# **Delirium Assessment in Acute Stroke: A Systematic Review and Meta-Analysis of Incidence, Assessment Tools, and Assessment Frequencies**

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#### ABSTRACT

PURPOSE: The purpose of this systematic literature review was to examine whether different assessment methods contribute to the variance in delirium incidence detected in populations of patients with acute stroke. Specifically, the aim was to address the influence of (1) choice of assessment tool, (2) frequency of assessment, and (3) type of health professional doing the assessment.

METHODS: We searched MEDLINE, EMBASE, and PsycINFO and included pro- and retrospective cohort studies assessing delirium during hospitalization of adult acute stroke patients.

RESULTS: In 30 articles, 24 unique populations were identified and included in the review. Delirium incidence ranged from 1.4% to 75.6% in total and a chi-square test showed a significant heterogeneity across studies ( $\chi^2$  = 536.5, df = 23, P<.0001). No studies had an assessment for delirium before a patient entered the study. No specific patterns regarding the influence of tool, assessment frequency or health professional were discernible.

DISCUSSION: Subgroups analyses were not conducted due to the heterogeneity across studies. Studies comparing delirium assessment tools directly with each other are needed.

CONCLUSIONS: Delirium is a common complication in acute stroke. No firm conclusions about a possible correlation of choice of tool, assessment frequency, and delirium incidence could be made due to the great heterogeneity of the study populations. Only 1 study compared 2 tools directly with each other. Further studies comparing delirium assessment tools directly with each other are needed

KEYWORDS: Delirium, delirium assessment, acute stroke

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## Introduction

Development of acute delirium is a serious complication in patients hospitalized with acute stroke. Delirium interferes with initiation of stroke rehabilitation and causes prolonged stay in hospital, worse functional outcome after stroke, and increased mortality.<sup>1</sup> In 2012, 2 reviews on the occurrence of delirium in acute stroke reported incidences in the ranges of 10% to 48%<sup>1</sup> and 2.3% to 66%,<sup>2</sup> respectively.

The DSM-V3 is the newest edition of the Diagnostic and Statistical Manual of Mental Disorders from the American Psychiatric Association. Previous editions also relevant to this review include the DSM-IV-TR, the DSM-IV, and the DSM-III-R.<sup>4-6</sup> The definition of delirium is the same in DSM-IV-TR and the DSM-IV and differs only slightly from the definition in the *DSM-V*.

The DRS (Delirium Rating Scale) is a 10-item scale made to rate the severity of delirium symptoms.7 The original version is from 1988 with a later revision in 1998 (the Delirium DECLARATION OF CONFLICTING INTERESTS: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Rating Scale Revised 1998 [DRS-R-98]). The DRS-R-98 consists of a 13-item symptom severity scale and 3 additional diagnostic items.<sup>8</sup> Both scales are intended to be completed by a clinician using all available information about the patient under assessment.

The Confusion Assessment Method (CAM) was developed to provide an easy-to-use tool to health staff members not specifically trained in psychiatry.9 The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) is an edition of the CAM designed for use in the intensive care setting.<sup>10</sup>

In patients with stroke, the diagnosis of delirium is complicated by the fact that acute stroke itself as well as dementia caused by previous vascular events may cause delirium-like symptoms differing only in time of onset and development. In addition, the symptoms and signs of delirium have a fluctuating course over hours and days. It may therefore be difficult for unexperienced observers to correctly identify delirium. Some classes of health professionals may also be better equipped than

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Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage). others in the assessment of delirium and this may affect a given tool's ability to identify delirium. Furthermore, it is possible that the frequency of assessments will influence the number of delirious patients found.

The purpose of this systematic literature review was to examine whether different assessment methods contribute to the variance in delirium incidence. Specifically, the aim was to address the influence of (1) choice of assessment tool, (2) frequency of assessment, and (3) type of health professional doing the assessment. It was not the purpose of this review to evaluate studies directly comparing 2 or more tools with each other.

#### Methods

A protocol for this review was published online at the PROSPERO register (ID CRD42017068360).<sup>11</sup> The protocol was based on the PRISMA-P guidelines.<sup>12</sup> The article has been written in accordance with the PRISMA guidelines.<sup>13</sup>

As described in detail in the systematic review protocol, we searched the databases MEDLINE, EMBASE, and PsycINFO. A health science librarian was consulted on the search strategy. The Medical Subject Headings (MeSH terms) 'stroke', 'cerebrovascular disorders', 'delirium', 'confusion' were searched in combination with the words 'cerebrovascular syndrome', 'brain ischemia', 'brain vascular accident', 'cerebrovascular accident', 'confusional state', 'psychosyndrome', 'brain syndrome', 'metabolic encephalopathy'. See review protocol for the exact MEDLINE search string.<sup>11</sup> The searches at EMBASE and PsycINFO were built on the same search words. No date restrictions were imposed on any of the searches and all searches were finalized in August 2017.

Screening, data extraction, and risk of bias assessments were done independently by 2 reviewers (J.S. and J.V.S.) and consensus established. Disagreement was sought to be resolved through discussion between J.S. and J.V.S. If consensus could not be reached, a third reviewer (T.C.) resolved the disagreement.

Study designs eligible for the review were prospective and retrospective observational cohort studies. Study designs excluded from the review were interventional studies, observational studies other than cohort studies, studies with 3 or less patients, and reviews.

To be included, studies had to estimate the delirium incidence, that is, new cases of delirium found during the study period, in a population of patients  $\geq$ 18 years of age admitted with acute stroke as hospital inpatients. Stroke populations with any combination of ischaemic stroke, intracerebral haemorrhages and subarachnoid haemorrhages were eligible. So were populations of patients with symptoms lasting less than 24 hours if they had relevant acute lesions on cerebral imaging. Patients with transient ischaemic attacks without demonstrable acute brain damage on brain imaging were excluded as they had full remission of symptoms and constituted a group which was treated heterogeneously, for example, in some institutions, these patients were admitted to an acute stroke wards and at other places they were handled via outpatient clinics. If a study encompassed patients both fulfilling and not fulfilling the inclusion criteria and the data from the patients fulfilling the inclusion criteria could be extracted for separate analysis, the study was considered eligible.

A 95% confidence interval (CI) for each study's delirium incidence was calculated. The chi square test of heterogeneity was performed and due to significant heterogeneity the DerSimonian and Laird Random Effects Model<sup>14</sup> was used to synthesize the overall delirium incidence estimate. Note that in the DerSimonian and Laird Random Effects Model each study is given a weight based on the number of patients, but the range of weights are compressed as compared with a fixed effects model. Data storage, analyses, and figures were done in Microsoft Excel and RStudio (©2009-2017 RStudio, Inc, Boston, MA, USA).

# Results

A total of 3748 unique titles were identified. A total of 134 articles were read in full length and 30 were included in the review.<sup>15-44</sup> In these 30 articles, 24 unique populations were identified (Figure 1). The discrepancy between the number of articles and the number of unique populations was caused by the fact that the same population was described in more than one article. Thus, 2 populations were described in 2 separate articles and 2 populations were reported on in 3 separate articles. The included studies were published during the years 1987 to 2017 and consisted of 2 retrospective and 22 prospective cohort studies. Table 1 is an overview of the included studies. A total of 21 studies reported a mean for age which was in the range of 51 to 79.2 years. The median age (range of 68-74 years) was available for those 3 studies which did not report a mean age.

## Delirium incidence

The delirium incidence range was 1.4% to 75.6% (see Figure 2). Figure 3 shows a graphic representation of the data synthesis for the delirium incidence. The chi-square test showed a significant heterogeneity across studies ( $\chi^2$ =536.5, *df*=23, *P*<0.0001). Cochrane *Q*=743.5 (*P*<.0001) and *I*<sup>2</sup>=96.9% and the random effects model showed a delirium incidence of 22.8%, 95% CI: 18.2-27.4 (23.9%, 95% CI: 19.5-28.4%, with the 2 retrospective studies removed from the model).

## Assessment tools

In 16 studies, the tools used were the CAM, CAM-ICU, DRS, and DRS-R-98 (exclusively, in combination with each other or in combination with *DSM* criteria). The study by McManus et al<sup>40</sup> reported 2 delirium incidences for the same population; one for the DRS (delirium incidence 26.8%) and one for the CAM (delirium incidence 28.1%). Six studies solely used some version of the *DSM* criteria (1 used *DSM-V*, 3 used *DSM-IV* or *DSM-IV-TR*, and 2 used *DSM-III-R* criteria) and 2 studies used some other specified criteria for delirium (see Table 1).

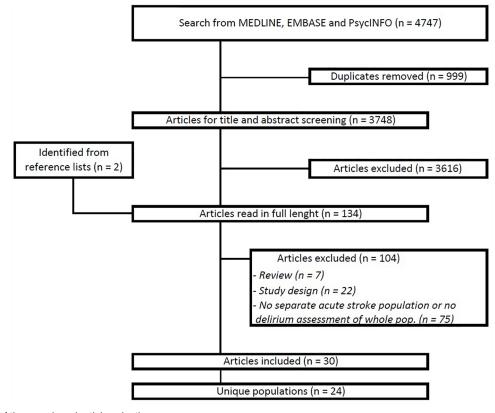


Figure 1. Flowchart of the search and article selection process.

Looking only at the studies using the CAM, CAM-ICU, DRS, and DRS-R-98 (alone or in combinations with each other or in combination with *DSM* criteria), the delirium incidences were within a narrower range of 6.6% to 35.3% (Figure 2).

## Frequency and timing of assessment tool use

In the prospective studies, delirium assessment was done once a day or more in 6 studies. The remaining 16 prospective studies assessed with a smaller frequency, for example, twice a week. The retrospective studies used patient records, either covering the entire admission or limited to days 1 through 7.

Marked in green in Table 1 are the 11 prospective studies that assessed roughly once a day (eg, daily except Sundays) or more often. Looking at the table, comparing these 11 studies with those that assessed with a frequency less than roughly daily, there is no discernible pattern with respect to delirium incidence.

## Type of health professional

Information about the type of health professional(s) using a specific tool was available from 20 studies (see Table 1). Study authors were contacted on 8 occasions to clarify the information about which type of health professional had done the delirium assessments in their studies. Nine prospective studies specifically stated that the persons using the tools had been trained to use their specific tool or to apply the delirium

criteria. No specific pattern as to whether the type of health professional doing the assessments had an influence on the delirium incidence was discernible.

#### Quality assessment

A panel of questions was designed to perform a quality assessment of the included studies. The questions were taken from Watt et al<sup>45</sup> and were, for some questions, modified slightly. Questions on exclusion of aphasic patients, delirium assessment before inclusion into a study, and the timeframes used for delirium assessments were added. Table 2 shows the questions and the answers for each study in this review. Of the 24 studies, 5 did not have clearly described characteristics regarding age, disease status, and preexisting cognitive impairment. The recruitment strategy was nonconsecutive in one population and unclear in another three. The inclusion and exclusion criteria were judged not to allow for appropriate selection of the respective studies' target populations in 2 cases (unclear in 3 cases) and aphasic patients were excluded in 9 studies. There were missing data on delirium assessments in 11 studies and 2 of these did not document reasons for this missing data. The delirium assessment was not performed by an independent assessor in 8 studies (unclear in an additional 6 studies) but only in 2 studies were the delirium assessments not done in a standard manner. No studies had an assessment negative for delirium before a patient entered the study and only 2 studies described the time frame used for a given tool's application.

Table 1. Summary of included studies.

| STUDY AND YEAR                           | COUNTRY                   | STROKE TYPES        | SIZE (N) | AGE, Y: MEAN (SD),<br>RANGE                  | STUDY DESIGN  | DELIRIUM CONSIDERED<br>PRESENT IF                                 | FREQUENCY AND TIMING OF<br>TOOL USE  | TYPES OF HEALTH<br>PROFESSIONALS<br>USING THE TOOL                              | DELIRIUM<br>INCIDENCE,<br>% |
|--|---------------------------|---------------------|----------|--|---------------|---|--|---|-----------------------------|
| Reijneveld et al. <sup>26</sup>          | Netherlands               | SAH                 | 646      | 51, <i>34-66</i> ª                           | Retrospective | Prespecified criteria for ACS fulfilled <sup>b</sup>              | Patient records from time of admission                                     | Not disclosed   | 1.4                         |
| Melkas et al. <sup>22</sup>              | Finland                   | AIS                 | 263      | 70.8 (7.4), 55-85                            | Retrospective | DSM-IV criteria fulfilled   | Medical records and nurses'<br>notes from between days 1<br>and 7          | A senior psychiatrist   | 19                          |
| Lim et al. <sup>15</sup>                 | Republic of<br>Korea      | AIS                 | 576      | 65.2, 23-93                                  | Prospective   | CAM to screen, if positive<br>then evaluation with<br>DRS-R-98°   | Daily  | Not disclosed   | 9.9                         |
| Dahl et al. <sup>23</sup>                | Norway                    | AIS, ICH, SAH       | 178      | 73   | Prospective   | CAM to screen, if positive<br>then evaluation with <i>DSM-IV</i>  | CAM was used twice daily   | CAM used by nurses,<br>DSM-IV criteria<br>applied by a<br>neurologist           | 10.1                        |
| Alvarez-Perez and<br>Paiva <sup>17</sup> | Portugal                  | AIS,<br>haemorrhage | 1072     | Median 68, Q1: 77,<br>Q3: 83                 | Prospective   | DSM-V criteria fulfilled  | Near continuously observed   | Nurses and other<br>medical staff   | £                           |
| Caeiro et al. <sup>44</sup>              | Portugal                  | AIS, ICH            | 190      | Delirium group: 63.6<br>(12.8), <i>33-84</i> | Prospective   | DRS score of ≽10 points and<br>DSM-IV-TR criteria fulfilled       | Day 1 whenever possible  | A psychologist  | 11.6                        |
| Oldenbeuving<br>et al. <sup>36</sup>     | Netherlands               | AIS, ICH            | 527      | 72, 29-96                                    | Prospective   | CAM positive  | Between days 2 and 4 and again between days 5 and 7                        | Neurological<br>residents   | 11.8                        |
| Lees et al. <sup>19</sup>                | ЛК                        | AIS,<br>haemorrhage | 101      | Median 74,<br>IQR:64-85 <sup>d</sup>         | Prospective   | CAM positive  | Once between days 1 and 4 after admission                                  | Four medical<br>students undertaking<br>a period of elective<br>study in stroke | 11.9                        |
| Oldenbeuving<br>et al. <sup>33</sup>     | Netherlands               | AIS, ICH            | 273      | 72, 31-99                                    | Prospective   | CAM positive  | Between days 2 and 4 and again between days 5 and 7                        | DM  | 15                          |
| Caeiro et al. <sup>42</sup>              | Portugal                  | SAH                 | 68       | 55.5 (14.5), 27-86                           | Prospective   | DRS score of ≫10 points and<br>DSM-IV-TR criteria fulfilled       | Day 1 whenever possible (all patients were scored within the first 4 days) | A psychologist  | 16.2                        |
| Kozak et al. <sup>31</sup>               | Turkey                    | AIS                 | 60       | 66.2 (12.5), 31-89                           | Prospective   | DRS score of ≽10 points and<br>DSM-IV criteria fulfilled          | Daily  | Same psychiatrist for every patient   | 18.3                        |
| Hénon et al. <sup>27</sup>               | France                    | AIS, ICH            | 202      | 75, 42-101                                   | Prospective   | DRS score of ≫10 points   | Day 1 and 2 for all, repeated if clinical change                           | Neurologist   | 24.3                        |
| Sheng et al. <sup>25</sup>               | Australia                 | AIS, ICH            | 156      | 79.2 (6.7)                                   | Prospective   | DSM-IV criteria fulfilled   | Once within 3 days of admission  | Same MD for all patients  | 25                          |
| Dostović et al. <sup>24</sup>            | Bosnia and<br>Herzegovina | AIS, ICH, SAH       | 233      | 70 (11.3)                                    | Prospective   | DRS-R-98 score >16 points<br>and <i>DSM-IV</i> criteria fulfilled | Once within 4 days after<br>stroke onset                                   | A neuropsychiatrist   | 25.3                        |
|  |                           |                     |          |  |               |   |  |   | (Continued)                 |

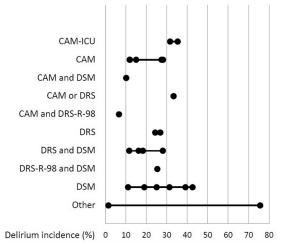
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| STUDY AND YEAR                     | COUNTRY           | STROKE TYPES        | SIZE (N) | AGE, Y: MEAN (SD),<br>RANGE                                    | STUDY DESIGN | DELIRIUM CONSIDERED<br>PRESENT IF                           | FREQUENCY AND TIMING OF<br>TOOL USE   | TYPES OF HEALTH<br>PROFESSIONALS<br>USING THE TOOL  | Delirium<br>Incidence,<br>% |
|------------------------------------|-------------------|---------------------|----------|--|--------------|---|---|---|-----------------------------|
| Miu and Yeung <sup>20</sup>        | China             | AIS, ICH, SAH       | 314      | 72.9 (10.3), 50-94   | Prospective  | CAM positive  | Daily between days 1 and 5  | Same geriatrician for<br>all patients   | 27.4                        |
| Kara et al. <sup>21</sup>          | Turkey            | AIS, ICH, SAH       | 150      | Delirium group: 68<br>(1.9). Non-delirium<br>group: 61.2 (1.3) | Prospective  | DRS score of ⇒10 points and<br>DSM-IV-TR criteria fulfilled | Close monitoring the first<br>5 days  | Not disclosed   | 28                          |
| McManus et al. <sup>41</sup>       | Ч                 | AIS, ICH            | 82       | 66.4 (15.9), 24-97   | Prospective  | CAM positive or DRS score<br>of ≥10 points                  | First assessment within first<br>4 days and then weekly until<br>a max. of 4 weeks or<br>discharge      | One assessor – a<br>senior Registrar in<br>Geriatric Medicine   | CAM: 28.1<br>DRS: 26.8      |
| Olsson et al. <sup>29</sup>        | Sweden            | AIS                 | 16       | 71 (11)  | Prospective  | DSM-III-R criteria fulfilled                                | Repeated assessments<br>between days 3 and 7  | MDs   | 31.3                        |
| Naidech et al. <sup>32</sup>       | NSA               | ICH                 | 98       | 63 (13.8) <sup>e</sup>   | Prospective  | CAM-ICU positive  | Twice daily   | ICU nurses  | 31.6                        |
| Ojagbemi et al. <sup>16</sup>      | Nigeria           | AIS,<br>haemorrhage | 66       | 61.1 (12.9)  | Prospective  | CAM positive or DRS score<br>of  ≥10 points                 | Two assessments within the<br>first 7 days of admission (a<br>maximum of 4 days between<br>assessments) | CAM: A research<br>assistant. DRS: A<br>psychiatrist  | 33.3                        |
| Rosenthal et al. <sup>18</sup>     | NSA               | ICH                 | 150      | 63.5 <sup>f</sup>  | Prospective  | CAM-ICU positive  | Twice daily   | Nursing staff   | 35.3                        |
| Fassbender<br>et al. <sup>28</sup> | Germany           | AIS                 | 23       | Median 72, range<br>39-89                                      | Prospective  | DSM-III-R criteria fulfilled                                | Observations during the first days of hospitalization   | Not disclosed   | 39.1                        |
| Mitasova et al. <sup>38</sup>      | Czech<br>Republic | AIS, ICH            | 129      | 71.2 (11.5), 30-93   | Prospective  | DSM-IV criteria fulfilled                                   | Daily except Sundays  | A team of at least 1<br>neurologist and 1<br>neuropsychologist, if<br>necessary also a<br>psychiatrist and/or a<br>speech therapist | 42.6                        |
| Mori and<br>Yamadori <sup>30</sup> | Japan             | AIS                 | 41       | 68.2 (10.9), <i>18-85</i>                                      | Prospective  | Prespecified criteria for ACS or AAD fulfilled9             | Within 2 weeks of onset   | Staff neurologists  | 75.6                        |

Abstract actual agriced delinum: ACS, acute contrusional state: AIS, acute ischaemic stroke. CAM: Corrtusion Assessment Method: Contrusion Assessment Method for the intensive care unit: DRS, Delinum Hating Scale: DRS-RH-06, DISM-IV-FR, Diagnostic and Statistical Manual of Mental Discordes (Furth Edition), DSM-IV-FR, Diagnostic and Statistical Manual of Mental Discordes (Furth Edition), DSM-IV-FR, Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-IV Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Diagnostic and Statistical Manual of Mental Discordes (Fifth Edition); DSM-V Discordes (Figth Edition); DSM-V Discordes (Fifth Edition); DSM-V Discordes (Fifth

#### Discussion

In our review, we found a large range in delirium incidences from 1.4% to 75.6%. It must be emphasized that none of the studies tested a certain screening method against a predefined golden standard. The study by Mitasova et al<sup>38</sup> was a study



**Figure 2.** Figure illustrating the delirium incidences categorized according to which assessment tools were used in each of the studies. Note that there are 4 studies using solely the CAM, 2 studies found incidences of 27.4% and 28.1%, respectively, and are almost nondiscernible from each other on the figure. Please note that the study by McManus et al is depicted twice, once for the CAM (delirium incidence 28.1%) and once for the DRS (delirium incidence 26.8%). Abbreviations: CAM, Confusion Assessment Method; CAM-ICU, Confusion Assessment Method for the intensive care unit;RS, Delirium Rating Scale; DRS-R-98, Delirium Rating Scale Revised 1998; DSM, *Diagnostic and Statistical Manual of Mental Disorders* (any edition).

comparing blinded assessments between a Czech version of the CAM-ICU and the *DSM-IV*; however, they reported delirium incidence for the *DSM-IV* only and therefore only this was included into this review. Based on the data in the included studies, we were able to calculate an overall estimate of delirium incidence of approximately 23%.

Even though all populations are acute stroke populations, heterogeneity across populations should be assumed. We did not do any test for a potential statistically significant difference between subgroups (ie, studies using the CAM, DRS, or DRS-R-98 vs the rest) as the studies were of observational design and the heterogeneity was, as mentioned, significant. This means that the subgroup pooled estimates and *I*<sup>2</sup> values might very well had turned out to be different for other reasons than the chosen subgrouping because of unknown confounders and any confident conclusions of such tests would therefore be impossible to make.

However, the narrower range of incidences from studies using the CAM, CAM-ICU, DRS, or DRS-R-98 generates the hypothesis that using standardized and validated delirium assessment tools such as the CAM, CAM-ICU, DRS, or DRS-R-98, a more precise detection of acute delirium may be obtained in patients with acute stroke. We emphasize that results from this review do not allow actual comparison of groups of studies with each other due to the heterogeneity of the studies. Only one study in this review compared 2 tools directly with each other. Further studies comparing delirium assessment tools directly with each other are needed.

A study by Infante et al<sup>46</sup> was not included into this review, because it had patients with transient ischaemic attack

| Study                     | Total number of patients | Number of delirious patients |   | Delirium incidence  | Weight |
|---------------------------|--------------------------|------------------------------|---|---------------------|--------|
| Lim et al. 2017           | 576                      | 38                           | <b>.</b>  | 6.6% [4.57;8.62]    | 4.7%   |
| Ojagbemi et al. 2017      | 99                       | 33                           | <b>_</b> _  | 33.3% [24.05;42.62] | 4.0%   |
| Alvarez-Perez et al. 2017 | 1072                     | 118                          |   | 11% [9.13;12.88]    | 4.7%   |
| Rosenthal et al. 2017     | 150                      | 53                           | _ <b>_</b>  | 35.3% [27.68;42.98] | 4.2%   |
| Kozak et al. 2017         | 60                       | 11                           |   | 18.3% [8.54;28.12]  | 3.9%   |
| Oldenbeuving et al. 2014  | 273                      | 41                           |   | 15% [10.78;19.26]   | 4.6%   |
| Lees et al. 2013          | 101                      | 12                           |   | 11.9% [5.57;18.19]  | 4.4%   |
| Miu et al. 2013           | 314                      | 86                           |   | 27.4% [22.46;32.32] | 4.5%   |
| Kara et al. 2013          | 150                      | 42                           |   | 28% [20.81;35.19]   | 4.3%   |
| Naidech et al. 2013       | 98                       | 31                           | <b>_</b>  | 31.6% [22.43;40.84] | 4.0%   |
| Melkas et al. 2012        | 263                      | 50                           | -   | 19% [14.27;23.75]   | 4.5%   |
| Mitasova et al. 2012      | 129                      | 55                           | <b>_</b>  | 42.6% [34.1;51.17]  | 4.1%   |
| Dahl et al. 2010          | 178                      | 18                           |   | 10.1% [5.68;14.54]  | 4.6%   |
| McManus 2009              | 82                       | 23                           |   | 28.1% [18.33;37.77] | 3.9%   |
| Dostovic et al. 2009      | 233                      | 59                           |   | 25.3% [19.74;30.91] | 4.5%   |
| Oldenbeuving et al. 2008  | 527                      | 62                           | <b>•</b>  | 11.8% [9.01;14.52]  | 4.7%   |
| Sheng et al. 2006         | 156                      | 39                           | _ <b>_</b>  | 25% [18.2;31.8]     | 4.3%   |
| Caeiro et al. 2005        | 68                       | 11                           |   | 16.2% [7.42;24.93]  | 4.1%   |
| Caeiro et al. 2004        | 190                      | 22                           |   | 11.6% [7.03;16.13]  | 4.6%   |
| Reijneveld et al. 2000    | 646                      | 9                            | •   | 1.4% [0.49;2.3]     | 4.8%   |
| Hénon et al. 1999         | 202                      | 49                           |   | 24.3% [18.35;30.17] | 4.4%   |
| Fassbender et al. 1994    | 23                       | 9                            |   | 39.1% [19.18;59.08] | 2.5%   |
| Olsson et al. 1992        | 16                       | 5                            |   | 31.3% [8.54;53.96]  | 2.2%   |
| Mori et al. 1987          | 41                       | 31                           |   | 75.6% [62.46;88.75] | 3.4%   |
| Total                     | 5647                     | 907                          | •   | 22.8% [18.24;27.41] | 100%   |
|                           |                          |                              | 0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 89<br>Percent |                     |        |

Figure 3. Forest plot. The size of each square visualizes a study's percentile weight, the horizontal bars indicate the 95% confidence interval (CI), the centre of the diamond indicates the overall delirium incidence estimate, and the width of the diamond represents the 95% CI of the overall estimate.

|                                       | WERE THE<br>CHARACTERISTICS<br>CHARACTERISTICS<br>(AGE, DISEASE STATUS,<br>CONSIDERATION OF<br>PREEXISTING COGNITIVE<br>IMPAIRMENT) OF<br>PATIENTS CLEARLY<br>DESCRIBED? | WAS THE<br>RECRUITMENT<br>STRATEGY<br>CONSECUTIVE? | DID THE INCLUSION<br>AND EXCLUSION<br>CRITERIA ALLOW<br>FOR APPROPRIATE<br>SELECTION OF<br>THE TARGET<br>POPULATION FOR<br>THE STUDY? | EXCLUSION<br>OF APHASIC<br>PATIENTS? | WAS THERE<br>ADEQUATE<br>DOCUMENTATION<br>FOR REASONS<br>OF MISSING DATA<br>(SKIP IF QUESTION<br>NOT APPLICABLE)? | WAS THE DELIRIUM<br>ASSESSMENT<br>PERFORMED BY<br>AN INDEPENDENT<br>ASSESSOR (IE, NOT<br>A MEMBER OF THE<br>CARE TEAM)? | WAS THE<br>DELIRIUM<br>ASSESSMENT<br>DONE IN A<br>STANDARD<br>MANNER<br>FOR ALL<br>PARTICIPANTS? | WAS THERE AN<br>ASSESSMENT<br>NEGATIVE<br>FOR DELIRIUM<br>BEFORE<br>PATIENTS<br>ENTERED THE<br>STUDY? | WAS THE TIME<br>FRAME FOR<br>THE TOOL<br>APPLICATION<br>DESCRIBED? |
|---------------------------------------|--|--|---|--------------------------------------|---|---|--|---|--|
| Reijneveld et al. <sup>26</sup>       | Yes  | Yes  | No  | No                                   | Yes   | Yes   | Yes  | No  | No   |
| Melkas et al. <sup>22</sup>           | Yes  | Yes  | Yes   | Yes                                  | No  | Yes   | Yes  | No  | Yes  |
| Lim et al. <sup>15</sup>              | Yes  | Yes  | Unclear   | No                                   | NA  | Unclear   | Yes  | No  | No   |
| Dahl et al. <sup>23</sup>             | Yes  | Yes  | Yes   | No                                   | Yes   | No  | Yes  | No  | No   |
| Alvarez-Perez and Paiva <sup>17</sup> | No   | Unclear  | Yes   | No                                   | NA  | No  | Yes  | No  | No   |
| Caeiro et al. <sup>44</sup>           | Yes  | Yes  | Yes   | No                                   | No  | Yes   | Yes  | No  | No   |
| Oldenbeuving et al. <sup>36</sup>     | Yes  | Yes  | Yes   | No                                   | Yes   | No  | Yes  | No  | No   |
| Lees et al. <sup>19</sup>             | Yes  | Yes  | Yes   | No                                   | Yes   | Yes   | Yes  | No  | No   |
| Oldenbeuving et al. <sup>33</sup>     | Yes  | Yes  | Yes   | Yes                                  | NA  | No  | Yes  | No  | No   |
| Caeiro et al. <sup>42</sup>           | Yes  | Yes  | Yes   | No                                   | NA  | Yes   | Yes  | No  | No   |
| Kozak et al. <sup>31</sup>            | No   | Yes  | Yes   | Yes                                  | NA  | Yes   | Yes  | No  | No   |
| Hénon et al. <sup>27</sup>            | Yes  | Yes  | No  | No                                   | NA  | Unclear   | Yes  | No  | No   |
| Sheng et al. <sup>25</sup>            | Yes  | Yes  | Yes   | Yes                                  | Yes   | No  | Yes  | No  | Yes  |
| Dostović et al. <sup>24</sup>         | Yes  | Yes  | Yes   | Yes                                  | NA  | Unclear   | Yes  | No  | No   |
| Miu and Yeung <sup>20</sup>           | Yes  | Yes  | Unclear   | No                                   | NA  | Unclear   | Yes  | No  | No   |
| Kara et al. <sup>21</sup>             | Yes  | Yes  | Yes   | Yes                                  | NA  | Unclear   | Yes  | No  | No   |
| McManus et al. <sup>41</sup>          | Yes  | Yes  | Yes   | No                                   | Yes   | Yes   | Yes  | No  | No   |
| Olsson et al. <sup>29</sup>           | No   | No   | Unclear   | No                                   | NA  | Yes   | Yes  | No  | No   |
| Naidech et al. <sup>32</sup>          | Yes  | Yes  | Yes   | No                                   | Yes   | No  | Yes  | No  | No   |
| Ojagbemi et al. <sup>16</sup>         | Yes  | Yes  | Yes   | Yes                                  | NA  | Yes   | Yes  | No  | No   |
| Rosenthal et al. <sup>18</sup>        | No   | Unclear  | Yes   | No                                   | Yes   | No  | Yes  | No  | No   |
| Fassbender et al. <sup>28</sup>       | No   | Unclear  | Yes   | No                                   | NA  | Unclear   | No   | No  | No   |
| Mitasova et al. <sup>38</sup>         | Yes  | Yes  | Yes   | No                                   | Yes   | Yes   | Yes  | No  | No   |
| Mori and Yamadori <sup>30</sup>       | Yes  | Yes  | Yes   | Yes                                  | NA  | No  | No   | No  | No   |

Table 2. Quality assessment table.

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Abbreviation: NA, not applicable.

(symptoms lasting less than 24 hours and no acute cerebral lesions demonstrated on imaging) intermixed in its population but is still worth mentioning. The study found a delirium incidence of 52% when using the 4AT instrument but a lower incidence of 32% when the DSM-V criteria were applied to the same patients by the same neurologist. The 4AT was available for the first time in 2011 and is designed as an instrument for rapid delirium screening.<sup>47</sup>

Concerning the types of health professionals using the tools and the delirium incidence found, no discernible pattern was evident from our review. As mentioned above, the heterogeneity among the studies was considerable and no subgroup analyses were therefore done. To our knowledge, no previous studies have specifically addressed the possible influence of the type of health professional on the detection rate of delirium. Yet, this question must remain unanswered.

Due to the fluctuating symptoms of delirium, it could be speculated that the frequency of assessments will have an impact on the detection rate of delirium. However, due to the multitude of different tools in use across these 22 prospective studies, no firm conclusions can be made for any of the tools as to whether there is a correlation between the frequency and delirium detection.

Several sources for bias may exist. An important bias is the fact that the studies had clearly different types of settings and spanned a rather wide range of publication years. For example, some were conducted in modern stroke wards, others in neurological semi-intensive care units and others again in older settings. The types of stroke also differed across studies. Some reported both on ischaemic and haemorrhagic strokes, others only one type. The underlying stroke etiology itself might also in some situations contribute to the development of delirium. Another potential bias may come in- or exclusion of aphasic patients. The exclusion of aphasic patients may result in a lower incidence of delirium. Thought content and attention may be harder to judge when language is impaired, and this makes severely aphasic patients more difficult to assess for delirium. A validated tool for assessing severely aphasic patients is obviously needed. The CAM-ICU<sup>10</sup> does not require the patient to speak but severe aphasia might still interfere with patient's ability to understand what is being said without confusion being present. In addition, perceptual deficits other than aphasia might also make a delirium assessment difficult. Data on perceptual deficits other than aphasia were not collected in this review.

Assessment for delirium before the patients entered a given study was not done in any of the included studies. It is quite conceivable that some patients might have been delirious before inclusion (and before admission or before their stroke). Another bias might come from the time frames used when evaluating patients for the presence of delirium. For a given tool, some studies might consistently have used longer time frames (eg, looking back 24 hours instead of 8 hours) than others. The effect this might have on the incidence of delirium is unknown.

## Conclusions

Delirium is a common complication in acute stroke. The wide ranges of delirium incidence reported in the different stroke studies imply that delirium can be difficult to recognize in patients with stroke, leading to both under- and overdiagnosis.

No firm conclusions about a possible correlation of choice of tool, assessment frequency, and delirium incidence could be made due to the great heterogeneity of the study populations. Only 1 study compared 2 tools directly with each other. Further studies comparing delirium assessment tools directly with each other are needed.

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## **Author Contributions**

JS and JVS researched literature. JS, JVS, and TC conceived the study. All authors were involved in protocol development and data analysis. JS wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

#### Ethical approval

Ethical approval was not sought for this article because there was no indication that any of the studies in review posed any ethical dilemma.

## **Informed consent**

Informed consent was not sought for this article because no patient identifiable data were obtained for this review from any of the studies reviewed. All studies included into the review featured anonymized patient data.

#### Guarantor

J.S. is the guarantor of this study.

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