CHF 49,440 in 2011 to CHF 55,940 in 2013. Both the crude and the adjusted model indicated that the median cost increase was significant (table 3).

Nursing hours per case

In 2011, nurses spent on average roughly 26 hours and in 2013, 29 hours per case on direct patient care. Although this difference appeared significant in the unadjusted model, adjustment for confounders indicated that it was non-significant (table 3).

Table 3: Effectiveness, costs and benefits of the delirium management guideline.

Endpoints/outcomes		2011	2013	Crude models (2013/ 2011)		Adjusted models (2013/2011)	
Logistic regression models		n/N		OR (95% CI)	p-value	OR (95% CI)	p-value
Delirium prevalence	ICD-10	200/1608	334/1684	1.8 (1.4–2.1)	<0.001	1.7 (1.4–2.1)	<0.001
	ICD-10 ICU 1	121/971	244/1102				
	ICD-10 ICU 2	79/636	90/578				
	ICDSC* ICU 1	201/971	371/1102	1.94 (1.6–2.4)	<0.001	1.8 (1.5–2.3)	<0.001
	ICSC ICU 2	No data					
Parametric survival models		Crude restricted mean (95% CI)		TR (95% CI)	p-value	TR (95% CI)	p-value
ICU LOS (days)		2.5 (2.4–2.6)	2.6 (2.5–2.7)	1.1 (1.0–1.1)	0.132	0.9 (0.9–1.0)	0.048
In-hospital LOS (days)		17.1 (16.4–17.8)	18.1 (17.4–18.8)	1.1 (1.0–1.1)	0.015	1.0 (1.0–1.1)	0.214
Delirium duration (days)*		3.3 (2.9–3.7)	3.6 (3.6–3.4)	1.1 (0.98–1.3)	0.102	1.1 (1.0–1.3)	0.059
Duration mechanical ventilation (days)		23.8 (22.8–24.8)	23.6 (22.6–24.6)	0.96 (0.9–1.1)	0.429	0.8 (0.8–0.9)	<0.001
Binomial general linear models		n/N	n/N	OR (95% CI)	p-value	OR (95% CI)	p-value
In-hospital mortality		84/1608	96/1684	1.1 (0.8–1.5)	0.548	0.68 (0.5–1.0)	0.063
Quantitative regression methods/models		Median difference (95% CI)	Median difference (95% CI)	Median difference (95% CI)	p-value	Median difference (95% CI)	p-value
Cost per case (thousands of CHF)		49.4 (47.4–51.5)	55.9 (54.0–57.9)	6.5 (3.7–9.3)	<0.001	3.8 (0.5–7.1)	0.023
Nursing hours/case		26.0 (24.3–27.7)	28.5 (26.9–30.5)	2.6 (0.2–5.0)	0.037	−0.09 (−4.0 − −3.9)	0.500

CI = confidence interval; ICD-10 = International Statistical Classification of Diseases and Related Health Problems 10th Revision; ICDSC = Intensive Care Delirium Screening Checklist; ICU = intensive care unit; LOS = length of stay; OR = odds ratio; TR = time ratio * For one ICU only Postintervention and historical control groups were investigated using multivariate models including the following potential confounders: gender (m/f), intervention heart (0/1), intervention neurological (0/1), septic shock (0/1), acute respiratory distress syndrome (0/1), acute renal insufficiency (0/1), chronic renal insufficiency (0/1), hepatic insufficiency (0/1), age (in decades), Richmond Agitation Sedation Scale, Charlson comorbidity index, Simplified Acute Physiology Score II.

Associations between delirious state and ICU LOS, hospital LOS and mechanical ventilation duration

For both the 2011 and 2013 groups, the adjusted model indicated that delirium was significantly associated with LOS – both in the ICU and in hospital – and duration of mechanical ventilation. Delirium increased predicted ICU LOS by a factor of 2.66 and increased hospital LOS by a factor of 1.62. Predicted duration of mechanical ventilation increased by a factor of 2.33 in delirious patients (table 4).

Discussion

The purpose of this study was to evaluate the effectiveness, costs and benefits of a standardised delirium management guideline implemented in two ICUs of a Swiss tertiary care hospital with reference to eight selected patient and healthcare system outcomes. After implementation of the guideline, the duration of mechanical ventilation decreased significantly as hypothesised. However, contrary to our hypothesis, ICU LOS, delirium prevalence and cost per case increased significantly. No significant changes occurred in hospital LOS, delirium duration, in-hospital mortality or nursing hours per case. These results are in line with those of previous studies that indicated delirium is a significant predictor for ICU LOS [4, 8, 33] and duration of mechanical ventilation [4, 33], and showed that the implementation of a multicomponent delirium programme increased the detection of delirium. These results do not support a connection between intensive care delirium and hospital LOS.

These mixed results call for a differentiated interpretation. On the one hand, they show that the implemented guideline led to a reduction in mechanical ventilation duration independent of multiple disease-associated factors. Since prolonged mechanical ventilation has been linked to several risk factors such as ventilator-associated pneumonia, increased costs and higher 1-year mortality [34, 35], this is a positive finding.

On the other hand, combined with the unexpected results demonstrated by significant changes contrary to what was hypothesised in three of the selected outcomes, the absence of significant changes in five more outcomes suggests extrinsic and intrinsic factors should be considered. For example, the (statistically significant, but clinically irrelevant) increase in the ICU LOS can be partly explained by changes in the hospital infrastructure (opening of a large new intermediate care facility [IMC]) and the more frequent use of certain treatments (e.g., extracorporeal membrane oxygenation). Due to the opening of the new IMC, to which all stable patients are transferred, the proportion of unstable critically ill patients requiring catecholamines, mechanical ventilation, etc., had risen in both of the ICUs observed. The significantly higher SAPS II scores [24] in the postimplementation group support this assumption. In the current study, it was not possible to control for such

changes. To increase external validity, it would be important for future studies to consider these and similar factors in their design.

As delirium is underdiagnosed in the absence of standardised screening (those with hypoactive symptomatology in particular are not recognised and are therefore underreported [36]), the establishment of standard diagnostics in everyday clinical practice results initially in a higher sensitivity and therefore in increased delirium detection and documentation, which explains the observed increases in delirium diagnoses. However, this effect is time dependent: the selected analytical timeframe (the time interval between the start of implementation and the evaluation of its effects) plays a decisive role. As such, this study's analytical timeframe might have been too short to show any effect on the selected outcomes, particularly with respect to changes in ICU infrastructure during the observational period.

Other aspects also need to be discussed and considered when interpreting the delirium prevalence rate. For example, the poor agreement between delirium prevalence rates based on delirium ICD-10 codes [30] and those based on ICDSC scores [22] may indicate either an underreporting bias when using the ICD-10 code or insufficient specificity of ICDSC scores. Although both the implemented delirium management guideline and the algorithm clearly specify that at the end of the diagnostic process any results indicating delirium need to be documented in the electronic patient record as either a medical or a nursing diagnosis, this step is sometimes omitted, i.e., implementation is not 100% successful. Reasons include the principle that, as successful implementation requires cultural change, its completeness differs between units: gaps and disruptions arise in interprofessional processes, especially communication, leading to differing consideration among the involved professionals regarding, for example, the idea that failures to correctly document delirium diagnoses can have negative consequences for a patient. With the involvement of interprofessional teams at the unit or clinic, we aimed to support this cultural change via adaptation, where appropriate, of the relevant processes. With regard to the overall success of an implementation, the importance of involving all relevant stakeholders, including senior leaders and frontline providers, is supported by the results of other studies and quality improvement projects that use Lean Sigma methodology [37]. Since a cultural change requires time, our chosen time-frame might simply have been too short to show an effect in the expected direction.

In addition, the manifold interdependencies between risk factors precipitating or predisposing to delirium and/or causes make recognising and managing those factors and causes very challenging. Furthermore, in the critical care setting, given the complexity and instability of the patient's other conditions, delirium risk factors may not receive top priority, or the underlying cause, such as sepsis or ARDS,

Table 4: Associations between delirium and ICU length of stay, hospital length of stay and mechanical ventilation.

Variables	Delirious patients	Non-delirious patients	TR (95% CI)	p-value
ICU length of stay (days)	4.57 (4.37–4.78)	2.11 (2.03–2.19)	2.66 (2.43–2.92)	<0.001
Hospital length of stay (days)	25.07 (23.63–26.51)	16.07 (15.58–16.56)	1.62 (1.52–1.74)	<0.001
Duration mechanical ventilation (hours)	34.20 (32.66–35.74)	20.98 (20.22–21.74)	2.33 (2.04–2.65)	<0.001

CI = confidence interval; ICU = intensive care unit; TR = time ratio

may not respond immediately to treatment. Therefore, it is impossible to prevent all delirium in ICU patients.

Although our results did not match our hypotheses, they fit well into the overall picture of previous literature on the implementation of delirium guidelines. Reports on the implementation of multifaceted care approaches for the prevention and mitigation of a delirium in ICU patients or the ABCDE (Awakening, Breathing, Coordination, Delirium Monitoring/ Management, and Early Exercise/Mobility) bundles also show contradictory results. In fact, the evidence remains inconclusive: several studies have found significant decreases in ICU and/or hospital LOS, in-hospital and short-term mortality, delirium prevalence and duration, duration of mechanical ventilation, and total cost of ICU hospitalisation, whereas others have found no significant changes in these outcomes [9, 14, 16, 18, 38–45].

This study has several notable strengths and limitations. Its strengths include the large sample size and a fully representative sample of patients. Relevant limitations include the chosen design, which allows neither causal inferences nor control of confounders or changes over time such as legislative/policy shifts or staff turnover over the 2 years between datasets. To calculate delirium prevalence rates and the other primary and secondary outcomes, we combined objective clinical data extracted from well-established databases with delirium assessment data generated via validated instruments such as the ICDSC [22] once per shift. This and our extensive process of data validation, which we conducted to ensure both the quality of the data and the internal validity of the study, are also strengths. However, as bases for delirium prevalence calculations, the ICD-10 codes [30] and ICDSC assessment scores [22] varied considerably. As we know from feedback from physicians working in the study hospital, delirium diagnosis was not always documented at the end of the diagnostic process as defined in the implemented delirium algorithm. This might have contributed to the differences between results.

To evaluate the effectiveness of the implemented standardise delirium management, we compared the entire control group with the entire postintervention group. This lack of selectivity may have led to significant unexpected changes in effect direction. In future studies of outcomes including ICU and hospital LOS, length of mechanical ventilation, mortality, cost and nursing hours per case, it would be advisable to include only patients diagnosed with delirium.

Conclusions

Standardised delirium management supports the detection of delirium in ICU patients and may contribute to improved outcomes in critical care cases, such as shorter length of stay in the ICU. However, the increased awareness of delirium after the implementation of a standardised multiprofessional, multicomponent management process leads to increased therapeutic effort, resulting in prolongation of ICU stay and higher costs but with no significant effect on mortality.

To overcome the influence of an initial learning effect on the delirium rates and to clarify this study's conflicting results, further research will be necessary in our study context. In order to better understand delirium's causal relationships with ICU and hospital LOS, costs and mortality, we strongly advise research teams to employ study designs that allow causal inferences.

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