Effect of organisational factors on the variation in incidence of delirium in intensive care unit patients: A systematic review and meta-regression analysis

Paul Rood, RN, MSc, CCRN a, b, *
Getty Huisman - de Waal, PhD b
Hester Vermeulen, RN, PhD b
Lisette Schoonhoven, PhD, FEANS c, d
Peter Pickkers, MD, PhD a
Mark van den Boogaard, RN, PhD, CCRN a

* Department of Intensive Care Medicine, Radboud University Medical Center, Nijmegen, The Netherlands
b Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands
c Faculty of Health Sciences, University of Southampton, Southampton, United Kingdom
d National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care (Wessex), United Kingdom

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ABSTRACT

Background: Delirium occurs frequently in intensive care unit (ICU) patients and is associated with numerous deleterious outcomes. There is a large variation in reported delirium occurrence rates, ranging from 4% to 89%. Apart from patient and treatment-related factors, organisational factors could influence delirium incidence, but this is currently unknown.

Objective: To systematically review delirium incidence and determine whether or not organisational factors may contribute to the observed delirium incidence in adult ICU patients.

Methods: Systematic review of prospective cohort studies reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Included articles were independently assessed by two researchers. Quality of the articles was determined using the Strengthening the Reporting of Observational Studies in Epidemiology checklist. Subsequently, apart from patient characteristics, a meta-regression analysis was performed on available organisational factors, including hospital type, screening method and screening frequency.

Data Sources: PubMed, Embase, CINAHL, and Cochrane Library databases were searched from inception to 27 January 2017, without language limitation.

Results: A total of 9357 articles were found, of which 19 articles met the inclusion criteria and were considered as true delirium incidence studies. The articles were of good methodological quality (median [interquartile range] 32/38 [30–35] points), published between 2005 and 2016, originated from 17 countries. A total of 9867 ICU patients were included. The incidence rate of delirium varied between 4% and 55%, with a mean ± standard deviation of 29 ± 14%. Data relating to three organisational factors were included in the studies, but they were not significantly associated with the reported delirium incidence: hospital type (p 0.48), assessment methods (p 0.41), and screening frequency (p 0.28).

Conclusions: The mean incidence of delirium in the ICU was 29%. The organisational factors found including methods of delirium assessment, screening frequency, and hospital type were not related to the reported ICU delirium incidence.

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1. Introduction

Delirium is a serious problem in the intensive care unit (ICU), as it is associated with numerous short-term adverse events such as
increased duration of mechanical ventilation and length of stay. Also, delirium is associated with long-term adverse effects such as persistent cognitive decline and increased 6-month mortality. Delirium occurs frequently in the ICU; a recent meta-analysis found that delirium occurs in approximately one-third of ICU patients, but a large variation is reported. Depending whether incidence, defined as a new onset of delirium after ICU admission, or prevalence, which also includes patients who were already delirious before ICU admission, is estimated, occurrence rates vary between 4% and 89%. The reason for this large variability is currently not fully understood.

From a research perspective, the collection of implementation data is essential for program evaluations, and multilevel causal factors are described to impact implementation outcomes, such as patient, provider, and organisational factors. First, several patient-related risk factors are clearly associated with the development of delirium, such as respiratory failure, a history of cognitive impairment, and urgent ICU admission. Although patient-related risk factors account for a considerable part of the variability, they do not explain all of it. Second, delirium incidence is also influenced by the provider through the ICU treatment. The current international delirium guideline emphasises that timely management of the cause is essential to reduce the delirium incidence, severity, and duration. Also aspects of care such as sedation management and early mobilisation are considered to influence the development of delirium. Third, organisational factors may contribute to delirium. These include the selection of the screening method (currently either the Confusion Assessment Method for the Intensive Care Unit [CAM-ICU] or the Intensive Care Delirium Screening Checklist [ICDSC]) are recommended, of which the performance is limited, even when performed by experts, daily screening frequency (as delirium may not be detected if screening frequency is too low because of its fluctuating course during the day), and hospital type (as variations in different types of hospitals may account for differences). Also, strategies used for education of staff and screening compliance as the measured delirium incidence may differ because of to fluctuating course of delirium and the adequate recognition of delirium symptoms.

Recent reviews have provided insight into patient- and provider-related risk factors, but did not address organisational factors. As there is empirical support that the level of implementation may affect the outcome in prevention programs, we feel that these should be clarified so they can be incorporated when collecting and analysing data. As the incidence of delirium can be collected and analysed data. As the incidence of delirium can be found in most of the reviewed articles, this tool was deemed most suitable for critical quality appraisal of the included articles. It allowed for structured and transparent assessment of bias and applicability of primary diagnostic accuracy articles. Each domain was assessed in terms of risk of bias, and a rating per item was given (2 = present, 1 = partially present, 0 = not present, NA = not applicable). Afterwards sum scores were calculated. A maximum score of 38 points could be obtained. The lower limit for inclusion in the review was set at 70% of achievable points.

Data extraction was performed by the primary researcher (PR) using a standardised data extraction form containing patients characteristics and treatment and organisational factors. For treatment factors, we aimed to gather data on delirium treatment algorithms, as well as analgesia, sedative, and sleep enhancement strategies. For organisational factors, articles were searched for factors regarding country and continent, hospital type, implementation strategies, staff knowledge, motivation, and screening compliance.

2. Material and methods

A systematic review and meta-regression analysis was performed, according to the Cochrane Handbook for systematic reviews and reported according to the steps of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. The selection of articles, data extraction, and methodological quality assessment were performed independently by two reviewers (PR and MvdB). Included articles were assessed for methodological quality using the "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) statement. Prospective cohort studies were included in which the ICU delirium incidence was determined in adult medical, surgical, or mixed ICU patients (18 years or older). Delirium incidence was defined as a new onset of delirium during ICU admission without delirium before ICU admission, diagnosed by a positive delirium screening using a validated screening tool or as a reported medical diagnosis. Articles were excluded when only delirium prevalence (i.e. delirium before ICU admission was not an exclusion criterion) was reported, when the focus was on other ICU subpopulations, or if no full-text article was available. To ensure the quality of reported delirium incidence rates, only prospective cohort studies designed to study delirium incidence were included.

2.2. Search

A systematic literature search was conducted in PubMed, Embase, CINAHL and Cochrane Library databases. References of included articles were searched for additional relevant articles. Databases were searched through combining “Delirium,” “Intensive Care Unit,” and “Incidence”, as well as relevant synonyms. The complete strategy is provided in an online supplemental. Languages were not limited during the search. Articles published from database inception until January 27th, 2017, were included. Data management was performed using Endnote X8 (Thomson Reuters).

2.3. Study selection

Eligibility of articles was independently assessed by screening title and abstract by two researchers (PR and MB) using the inclusion criteria. Eligible articles were obtained in full-text by the first author; if not possible, we planned to contact the authors of the article. Articles that were irretrievable would have been excluded from further analysis. Both turned out not to be necessary, as all articles could be obtained. After independent full-text assessment of the eligible articles, discrepancies were discussed. In case of disagreement, a third researcher (HV) was asked to make a final judgement.

2.4. Methodological quality

The selected articles were screened for methodological quality using the “STROBE statement”. Because an index test was not included in the list of the reviewed articles, this tool was deemed most suitable for critical quality appraisal of the included articles. It allowed for structured and transparent assessment of bias and applicability of primary diagnostic accuracy articles. Each domain was assessed in terms of risk of bias, and a rating per item was given (2 = present, 1 = partially present, 0 = not present, NA = not applicable). Afterwards sum scores were calculated. A maximum score of 38 points could be obtained. The lower limit for inclusion in the review was set at 70% of achievable points.

2.5. Data collection

Data extraction was performed by the primary researcher (PR) using a standardised data extraction form containing patients characteristics and treatment and organisational factors. For treatment factors, we aimed to gather data on delirium treatment algorithms, as well as analgesia, sedative, and sleep enhancement strategies. For organisational factors, articles were searched for factors regarding country and continent, hospital type, implementation strategies, staff knowledge, motivation, and screening compliance.
2.6. Statistics

Extracted measures were reported using descriptive statistics: Patient characteristics, ICU treatment, and organisational factors as available in all included articles were extracted. To determine the association of organisational factors with the reported delirium incidences, a meta-regression analysis was performed. Owing to heterogeneity and a limited number of included articles, we performed a univariate analysis using a random effects model. Mean ± standard deviation, or median (interquartile range) are reported, depending on the normality of the distribution of data. Data were analysed using IBM SPSS Statistics 22 and R statistics 3.2.4. The standard error of the incidence was calculated for each study as \( (\text{Incidence}-(1-\text{Incidence})/N)^2 \). A \( p \)-value of \( \leq 0.05 \) was considered statistically significant.

3. Results

3.1. Study selection

The search yielded a total of 9357 articles, of which after removal of duplicates 8178 unique articles remained. Based on analysing title and abstract, 8060 articles were excluded, leaving 118 articles. Another 71 articles were excluded as only a conference abstract was available, and 28 articles were excluded because incidence rates were not mentioned in the full-text article. Finally, in total, 19 articles were included in this meta-regression analysis (Fig. 1).

A total of 9867 ICU patients were included in the articles. Sample size varied from 80 to 4450 patients. All articles were published between 2005 and 2016. Nine studies were conducted in a general ICU population, four only included medical and six only surgical patients (Table 1).

3.2. Organisational risk factors

In 16 articles, a screening tool validated for the ICU was used (eleven studies used the CAM-ICU, five used the ICDSC). In two studies, a general delirium screening tool (Delirium rating scale-revised-98, Nursing Delirium Symptom Checklist) was used, and in one study the formal diagnostic criteria according to the Diagnostic Statistical Manual IV–Third Revision were applied. Nine articles originated from Europe, six from Asia, two from Northern America, one from Southern America, and one from Oceania. Sixteen studies were performed in one or more university hospitals and three were performed in general hospitals. Nine articles reported the number of ICU beds, which varied between 8 and 33 beds. Daily screening frequency varied between 1 and 3 times a day, the time window in which the first, follow-up, and last delirium screening was performed varied greatly. In 10 studies, the delirium screening was performed by ICU nurses, in five by ICU physicians, in two studies by dedicated research personnel, and in two studies by psychiatrists (Table 2).

3.3. Methodological quality

Of the 19 included articles, STROBE quality assessment yielded a median score of 32 (possible 38) points. All articles obtained a quality score over 70% and were considered of sufficient methodological quality for inclusion in the analysis. Most elements were reported in the majority of the articles, except for bias (mentioned in 13% of articles) and funding (mentioned in 50% of articles). An overview of the individual assessment scores is provided in the online supplement 2.

3.4. Results of individual articles

The mean delirium incidence rate was 29 ± 14%; the lowest incidence found was 4%, and the highest was 55%. The samples that were included were heterogeneous. Overall, most studies included older patients, who originated from medical, surgical, or mixed ICU populations, and more males than females were included. A broad variation was observed in admission type, severity of illness, length of stay, and mortality rates (Table 1).

3.5. Associations of ICU treatment and organisational factors

Using a meta-regression analysis, we assessed the association of organisational factors to reported delirium incidence rates. No significant differences in delirium incidence were found between university hospitals (median 28%, in 9463 patients) and non-university hospitals (33% in 404 patients \( p = 0.48 \)). Related to the screening method used to detect delirium, five different methods were described. In 11 studies that used the CAM-ICU, a median incidence of 24% was found in 3767 patients. In five studies that used the ICDSC, a median incidence of 32% was found in 5654 patients. Three non-ICU specific methods were used: (i) one study used the Delirium rating scale-revised and found an incidence of 24% in 140 patients; (ii) one study used a psychiatric interview according to the Diagnostic Statistical Manual IV–Third Revision criteria and found an incidence of 55% in 142 patients; and (iii) one study used the Nursing Delirium Symptom Checklist and found an incidence of 44.5% in 164 patients. The incidence of delirium did not differ significantly between screening methods \( p = 0.28 \). Finally, the influence of the daily screening
<table>
<thead>
<tr>
<th>Reference</th>
<th>Delirium incidence</th>
<th>N</th>
<th>Age</th>
<th>Population</th>
<th>Male (N, %)</th>
<th>Urgent admission (N, %)</th>
<th>Severity of illness score</th>
<th>Mechanically ventilated (N, %)</th>
<th>LOS-ICU</th>
<th>LOS hospital</th>
<th>Mortality rate (N, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayllon Garrido et al.60</td>
<td>41.3%</td>
<td>112</td>
<td>63 (±18)</td>
<td>Mixed</td>
<td>67 (60)</td>
<td>–</td>
<td>APACHE II 47 (42)</td>
<td>3 [2–8]</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Bilge et al.61</td>
<td>18.4%</td>
<td>250</td>
<td>60 (±13)</td>
<td>Surgical</td>
<td>D 21 (46) ND 121 (59)</td>
<td>–</td>
<td>APACHE II 47 (±7)</td>
<td>14 (±7)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Kanova et al.62</td>
<td>31.2%</td>
<td>125</td>
<td>64 (±21)</td>
<td>Mixed</td>
<td>87 (61%)</td>
<td>–</td>
<td>APACHE II 12 (±4)</td>
<td>61 (43)</td>
<td>3 (±6)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lahary et al.63</td>
<td>9.3%</td>
<td>309</td>
<td>D 62 (±14); ND 57 (±13)</td>
<td>Medical</td>
<td>D 51 (63) ND 30 (37)</td>
<td>D 78 (96) ND 205(90)</td>
<td>APACHE II D 15 (±5)</td>
<td>–</td>
<td>D 2 (±2)</td>
<td>ND 2 (±1)</td>
<td>–</td>
</tr>
<tr>
<td>Limpawattana et al.64</td>
<td>22.2%</td>
<td>99</td>
<td>D 79 (±7); ND 75 (±7)</td>
<td>Medical</td>
<td>D 24 (40) ND 22 (55)</td>
<td>–</td>
<td>APACHE II D 24 (±1)</td>
<td>D 30 (68) ND 18 (33)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mori et al.64</td>
<td>46.3%</td>
<td>149</td>
<td>D 65 [53–80]; ND 54 [30–68]</td>
<td>Mixed</td>
<td>D 42 (61) ND 49 (61)</td>
<td>–</td>
<td>APACHE II 61 (43)</td>
<td>3 (±6)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Norkiene et al.65</td>
<td>13.3%</td>
<td>87</td>
<td>D 68 (±10); ND 65 (±11)</td>
<td>Surgical</td>
<td>–</td>
<td>0 (0)</td>
<td>–</td>
<td>–</td>
<td>87 (100)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ouimet et al.66</td>
<td>31.8%</td>
<td>820</td>
<td>D 65 (±14); ND 63 (±15)</td>
<td>Mixed</td>
<td>D 147 (61) ND 303 (58)</td>
<td>–</td>
<td>APACHE II D 18 (±8)</td>
<td>645 (79)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Page et al.67</td>
<td>31.0%</td>
<td>80</td>
<td>D 70 [56–76]; ND 73 [60–77]</td>
<td>Mixed</td>
<td>D 16 (72) ND 34 (69)</td>
<td>D 22 (45) ND 27 (55)</td>
<td>APACHE II D 17 (63) ND 10 (37)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Peterson et al.68</td>
<td>24.4%</td>
<td>614</td>
<td>53 (±18)</td>
<td>Medical</td>
<td>309 (50)</td>
<td>–</td>
<td>APACHE II 298 (49)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Roberts et al.70</td>
<td>45.0%</td>
<td>185</td>
<td>D 64; ND 60</td>
<td>Mixed</td>
<td>D 52 (62) ND 56 (55)</td>
<td>–</td>
<td>APACHE II D 21 ND 17</td>
<td>–</td>
<td>D 10 [7] ND 7 [5]</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sharma et al.72</td>
<td>24.4%</td>
<td>140</td>
<td>D 50 (±19); ND 37 (±14)</td>
<td>Mixed</td>
<td>D 43 (57) ND 29 (45)</td>
<td>–</td>
<td>APACHE II D 20 (±6)</td>
<td>D 60 (80) ND 34 (52)</td>
<td>D 8 [5–13] ND 5 [3–6]</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Smulter et al.74</td>
<td>54.9%</td>
<td>142</td>
<td>D 77 (±5); ND 76 (±4)</td>
<td>Surgical</td>
<td>D 54 (69) ND 38 (59)</td>
<td>–</td>
<td>APACHE II D 13 (±4) ND 7 (±4)</td>
<td>–</td>
<td>D 11 [±1] ND 0.76 (±0.23)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Svenningsen et al.75</td>
<td>40.2%</td>
<td>139</td>
<td>D 63; ND 64</td>
<td>Mixed</td>
<td>78 (56)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>D 21 ND 14</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Woien et al.77</td>
<td>23.4%</td>
<td>139</td>
<td>55 (±15)</td>
<td>Medical</td>
<td>87 (63)</td>
<td>–</td>
<td>SAPS II 138 (99)</td>
<td>5 (range 1–53)</td>
<td>–</td>
<td>–</td>
<td>25 (18)</td>
</tr>
</tbody>
</table>

D = delirious patients, ND = non-delirious patients; LOS = length of stay; ICU = intensive care unit.
Illness severity scores: APACHE-II score = Acute Physiology and Chronic Health Evaluation-II score, ASA Score = American Society of Anaesthesiologists score, SAPS II/III = Simplified Acute Physiology Score, EUROSCORE II = European System for Cardiac Operative Risk Evaluation II.
Data are expressed as number and percentage (N%), mean (±standard deviation) or median [interquartile range], unless mentioned otherwise.
Table 2
Organisational characteristics of included articles.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Incidence</th>
<th>Year</th>
<th>N</th>
<th>Type center</th>
<th>Beds</th>
<th>Country</th>
<th>Screening method</th>
<th>Daily screening frequency</th>
<th>Screening by</th>
<th>Comments</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayllon Garrido et al.</td>
<td>41.3%</td>
<td>2007</td>
<td>112</td>
<td>UMC</td>
<td>8</td>
<td>Spain</td>
<td>ICDS</td>
<td>1 Nurses</td>
<td></td>
<td>Only patients admitted &gt;72 h were included; Patients were assessed once. Patients who required post-operative mechanical ventilation were excluded.</td>
<td>34/38</td>
</tr>
<tr>
<td>Bilge et al.</td>
<td>18.4%</td>
<td>2015</td>
<td>250</td>
<td>UMC</td>
<td>–</td>
<td>Turkey</td>
<td>CAM-ICU</td>
<td>1 Physicians</td>
<td></td>
<td>36/38</td>
<td></td>
</tr>
<tr>
<td>Kanova et al.</td>
<td>31.2%</td>
<td>2015</td>
<td>125</td>
<td>UMC</td>
<td>–</td>
<td>Czech Republic</td>
<td>CAM-ICU</td>
<td>1 Physicians</td>
<td></td>
<td>Prevalence 29%, incidence defined as first positive score &gt;24 after admission. First CAM-ICU was performed within 48 h after admission. Readmitted patients and patients/family who refused cooperation were excluded from analysis.</td>
<td>30/38</td>
</tr>
<tr>
<td>Lahariya et al.</td>
<td>9.3%</td>
<td>2014</td>
<td>309</td>
<td>UMC</td>
<td>22</td>
<td>India</td>
<td>CAM-ICU; DSM-IV-TR</td>
<td>1 Clinicians—psychiatrists</td>
<td></td>
<td>31/38</td>
<td></td>
</tr>
<tr>
<td>Limpawattana et al.</td>
<td>22.2%</td>
<td>2016</td>
<td>99</td>
<td>UMC</td>
<td>–</td>
<td>Thailand</td>
<td>CAM-ICU</td>
<td>1 Nurses</td>
<td></td>
<td>33/38</td>
<td></td>
</tr>
<tr>
<td>Mori et al.</td>
<td>46.3%</td>
<td>2016</td>
<td>149</td>
<td>UMC</td>
<td>17</td>
<td>Brazil</td>
<td>CAM-ICU</td>
<td>2 Nurses</td>
<td></td>
<td>Screening was started 24 h after surgery, repeated every 8 h during ICU stay (max 5 days).</td>
<td>34/38</td>
</tr>
<tr>
<td>Norkiene et al.</td>
<td>13.3%</td>
<td>2013</td>
<td>87</td>
<td>UMC</td>
<td>–</td>
<td>Lithuania</td>
<td>ICDSC</td>
<td>3 Clinicians</td>
<td></td>
<td>30/38</td>
<td></td>
</tr>
<tr>
<td>Ouimet et al.</td>
<td>31.8%</td>
<td>2007</td>
<td>820</td>
<td>UMC</td>
<td>16</td>
<td>Canada</td>
<td>ICDSC</td>
<td>1 Clinicians</td>
<td></td>
<td>29/38</td>
<td></td>
</tr>
<tr>
<td>Page et al.</td>
<td>31.0%</td>
<td>2009</td>
<td>80</td>
<td>Gen</td>
<td>8</td>
<td>United Kingdom</td>
<td>CAM-ICU</td>
<td>2 Nurses</td>
<td></td>
<td>27/38</td>
<td></td>
</tr>
<tr>
<td>Peterson et al.</td>
<td>24.4%</td>
<td>2006</td>
<td>614</td>
<td>UMC</td>
<td>14</td>
<td>USA</td>
<td>CAM-ICU</td>
<td>2 Nurses</td>
<td></td>
<td>Prevalence 36.6%</td>
<td>35/38</td>
</tr>
<tr>
<td>Pipanmekaporn et al.</td>
<td>3.6%</td>
<td>2015</td>
<td>4450</td>
<td>UMC</td>
<td>–</td>
<td>Thailand</td>
<td>ICDSC</td>
<td>1 Nurses</td>
<td></td>
<td>Range between SICU’s: 0–13.9%. Exclusion: &lt;24 h stay, neurosurgical and cardiac admission, Inclusion of 185/2568 patients admitted due to exclusion when ICU LOS &lt;36 h or hospital stay &gt;96 h prior to ICU admission.</td>
<td>31/38</td>
</tr>
<tr>
<td>Roberts et al.</td>
<td>45.0%</td>
<td>2005</td>
<td>185</td>
<td>Gen</td>
<td>–</td>
<td>Australia/New Zealand</td>
<td>ICDSC</td>
<td>2 Researchers or trained professionals</td>
<td></td>
<td>31/38</td>
<td></td>
</tr>
<tr>
<td>Sabol et al.</td>
<td>20.8%</td>
<td>2015</td>
<td>250</td>
<td>UMC</td>
<td>–</td>
<td>Slovakia</td>
<td>CAM-ICU</td>
<td>2 Nurses</td>
<td></td>
<td>32/38</td>
<td></td>
</tr>
<tr>
<td>Sharma et al.</td>
<td>24.4%</td>
<td>2012</td>
<td>140</td>
<td>UMC</td>
<td>8</td>
<td>India</td>
<td>DRS-R-98</td>
<td>1 Psychiatrists</td>
<td></td>
<td>35/38</td>
<td></td>
</tr>
<tr>
<td>Shi et al.</td>
<td>44.5%</td>
<td>2010</td>
<td>164</td>
<td>UMC</td>
<td>–</td>
<td>China</td>
<td>Nu-DESC</td>
<td>3 Physicians and nurses</td>
<td></td>
<td>Delirium assessment was performed until day 7 post-operative or the disappearance of delirious symptoms for 2 consecutive days. Patients were assessed pre-operatively and on day 1 and day 4 post-operatively. Patients were assessed &gt;48 h after ICU admission until discharged.</td>
<td>29/38</td>
</tr>
<tr>
<td>Smulter et al.</td>
<td>54.9%</td>
<td>2013</td>
<td>142</td>
<td>UMC</td>
<td>–</td>
<td>Sweden</td>
<td>DSM-IV-TR</td>
<td>1 Trained research nurses</td>
<td></td>
<td>32/38</td>
<td></td>
</tr>
<tr>
<td>Svenningsen et al.</td>
<td>40.2%</td>
<td>2011</td>
<td>139</td>
<td>UMC</td>
<td>28</td>
<td>Denmark</td>
<td>CAM-ICU</td>
<td>2 Nurses</td>
<td></td>
<td>28/38</td>
<td></td>
</tr>
<tr>
<td>Van den Boogaard et al.</td>
<td>25.5%</td>
<td>2012</td>
<td>1613</td>
<td>UMC</td>
<td>33</td>
<td>The Netherlands</td>
<td>CAM-ICU</td>
<td>3 Nurses</td>
<td></td>
<td>35/38</td>
<td></td>
</tr>
<tr>
<td>Woen et al.</td>
<td>23.4%</td>
<td>2013</td>
<td>139</td>
<td>Gen</td>
<td>–</td>
<td>Norway</td>
<td>CAM-ICU</td>
<td>3 Nurses</td>
<td></td>
<td>35/38</td>
<td></td>
</tr>
</tbody>
</table>

LOS = length of stay; ICU = intensive care unit; CAM-ICU = Confusion Assessment Method for the Intensive Care Unit; ICDSC = Intensive Care Delirium Screening Checklist; DRS-R-98 = Delirium rating scale-revised-98; DSM-IV-TR = Diagnostic Statistical Manual IV—Third Revision; Nu-DESC = Nursing Delirium Symptom Checklist; SICUs = Surgical Intensive Care Units.
frequency was assessed. A median incidence of 26% from 14 to 38 was found in 6447 patients in nine studies in which patients were screened for delirium once daily. 34% to 46 in 1417 patients in six studies which screened twice daily, and 27% to 47 in 2003 patients in the studies which screened three times daily. No significant differences were observed (p = 0.41) (Table 3).

### 4. Discussion

In this meta-analysis we found 19 good quality articles (median [interquartile range] score 32 [30–35] of possible 38 points), published between 2005 and 2016, originated from 17 countries. A total of 9867 ICU patients were included. All articles specifically described delirium incidence. A mean ICU delirium incidence of 29 ± 14 was found, ranging from 4% to 55%, which is in concordance with previous reviews. Organisational factors were scarcely reported. The variation in reported ICU delirium incidence could not be explained by hospital type, screening methods used, or daily screening frequency.

Several studies have been conducted to examine patient- and treatment-related factors that contribute to the development of delirium in the ICU, like need for mechanical ventilation (odds ratio [OR] = 7.0; 95% confidence interval [CI] = 3.4–14.8), need for physical restraints (OR = 33.8; 95% CI = 11.2–102.4), and use of sedatives (OR = 13.66; 95% CI = 7.2–26.1). Based on these risk factors, delirium prediction models accurately predict if a patient will develop delirium or not in 77% of the patients. Although these patient- and treatment-related factors may account for a considerable part of the variability, they do not fully explain the observed delirium incidence. Identifying potentially modifiable organisational factors that might contribute to enhanced delirium recognition or occurrence may improve delirium management. In our meta-analysis, only three organisational factors could be extracted from the articles. First, the hospital type could have contributed to the delirium incidence found because of differences in severity of illness. Second, the daily screening frequency might have added to the sensitivity of the observed incidence owing to the known fluctuating nature of delirium during the day. Third, the used assessment methods might have influenced the incidence found because the validity and psychometric properties of some screening instruments remain controversial, and differences in delirium incidence have been reported when both the CAM-ICU and the ICDSC are used simultaneously. However, based on our findings, no significant association with delirium incidence can be concluded.

Delirium is found in up to 89% of critically ill patients. However, we showed these highest estimates reflect prevalence rather than incidence. These high prevalence figures probably reflect onset of delirium before ICU admission. For clinical practice, it is important to have insight in the incidence of ICU delirium, so that effects of interventions and quality improvement programs, for example decreasing sedation-management or improving early mobilisation, can be assessed. Future studies should strive to discriminate between ICU-acquired “incidence” and pre-ICU—acquired “prevalence” figures and also incorporate organisational and treatment aspects as robust data on effectiveness of specific non-organisational are scarce.

Although not significantly associated with the delirium incidence, a broad consensus on which occurrence measure, diagnostic instrument, and which screening algorithm to use might help to optimise delirium treatment and reduce its incidence. The current international Society of Critical Care Medicine (SCCM) delirium treatment ICU guideline recommends the use of a standardised validated ICU delirium screening instrument. Both the CAM-ICU and the ICDSC are recommended despite their methodological differences in assessment of delirium (testing patient performance versus observation by the professional). In our meta-analysis, we did not find that the assessment tools used explained differences in delirium incidence. Potentially, because of the difference in assessment methods, a tool that combines testing patient performance with observation by a professional may provide even better screening performances and insight in the exact proportion of delirium in the ICU, but this has not been tested.

Some limitations of our study should be addressed. First, the number of organisational factors that could be analysed was limited to only three, as these were the only three that are currently reported. There might be other important organisational factors, such as structure and process factors like implementation and educational strategies, staff knowledge, motivation, and screening compliance, which may influence delirium incidence. However, these are difficult to quantify and therefore will be challenging to assess to what extent they may influence delirium incidence. Delirium is a multifactorial syndrome, which is often the result of several interacting processes. It is vital to have good insight in causal linkages of the organisational processes and the outcomes of care by perceiving insights in these processes. Although, we did not find these associations, this does not exclude that other not reported organisational factors, such as delirium education, implementation strategies, staff knowledge, motivation, and screening compliance, may contribute to the observed delirium incidence as they are known to affect other outcomes in the ICU, such as infections.

In our study, we found articles of good methodological quality, assessed by the STROBE criteria. Therefore, the data we found are likely to be valid. Notably, however, the lowest delirium incidence rate (4%) was found in the largest study. Although this study fulfilled the criteria for a good methodological quality, the low reported incidence contrasts to previous results and may be the result of a suboptimal screening regime, as in this national study some participating centres found incidences of 0%, which is unlikely to be accurate, considering the severity of illness (Acute Physiology and Chronic Health Evaluation-II) in the population as well as previous incidences found in large meta-analyses.

Because this national study was not only primarily focused on delirium incidence but also on all other adverse events and outcomes associated with critically ill surgical patients, we hypothesised that this would probably affect their reported delirium incidence rates. However, the results of this study did not statistically affect our reported mean delirium incidence of 29%.

It is possible that we were not able to detect an effect of organisational factors on delirium incidence because important

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Meta-regression analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>Estimates</td>
</tr>
<tr>
<td>Type of hospital</td>
<td>0.279</td>
</tr>
<tr>
<td>University</td>
<td>0.332</td>
</tr>
<tr>
<td>Non-university</td>
<td>0.290</td>
</tr>
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<td>Daily screening frequency</td>
<td>0.343</td>
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<td>1</td>
<td>0.266</td>
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<tr>
<td>2</td>
<td>0.262</td>
</tr>
<tr>
<td>Screening method</td>
<td>0.268</td>
</tr>
<tr>
<td>CAM-ICU</td>
<td>Other</td>
</tr>
</tbody>
</table>

CAM-ICU – Confusion Assessment Method for the Intensive Care Unit; ICDSC – Intensive Care Delirium Screening Checklist.

* Forest plots available in an online supplement.
organisational factors were simply not addressed. To enable uniform and comparable research addressing all potentially important aspects of delirium, it may be useful to compose a minimal data set for delirium research, which is already used within critical care and other fields of health care, and might be useful for defining consensus-based patient and nursing sensitive outcomes, such as screening compliance and education type e-learning and hands on learning. This data set might have most potential when added to the current ICU delirium management guidelines and ICU delirium research agenda. Second, Because of the limited number of studies which specifically reported delirium incidence in the context of organisational factors, we could not perform a multivariate regression analysis. This analysis would have enabled us to assess the associations between the extracted factors related to the delirium incidence found. Although optimal recognition of delirium does not reduce its burden on patients directly, it might help to provide optimal delirium care which may reduce its burden on patients. Further research may align the understanding of the variation in the occurrence of delirium in the ICU, through which lessons may be learned to minimise the burden of delirium in ICU patients.

5. Conclusions

This systematic review showed that 29% of patients develop delirium during their ICU stay. We were unable to demonstrate that organisational factors including methods of delirium assessment, screening frequency, and hospital type were related to the reported incidence of delirium in ICU patients.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.aucc.2018.02.002.

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