

Systematic Review

4 AT? delirium assessment tool in hospitalized non-ICU patients (≥65years): A systematic review on validity and reliability

Comment [m1]:

Comment [m2]: the title should not contain not clear words

ABSTRACT

Background: Delirium is a frequent acute neuropsychiatric illness that affects attention, consciousness, and cognition. **Objectives:** The 4AT evaluation tool's validity and reliability in hospitalized non-ICU patients over 65 were assessed in this systematic study. **Method:** PRISMA? guidelines and the PICO? framework were used, and relevant research papers were found utilizing several databases (PubMed, Scopus, Web of Sciences, and ScienceDirect). The Mixed Methods Appraisal Tool was used to evaluate the study's quality. **Results:** A257 relevant publications were found, and only ten articles were selected based on inclusion criteria after the screening. Several studies were reported from various regions, including Asia, Europe, Canada, and Australia. Furthermore, studies found varying prevalence levels for 4AT and control groups, with the greatest for the 4AT group being 40.32%. Moreover, most research employed DSM-5 criteria, while some relied on CAM, DSM-4, and Psychiatric examination by qualified clinicians. Meanwhile, the sensitivity varied from 70% to 100%, and the specificity ranged from 71.6% to 99.2%. In contrast, other assessment tools, such as CAM and OBS, also demonstrated sensitivity and specificity. The main advantage was the time taken to complete the 4AT tool, which required 2-3 minutes, whereas the other tools took 3.6 and 12.46 minutes, respectively. The 4AT tool was a rapid, validated, easy patient assessment tool. In addition, it was found to improve delirium diagnosis. **Conclusion:** The tool has been found to have good sensitivity and specificity, and it may be completed quickly by non-specialists.

Comment [m3]: first mention of abbreviation should write the full name

Comment [m4]: first mention of the abbreviation should write the full name

Comment [m5]: first mention of abbreviation should write the full name

Comment [m6]: full names?

Comment [m7]: full name?

Keywords: 4AT delirium assessment tool, sensitivity, specificity, geriatric population, non-ICU patients

Comment [m8]: ? not need in keywords

1. INTRODUCTION

Delirium is a psychiatric illness that causes severe cognitive impairment. This disease frequently strikes older people and can be fatal if left untreated [1]. It is also an acute confusional condition marked by inattention and heightened consciousness [2]. Adverse delirium outcomes, such as the onset of dementia symptoms in preclinical dementia or the acceleration of cognitive loss in those with dementia, may also be delayed by delirium-preventative strategies [2]. However, when it comes to the individual's quality of life (QoL) and ability to function, as well as the societal impact and financial burden of health care, delirium is frequently overlooked [1]. Furthermore, research studies and clinical observations have revealed that delirium may have long-lasting effects. Hence, delirium is a leading cause of functional deterioration, institutionalization, loss of independence, and mortality in older people. Meanwhile, 14% and 56% of all elderly hospital patients suffer from delirium. It is estimated that at least 20% of the 12.5 million individuals > 65 years old hospitalized annually in the United States suffer from delirium-related issues while in hospital [3, 4]. Moreover, delirium was prevalent in 17% aged 85, 21% aged 90, and 39% aged 95 and more. Those without dementia were less likely to have delirium (5%) than those with dementia (52%) [5]. The incidence is also relatively high in long-term care (LTC) facilities and nursing homes. Delirium may have serious repercussions, including an increased chance of hospital death, reduced cognitive function over time, a loss of independence, and an increased likelihood of institutionalization [6]. Among older patients with cognitive impairment, those with delirium had significantly higher hospital expenditures than those without delirium, and this was seen across a diverse population of patients [7]. For instance, in the US, the cost of inpatient delirium was estimated at \$806 and \$24,509 [8]. Furthermore, infections seem to be the most prevalent cause of delirium among the elderly living in the community, followed by medications and hydro electrolytic illnesses [9]. If these risk factors are known, metabolic imbalances may be treated sooner, reducing the duration of delirium [10]. Medication usage for either prevention or therapy is not

supported by strong evidence while non-pharmacological treatments and decreased medication usage for sedation and pain alleviation are advised [11]. Several delirium evaluation instruments have operationalized the primary diagnostic criteria for delirium, although they have mostly remained research tools.

There are several delirium screening and diagnostic methods available [12] such as the Confusion Assessment Method (CAM) for the Intensive Care Unit (CAM-ICU), the Richmond Agitation-Sedation Scale (RASS) for delirium shown good sensitivity and specificity in older patients, the Brief Confusion Assessment Method (bCAM) and the Delirium Triage Screen (DTS) were utilized to construct a rapid two-step approach for delirium monitoring [13]. The assessment tools utilization increases the likelihood of spotting delirium early on, which is crucial for maximizing positive results [14]. The CAM is the most widely suggested screening tool for use in routine clinical care, even though it takes around 10 minutes to complete and has adequate sensitivity and specificity in the hands of skilled personnel [15] because it first necessitates a cognitive assessment like the Modified Mini-Cog [16]. However, the 4 'A's Test (4AT) tool was also used widely. Moreover, the 4AT is a rapid (2 minutes) test for detecting delirium widely adopted as an assessment tool for clinical use worldwide [17]. Due to patient load and cognitive test practice effects, the tool is episodic and is not intended for daily monitoring or daily use for a more extended period [18]. However, it detects delirium without the need for advanced medical knowledge and can be used by anyone [19]. It has been translated into other languages, and validation tests demonstrate good sensitivity and specificity for identifying delirium throughout the screening procedure [20]. The 4AT is designed to consolidate the AMT4 and the Months Backwards test, two existing quick tests for cognitive function, into a single instrument that may be used in place of both.[20] Several studies have assessed 4AT performance since its development [21]. The 4AT has a specificity and sensitivity of 88% for delirium screening, according to a recent meta-analysis that included patients (3702)?[17]. In addition, when used in a clinical setting, 4AT demonstrated adequate sensitivity and specificity [22]. It has various benefits over other assessment tools, such as no specific medical training needed before using the 4AT, and is rapid and straightforward to administer. Patients who cannot communicate can be assessed (patients with severe agitation or drowsiness) [23]. That's why several guidelines[24] and clinical practice [25] now include the 4AT as a recommended tool. Additionally, 95% adherence rates have been reported for the 4AT in the United Kingdom [26], making it the most widely used evaluation tool for delirium there. Unfortunately, there needs to be more information about the therapeutic application of the 4AT, and research has yet to examine the obstacles to taking this test [17]. Similarly, there are different barriers to the use of the 4AT, such as reduced alertness of patients, communication barriers including language, aphasia, dysarthria, and deafness), Considering patients' comfort first includes prioritizing their sleep, treating their pre-existing cognitive impairments, doing unstructured delirium evaluations, and dealing with their essential diseases and end-of-life concerns and symptoms [27]. Moreover, the 4AT is a preliminary screening instrument rather than a final diagnostic tool. Thus, a further in-depth evaluation by an appropriately qualified expert ought to be triggered by a score indicative of delirium [21]. Therefore, the current systematic review aimed to assess the validity and reliability of the 4AT assessment tool in detecting delirium in older patients. Moreover, there were different objectives 1). To determine the validity, reliability, and impact of associated factors on the 4AT tool for detecting delirium in hospitalized patients. 2). To examine the 4AT's efficacy concerning competing delirium screening techniques regarding sensitivity, specificity, and overall accuracy. 3). To evaluate the potential clinical utility of the 4AT tool for detecting delirium in hospitalized patients.

Comment [M9]: Full name?

Comment [M10]: ? what meanig this number?

Comment [M11]: Need more adjustment

Comment [M12]: Unifying and concentrating the aim of review is required

Comment [M13]: Just methodology is enough

Comment [M14]:

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS/ METHODOLOGY

The current study followed the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [28].

2.1. Literature search

The search strategy was established according to the participants, intervention, comparators or controls, and outcome (PICO) framework [29]. Population – Non-ICU above 65 hospitalized patients with suspected delirium intervention – 4AT tool-based delirium assessment. Comparator – Other delirium assessment tools / or clinical assessment by the clinician. Outcome – To what extent 4AT assessment tool is reliably assessing delirium? Different databases such as PubMed, Scopus, Web of Sciences, and ScienceDirect were searched for the relevant research articles using various keywords such as ("Delirium" OR "Dementia" OR "Brain failure") AND ("4 AT assessment tool" OR "4 A's test"

OR "4AT") AND ("hospitalized patients" OR "Older patients"). [MeSH] terms were used, as well as combinations of those terms. The references were reviewed to find studies that validated the 4AT screening tool for delirium in hospital inpatients.

Comment [M15]: ?

2.2. Inclusion criteria

Only studies meeting the following criteria were considered: 1) Original research studies reporting the validity and reliability of the 4AT tool for delirium detection in non-ICU hospitalized patients above 65 years. 2) Non-ICU hospitalized patients above 65 years. 3) Studies published in English. 4) Studies published from 2016 to 2022.

2.3. Exclusion criteria

The following were not considered for inclusion in the study: 1) Studies reporting the validity and reliability of the 4AT tool in non-hospitalized or ICU patients. 2) Studies not published in English. 3) Studies published before 2016.

2.4. Study selection and assessment

There was an independent evaluation of the original research articles, study titles, and abstracts. Two reviewers independently evaluated and assessed the full texts of research papers that met the inclusion requirements, and their conclusions were discussed to reach a consensus. Any disagreements were resolved with the third independent reviewer and settled through agreement if there were any.

2.5. Data extraction

Data extraction was done on the shortlisted studies that matched the requirements for inclusion. A data extraction form was used to record the data extracted after screening the research articles. Two reviewers independently document each study's authors, year of publication, study design, mean age, medical conditions, the prevalence of delirium, an assessment tool used, comparison (tool), sensitivity, specificity, accuracy, conclusion, and limitations.

Sensitivity and specificity are used to assess validation studies. The ability of a diagnostic test to correctly identify patients with the disease or condition being tested for is called its "sensitivity." This means there will be few missed diagnoses with a susceptible test. A diagnostic test's specificity is its ability to exclude false-positive results when the condition is absent. This review utilized the following criteria to rank the sensitivity and specificity of the 4AT tool included in the study: Excellent >95%, Good between 80% and 94%, Average between 70% and 79%, and Poor below 70% [30].

2.6. Quality assessment

Methodological quality assessment of other than Randomized Control Trial (RCTs) research articles was done using the Mixed Methods Appraisal Tool (MMAT), and quality scores were calculated using the approach described.[31] Studies were classified as either low (scoring ≤ 3) or high (score >3) depending on whether participants answered: "yes" (1 point) or "no" (0 points) [32].

2.7. Data analysis

Qualitative analysis was used to compile the articles included in the systematic review. A systematic literature review was performed using the PRISMA checklist, and a detailed procedure for selecting articles was also provided.

3. RESULTS

3.1. Literature searched

In all, 257 relevant papers were identified by a search of the literature using electronic databases (Scopus, ScienceDirect, PubMed, Web of Sciences). Eighty research articles of duplicates had to be removed. We reviewed the titles and abstracts of the remaining 177 publications and eliminated another 164 that didn't pertain to our research. Three of the thirteen full-text articles that remained

after a careful review was dropped for various reasons. (Figure 1). Tables and brief descriptions of the ten publications are provided.

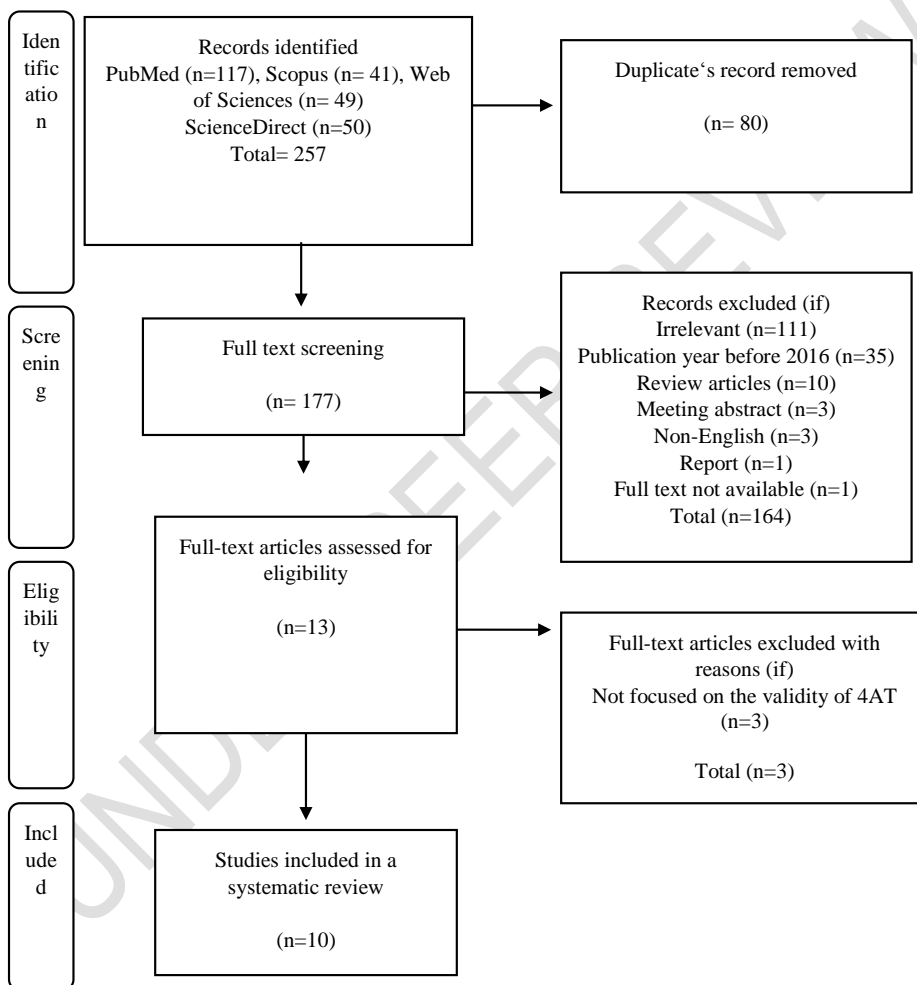


Figure 1. PRISMA flow chart

3.2. Characteristics of studies

Studies were reported from 10 different countries from Asia, Europe, Australia, and Canada (Figure 2), including Iran [33], Canada [34], UK [21], Germany [35], Italy [36], Sweden [14], Norway [22], Australia [37], Spain [38] and Switzerland [19] (Figure 2).

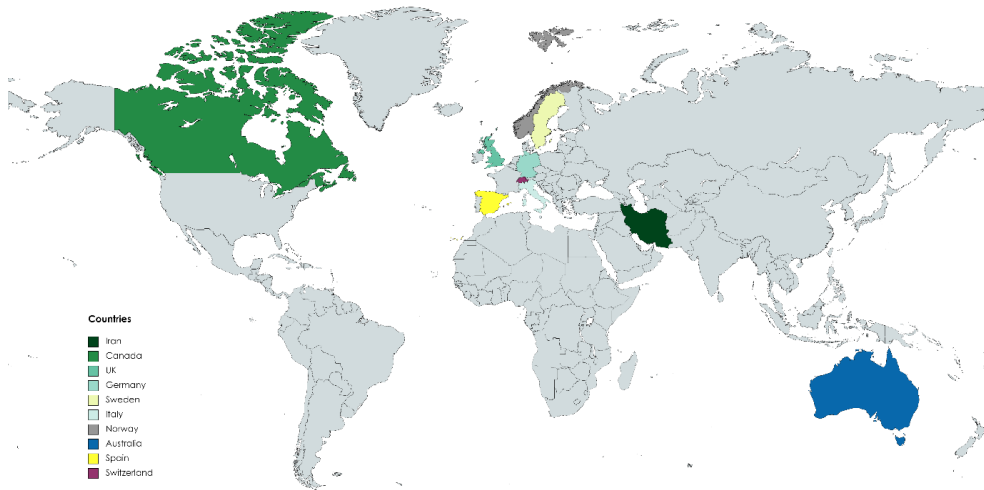


Figure 2. Studies reported from different countries

Most of the studies followed a prospective study design [19, 21, 22, 33, 35, 37, 38], a retrospective study design [36], quantitative descriptive (interview/survey) [34] and mixed method [14]. The maximum number of participants was 785, [21] and the minimum number of participants was 121 [19]. All of the studies include participants >65 years of age. Even then maximum age was 86.6 [22], while the minimum was 69.3 years [33]. Participants in the included studies had different medical conditions, such as dementia, cognitive impairment, and hearing impairment (Table 1). Moreover, in terms of prevalence, studies reported different levels for 4AT and control groups maximum was 40.32% for the 4AT group [38], while the minimum was 4.40% [35]. Most of the studies were conducted in ED?; however, patients from other departments or wards were included, as indicated in Table 1. Furthermore, most studies used DSM-5 criteria, while some used CAM, DSM-4, and Psychiatric evaluation by experienced clinicians [14, 21, 34, 35] (Table 1).

Comment [M16]: 36?

Comment [M17]: 34?

Comment [M18]: ?

UNDER

Table 1. Characteristics of included studies.

Ref.	Study design	N	Age	Medical condition	Prevalence (delirium)	Population tested	Criteria on which based
[33]	A prospective study	164	69.3	Cognitive impairment	NA	ED	DSM-5
[34]	Interview	320	76.8	Cognitive impairment	25%	ED	CAM
[21]	A prospective diagnostic test accuracy	785	81.4	NA	Reference standard=12.1%, 4AT=14.3%, CAM=4.7%	ED, Acute general medical ward, hospital ward	DSM-4
[35]	A perspective	543	51-76	NA	4.40%	PACU	Psychiatric evaluation by experienced clinicians
[14]	Mixed method a qualitative and a quantitative approach	200	80	Dementia	Reference standard=19%, 4AT=18%	Geriatric stroke/multimorbidity, neurology, orthopedic, severe cognitive impairment, and urology.	DSM-4-TR
[36]	A retrospective study	257	>75	Dementia diagnosis, chronic neuroleptics use, hearing impairment	Training sample=16.1%, Testing sample=34.6%	ED Observation Unit	NA
[22]	A prospective study	228	86.6	Dementia	DSM-5=34.2% 4AT=35.1%	Medical geriatric ward	DSM-5
[37]	A prospective diagnostic test accuracy study	271	76.9	Cognitive impairment	16.20%	PACU	DSM-5
[38]	A prospective study	121	>70	Dementia, Cognitive impairment	40.32% (50)	Medical and Surgical	DSM-5
[19]	A prospective, cross-sectional study	116	73	Dementia, neurocognitive disorder patients	mCAM-ED=6.9% A4T=13.8%	ED	DSM

Abbreviation: PACU= Post-Anaesthesia Care Unit; DSM-4, 5=Diagnostic and Statistical Manual on Mental Disorders, 4th and 5th ed. DSM-4-TR= Diagnostic and Statistical Manual on Mental Disorders, 4th ed. Text Revision; NA=Not Available

3.3. AT Sensitivity and Specificity

4AT assessment tool was used in all studies compared to other assessment tools such as CAM, Nu-DSS, OBS, 3D-CAM, and mCAM-ED. 100% sensitivity was shown in the study conducted by Muser, Seiler [19], while the minimum was 70% [14]. In terms of specificity, a maximum of 99.2% was observed in a study conducted by [35] and a minimum of 71.6% [33]. Overall, good accuracy was found across all the studies. However, the maximum accuracy was 93% [33]. In contrast, other tools also showed good sensitivity and specificity (Table 2). Other than sensitivity, specificity, and accuracy, the main benefit was the time taken to complete the 4AT assessment tool. As 4AT tool took 2-3 minutes, and other tools took 3.6 [37] and 12.46 [14] minutes to completion.

Table 2. Sensitivity and specificity of the 4AT assessment tool compared to other tools.

Ref	4 AT assessment tool				Comparative tool				
	Sensitivity	Specificity	Accuracy	Time taken (Min)	Tool used	Sensitivity	Specificity	Accuracy	Time taken (Min)
[33]	95.2%-34.7%	71.6%-97.2%	93%	<2	NA	NA	NA	NA	NA
[34]	84%	74%	Good	NA	CAM	NA	NA	NA	NA
[21]	76%	94%	90%	NA	CAM	40%	100%	NA	NA
[35]	95.5%	99.2%	Good	NA	Nu-DSS	27.3%	99.4%	NA	NA
[14]	70%	92%	88%	2.53	OBS	NA	NA	NA	12.46
[36]	>80%	>90%	NA	NA	NA	NA	NA	NA	NA
[22]	72%	84%	88%	NA	NA	NA	NA	NA	NA
[37]	93%	89%-87%	NA	2.8	3D-CAM	100%	93%-91%	Excellent	3.6
[38]	96%	83.1%	91.80%	NA	Unclear	NA	NA	NA	NA
[19]	100%	93%	NA	NA	mCAM-ED	NA	NA	NA	NA

Abbreviations: NA=Not Available; CAM=Confusion Assessment Method; Nu-DSS=Nurse Delirium Screening Scale; OBS=Organic Brain Syndrome Scale

3.4. Outcomes

According to Table 3, the 4AT tool was a rapid, validated, easy assessment tool for patients. In addition, it was found to improve delirium diagnosis [21], especially in older patients [36]. Moreover, it can be used in different departments, such as emergency units of various wards [34] and PACU [37]. However, the 4AT has a significant false-positive rate in this initial comparison, which may need further in-depth examinations [19].

Even though, with a high level of sensitivity and specificity, there are still limitations such as sample size, generalizability, response rate, etc. (Table 3).

Table 3. Included studies' conclusions and limitations.

Ref	Conclusion	Limitations
[33]	The findings supported the validity of the 4AT and its applicability.	NA
[34]	ED?delirium and cognitive impairment screening is rapid and accurate using the 4AT-F. Its quick administration time permits routine screening of patients at risk of delirium without considerably increasing ED staff effort.	Underrepresentation of participants, methodological biasness.
[21]	The short, pragmatic 4AT may improve delirium diagnosis in everyday clinical treatment.	Selection process, researcher bias.

[35]	These data imply that the 4AT is a reliable post-anesthesia care unit delirium screening tool.	Single center, did not perform two blinded assessments.
[14]	The Swedish version of 4AT is reliable for diagnosing delirium in hospitalized patients across medical specialties and professional levels.	Underestimation of the delirium rates, under-reporting cognitive impairment,
[36]	Risk assessment tools may assist older ED patients in recognizing delirium.	The timing of delirium development data is not available.
[22]	Clinically, 4AT demonstrated good sensitivity and specificity.	Study design, reference test was not blinded, generalizability.
[37]	Screening tools like the 3D-CAM and the 4AT may be utilized to identify delirium in the PACU's elderly population because of their high sensitivity and specificity.	The single-center study did not assess the delirium severity, underrepresentation of dementia patients, and no screening tools feasibility was performed.
[38]	The 4AT-ES showed excellent validity, sensitivity, and specificity	Absence of external criterion, not calculated index of interrater reliability, small sample size.
[19]	The 4AT has a significant false-positive rate in this initial comparison, which may need further in-depth examinations.	Response rate, a very heterogeneous sample, also includes neurocognitive disorder patients.

Abbreviations: NA=Not Available; ED=Emergency Department; CAM=Confusion Assessment Tool; PACU= Post-Anaesthesia Care Unit

3.5. Quality assessment

The quality of the listed studies' methodology was evaluated using the Mixed Methods Appraisal Tool (Table 4 and Appendix 1). You may find the questions in Appendix 1. All the investigations were of excellent methodological quality, whether prospective, retrospective, quantitative descriptive (interview/survey) or mixed methods.

Table 4. Quality assessment of included studies.

Ref.	Study design	MMAT Criteria for different studies				
		3.1	3.2	3.3	3.4	3.5
[33]	A Prospective study design	Yes	Yes	Yes	Yes	Yes
[21]	A Prospective study design	No	Yes	Yes	Yes	Yes
[35]	A Prospective study design	Yes	Yes	Yes	Yes	Yes
[36]	A Retrospective study design	Yes	Yes	Yes	Yes	Yes
[22]	A Prospective study design	Can't tell	Yes	Yes	Yes	Yes
[37]	A Prospective study design	Yes	Yes	Yes	Yes	Yes
[38]	A Prospective study design	Yes	Yes	Yes	Yes	Can't tell
[19]	A Prospective study design	No	Can't tell	Yes	Yes	Yes
		4.1	4.2	4.3	4.4	4.5
[34]	Quantitative descriptive (Interview/survey)	Yes	No	Yes	Yes	Yes
		5.1	5.2	5.3	5.4	5.5
[14]	Mixed Method	Yes	Yes	Yes	Yes	Yes

4. DISCUSSION

Recent studies continue to indicate the underdetection of delirium, making it difficult to identify [39]. The accessibility of approved evaluation tools used in clinical practice is crucial in enhancing detection. There are different validated assessment tools, such as the CAM, the Delirium Rating Scale (DRS), OBS or 4AT are often used by healthcare providers to identify delirium because of their specificity in measuring the symptoms and indicators of delirium. These tools help monitor the efficacy of interventions and ensure the right people get the right treatments. The main advantage of using

well validated tool to minimize the risk of misdiagnosis or underdiagnosis of delirium, which offers a consistent and objective approach to examining patients [40]. As well as, it facilitates enhanced communication between healthcare providers on a patient's status and treatment, leading to better-coordinated care. All of the assessment tools has its own benefits and limitations however, the 4AT's reliability and validity as a delirium evaluation tool have been shown by extensive research. Thus, this systematic study sought to evaluate the validity, accuracy and precision of the 4AT assessment tool for identifying delirium in the elderly (>65 years) population.

In the present study, there were different levels of prevalence for 4AT and control groups maximum was 40.32% for the 4AT group and there was very minor difference when results of 4AT compared to standard reference diagnosis test. Question can arise, why 4AT is better or has very minor difference when compared with standard reference assessment tools. The possible explanation can be that the diagnostic criteria employed for delirium in the various instruments may account for some variation. The 4AT identifies delirious patients by testing them across four different cognitive domains: awareness, orientation, attention, and sudden changes in cognition. Other diagnostic criteria, such as behavioral or perceptual shifts, may be used by alternative reference tools. Another factor can be the education and experience of the medical staff making the diagnosis. Physicians with differing degrees of experience and training in recognizing delirium may interpret their patients' replies differently. Another study also reported the similar results, the prevalence of delirium was 12.1% based on the reference standard, 14.3% based on the 4AT, and 4.7% based on the CAM [21]. In contrast, overall, 24.2% (95% CI: 17.8-32.1%; range: 10.5%-61.9%) of people were diagnosed with delirium using 4AT diagnosis tool [17].

In the present study, maximum 100% sensitivity, 99.2% specificity and good accuracy was observed when compared with other assessment tool such as CAM, OBS. Our findings are in line with the findings of another study, when reference standard delirium was diagnosed by a positive 4AT score (> 3), which had a 95% specificity [95% CI 92% to 97%] and a sensitivity of 76% [95% CI 61% to 87%] [41]. In addition, high sensitivity and specificity for predicting delirium in ED patients have been shown in validation studies of 4AT [34, 42]. Moreover, the prevalence of delirium was detected with a sensitivity of 90% and a specificity of 84% in a validation study of elderly inpatients (n = 234) [20]. Sensitivity for diagnosing delirium was 100% (n = 110), and specificity was 82% (n = 110) in another investigation of stroke patients [43]. Indeed, the 4AT showed promising results when applied to patients with a dual diagnosis of dementia and delirium, but it needs further research [30]. Meanwhile, there has been a rise in website views, and the 4AT has been translated into various languages such as French [34], Swedish [14], Spanish [38]. The 4AT is featured in several international and national policy statements and recommendations [24]. Delirium specialists or trained research assistants have conducted 4AT in various studies, although it has often been done after patients have been admitted to the hospital. Depending on the operators and the assessment time, the 4AT's validity may suffer in various contexts [44]. There may be different reasons for the 4AT's high sensitivity and specificity, come in part from the fact that it accounts for attention, acute alterations in cognition, and altered degrees of consciousness—all known to be linked with delirium. The 4AT's ease of use and adaptability to different situations make it a valuable resource for healthcare providers. Since the 4AT is short and to the point, it may be used for more frequent clinical tests, contributing to its improved sensitivity and specificity. In addition, because of this, the technique may identify delirium in individuals who may have trouble describing their condition due to factors like severe cognitive impairment or a language barrier [27]. Finally, the 4AT's accuracy and reliability as a delirium assessment tool have been established via comprehensive validation across a variety of hospital settings and patient types [18, 45]. Our findings also demonstrated that the 4AT test took 2-3 minutes while other test took from 3 to 12.46 minutes, which is another advantage of 4AT over other tools. Even though, a clinician's professional judgment should always be utilized in tandem with any evaluation instrument since no single tool is foolproof. Therefore, further research is required to investigate its applicability in other contexts.

Our study's strength is that it includes publications on older adults experiencing cognitive impairment and delirium; patient populations are often left out of clinical investigations. In addition, we looked at using a delirium screening tool, 4AT, in several hospital wards upon admission to the ED. However, there are several limitations such as, the diagnostic accuracy of the 4AT was evaluated by looking at data from both prospective and retrospective investigations. Despite the fact that selection bias is a major problem in retrospective research. Moreover, in order to be as thorough as possible, we included studies that used either CAM, DSM-IV, or DSM-V criteria, as their reference standard,

despite the fact that the Cochrane criteria encourage adopting a single reference standard to avoid bias or ambiguity.

Despite a large number of current validation studies, more research is needed to validate the 4AT delirium assessment tool in various settings and populations. In addition, future research may investigate the feasibility of using a mobile app or digital platform to provide the 4AT because of technological advancements. This could enhance the tool's use, precision, and dependability. Finally, it is suggested that clinical judgment be utilized in combination with the 4AT tool to offer a thorough examination of patients. This may aid in making sure correct diagnoses are made and effective treatments are administered.

5. CONCLUSION

The systematic evaluation of the 4AT delirium assessment tool found it valid and valuable for diagnosing delirium in hospitalized non-ICU patients > 65. The research indicated that the 4AT was highly sensitive and specific, making it a useful tool for detecting delirium in this group. Furthermore, the study found that the 4AT is simple to administer and requires little training, making it a valuable tool for healthcare providers. The 4AT is a helpful tool for diagnosing delirium in hospitalized non-ICU patients over 65, despite significant limitations such as the need for additional validation in particular patient groups. Further study is required to verify the 4AT across situations and people and compare its performance to that of other delirium assessment tools in combination with clinical investigations.

REFERENCES

1. Oh Esther S., Fong Tamara G., Hsieh Tammy T. and Inouye Sharon K., Delirium in Older Persons: Advances in Diagnosis and Treatment. *JAMA*, 2017; 318(12): 1161-1174. 10.1001/jama.2017.12067.
2. Fong Tamara G. and Inouye Sharon K., The inter-relationship between delirium and dementia: the importance of delirium prevention. *Nature Reviews Neurology*, 2022; 18(10): 579-596. 10.1038/s41582-022-00698-7.
3. Inouye S. K., Predisposing and precipitating factors for delirium in hospitalized older patients. *Dementia and Geriatric Cognitive Disorders*, 1999; 10(5): 393-400. 10.1159/000017177.
4. Inouye S. K., Delirium in hospitalized older patients: recognition and risk factors. *Journal of Geriatric Psychiatry and Neurology*, 1998; 11(3): 118-25. 10.1177/089198879801100302.
5. Mathillas J., Olofsson B., Lövheim H. and Gustafson Y., Thirty-day prevalence of delirium among very old people: a population-based study of very old people living at home and in institutions. *Archives Gerontology Geriatrics*, 2013; 57(3): 298-304. 10.1016/j.archger.2013.04.012.
6. Kukreja D., Günther U. and Popp J., Delirium in the elderly: Current problems with increasing geriatric age. *Indian Journal of Medical Research*, 2015; 142(6): 655-62. 10.4103/0971-5916.174546.
7. Igarashi Masakazu, Okuyama Kotoba, Ueda Naoya, Sano Hideki, Takahashi Kanae, P Qureshi Zaina et al., Incremental medical cost of delirium in elderly patients with cognitive impairment: analysis of a nationwide administrative database in Japan. *BMJ Open*, 2022; 12(12): e062141. 10.1136/bmjopen-2022-062141 %J BMJ Open.
8. Kinchin I., Mitchell E., Agar M. and Trépel D., The economic cost of delirium: A systematic review and quality assessment. *Alzheimer's and Dementia*, 2021; 17(6): 1026-1041. 10.1002/alz.12262.
9. Magny E., Le Petitcorps H., Pociumban M., Bouksani-Kacher Z., Pautas É., Belmin J. et al., Predisposing and precipitating factors for delirium in community-dwelling older adults admitted to hospital with this condition: A prospective case series. *PLoS One*, 2018; 13(2): e0193034. 10.1371/journal.pone.0193034.
10. Pisani M. A., Murphy T. E., Van Ness P. H., Araujo K. L. and Inouye S. K., Characteristics associated with delirium in older patients in a medical intensive care

- unit. *Archives of Internal Medicine*, 2007; 167(15): 1629-34. 10.1001/archinte.167.15.1629.
11. Inouye S. K., Westendorp R. G. and Saczynski J. S., Delirium in elderly people. *Lancet*, 2014; 383(9920): 911-22. 10.1016/s0140-6736(13)60688-1.
 12. Bellelli Giuseppe, Brathwaite Justin S. and Mazzola Paolo, Delirium: A Marker of Vulnerability in Older People. *Frontiers in Aging Neuroscience*, 2021; 13: 10.3389/fnagi.2021.626127.
 13. Mariz J., Costa Castanho T., Teixeira J., Sousa N. and Correia Santos N., Delirium Diagnostic and Screening Instruments in the Emergency Department: An Up-to-Date Systematic Review. *Geriatrics (Basel)*, 2016; 1(3). 10.3390/geriatrics1030022.
 14. Johansson Y. A., Tsevis T., Nasic S., Gillsjö C., Johansson L., Bogdanovic N. et al., Diagnostic accuracy and clinical applicability of the Swedish version of the 4AT assessment test for delirium detection, in a mixed patient population and setting. *BMC Geriatrics*, 2021; 21(1): 568. 10.1186/s12877-021-02493-3.
 15. Inouye S. K., van Dyck C. H., Alessi C. A., Balkin S., Siegel A. P. and Horwitz R. I., Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Annals of Internal Medicine*, 1990; 113(12): 941-8. 10.7326/0003-4819-113-12-941.
 16. Borson S., Scanlan J., Brush M., Vitaliano P. and Dokmak A., The mini-cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *International Journal of Geriatric Psychiatry*, 2000; 15(11): 1021-7. 10.1002/1099-1166(200011)15:11<1021::aid-gps234>3.0.co;2-6.
 17. Tiegies Z., MacLulich A. M. J., Anand A., Brookes C., Cassarino M., O'Connor M. et al., Diagnostic accuracy of the 4AT for delirium detection in older adults: systematic review and meta-analysis. *Age and Ageing*, 2021; 50(3): 733-743. 10.1093/ageing/afaa224.
 18. Wilson J. E., Mart M. F., Cunningham C., Shehabi Y., Girard T. D., MacLulich A. M. J. et al., Delirium. *Nature Reviews Disease Primers*, 2020; 6(1): 90. 10.1038/s41572-020-00223-4.
 19. Muser Olga, Seiler Kevin, Bachnick Stefanie, Gehri Beatrice, Zúñiga Franziska and Hasemann Wolfgang, Delirium detection in hospitalized adults: the performance of the 4A's Test and the modified Confusion Assessment Method for the Emergency Department. A comparison study. *Bulletin of the National Research Centre*, 2022; 46(1): 179.
 20. Bellelli G., Morandi A., Davis D. H., Mazzola P., Turco R., Gentile S. et al., Validation of the 4AT, a new instrument for rapid delirium screening: a study in 234 hospitalised older people. *Age and Ageing*, 2014; 43(4): 496-502. 10.1093/ageing/afu021.
 21. Shenkin S. D., Fox C., Godfrey M., Siddiqi N., Goodacre S., Young J. et al., Delirium detection in older acute medical inpatients: a multicentre prospective comparative diagnostic test accuracy study of the 4AT and the confusion assessment method. *BMC Medicine*, 2019; 17(1): 138. 10.1186/s12916-019-1367-9.
 22. Evensen S., Hølen R., Ranhoff A., Lydersen S. and Saltvedt I., The delirium screening tool 4AT in routine clinical practice: prediction of mortality, sensitivity and specificity. *European Geriatric Medicine*, 2021; 12(4): 793-800. 10.1007/s41999-021-00489-1.
 23. Arnold E., Finucane AM, Spiller JA, Tiegies Z and MacLulich AMJ, Validation of the 4AT tool for delirium assessment in specialist palliative care settings: protocol of a prospective diagnostic test accuracy study [version 1; peer review: 2 approved]. *AMRC Open Research* 2021; 3(16). 10.12688/amrcopenres.12973.1.
 24. Davis Daniel, Searle Samuel D and Tsui Alex, The Scottish Intercollegiate Guidelines Network: risk reduction and management of delirium. *Age Ageing*, 2019; 48(4): 485-488.
 25. Vardy E., Collins N., Grover U., Thompson R., Bagnall A., Clarke G. et al., Use of a digital delirium pathway and quality improvement to improve delirium detection in the emergency department and outcomes in an acute hospital. *Age and Ageing*, 2020; 49(4): 672-678. 10.1093/ageing/afaa069.

26. Tiegies Zoë, Lowrey Jacqueline and MacLulich Alasdair MJ, What delirium detection tools are used in routine clinical practice in the United Kingdom? Survey results from 91% of acute healthcare organisations. *European Geriatric Medicine*, 2021; 12(6): 1293-1298.
27. Alhaidari Abdullah A. O. and Matsis Kyriakos P., Barriers to completing the 4AT for delirium and its clinical implementation in two hospitals: a mixed-methods study. *European Geriatric Medicine*, 2022; 13(1): 163-172. 10.1007/s41999-021-00582-5.
28. Page Matthew J, Moher David and McKenzie Joanne E, Introduction to PRISMA 2020 and implications for research synthesis methodologists. *Research Synthesis Methods*, 2022; 13(2): 156-163.
29. Schardt Connie, Adams Martha B., Owens Thomas, Keitz Sheri and Fontelo Paul, Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Medical Informatics and Decision Making*, 2007; 7(1): 16. 10.1186/1472-6947-7-16.
30. De J. and Wand A. P., Delirium Screening: A Systematic Review of Delirium Screening Tools in Hospitalized Patients. *Gerontologist*, 2015; 55(6): 1079-99. 10.1093/geront/gnv100.
31. Charette Martin, McKenna Lisa G., Deschênes Marie-France, Ha Laurence, Merisier Sophia and Lavoie Patrick, New graduate nurses' clinical competence: A mixed methods systematic review. *Journal of Advance Nursing*, 2020; 76(11): 2810-2829. <https://doi.org/10.1111/jan.14487>.
32. Hong Quan Nha, Fàbregues Sergi, Bartlett Gillian, Boardman Felicity, Cargo Margaret, Dagenais Pierre et al., The Mixed Methods Appraisal Tool (MMAT) version 2018 for information professionals and researchers. *Education Information*, 2018; 34(4): 285-291.
33. Asadollahi Abdolrahim, Saberi Mohammad, Entezari Mariam, Hoseini Zohreh, Hasani Syed Abdolmotalleb, Saberi Laleh Fani et al., Iranian version of 4AT, an instrument for rapid delirium screening for later life. *International Journal of Advanced and Applied Sciences*, 2016; 3: 33-38.
34. Gagné A. J., Voyer P., Boucher V., Nadeau A., Carmichael P. H., Pelletier M. et al., Performance of the French version of the 4AT for screening the elderly for delirium in the emergency department. *Canadian Journal of Emergency Medicine*, 2018; 20(6): 903-910. 10.1017/cem.2018.367.
35. Saller T., MacLulich A. M. J., Schäfer S. T., Crispin A., Neitzert R., Schüle C. et al., Screening for delirium after surgery: validation of the 4 A's test (4AT) in the post-anaesthesia care unit. *Anaesthesia*, 2019; 74(10): 1260-1266. 10.1111/anae.14682.
36. Zucchelli A., Apuzzo R., Paolillo C., Prestipino V., De Bianchi S., Romanelli G. et al., Development and validation of a delirium risk assessment tool in older patients admitted to the Emergency Department Observation Unit. *Aging Clinical and Experimental Research*, 2021; 33(10): 2753-2758. 10.1007/s40520-021-01792-4.
37. Aldwikat R. K., Manias E., Holmes A., Tomlinson E. and Nicholson P., Validation of Two Screening Tools for Detecting Delirium in Older Patients in the Post-Anaesthetic Care Unit: A Diagnostic Test Accuracy Study. *International Journal of Environmental Research and Public Health*, 2022; 19(23). 10.3390/ijerph192316020.
38. Delgado-Parada E, Morillo-Cuadrado D, Saiz-Ruiz J, Cebollada-Gracia A, Ayuso-Mateos JL and Cruz-Jentoft AJ, Diagnostic accuracy of the Spanish version of the 4AT scale (4AT-ES) for delirium screening in older inpatients. *The European Journal of Psychiatry*, 2022; 36(3): 182-190.
39. GMRC, Delirium is prevalent in older hospital inpatients and associated with adverse outcomes: results of a prospective multi-centre study on World Delirium Awareness Day. *BMC Medicine*, 2019; 17(1): 229. 10.1186/s12916-019-1458-7.
40. Hercus Catherine and Hudaib Abdul-Rahman, Delirium misdiagnosis risk in psychiatry: a machine learning-logistic regression predictive algorithm. *BMC Health Services and Research*, 2020; 20(1): 151. 10.1186/s12913-020-5005-1.

41. MacLulich A. M., Shenkin S. D., Goodacre S., Godfrey M., Hanley J., Stíobhairt A. et al., The 4 'A's test for detecting delirium in acute medical patients: a diagnostic accuracy study. *Health Technology Assessment*, 2019; 23(40): 1-194. 10.3310/hta23400.
42. O'Sullivan D., Brady N., Manning E., O'Shea E., O'Grady S., N O. ' Regan et al., Validation of the 6-Item Cognitive Impairment Test and the 4AT test for combined delirium and dementia screening in older Emergency Department attendees. *Age and Ageing*, 2018; 47(1): 61-68. 10.1093/ageing/afx149.
43. Lees R., Corbet S., Johnston C., Moffitt E., Shaw G. and Quinn T. J., Test accuracy of short screening tests for diagnosis of delirium or cognitive impairment in an acute stroke unit setting. *Stroke*, 2013; 44(11): 3078-83. 10.1161/strokeaha.113.001724.
44. Inouye S. K., Leo-Summers L., Zhang Y., Bogardus S. T., Jr., Leslie D. L. and Agostini J. V., A chart-based method for identification of delirium: validation compared with interviewer ratings using the confusion assessment method. *Journal of the American Geriatrics Society*, 2005; 53(2): 312-8. 10.1111/j.1532-5415.2005.53120.x.
45. Anand Atul, Cheng Michael, Ibitoye Temi, MacLulich Alasdair M J and Vardy Emma R L C, Positive scores on the 4AT delirium assessment tool at hospital admission are linked to mortality, length of stay and home time: two-centre study of 82,770 emergency admissions. *Age and Ageing*, 2022; 51(3). 10.1093/ageing/afac051.

APPENDIX

Appendix 1: Key to quality assessment questions

3.1	Are the participants representative of the target population?
3.2	Are measurements appropriate regarding both the outcome and intervention (or exposure)?
3.3	Are there complete outcome data?
3.4	Are the confounders accounted for in the design and analysis?
3.5	During the study period, is the intervention administered (or exposure occurred) as intended?
4.1	Is the sampling strategy relevant to address the research question?
4.2	Is the sample representative of the target population?
4.3	Are the measurements appropriate?
4.4	Is the risk of nonresponse bias low?
4.5	Is the statistical analysis appropriate to answer the research question?
5.1	Is there an adequate rationale for using a mixed methods design to address the research question?
5.2	Are the different components of the study effectively integrated to answer the research question?
5.3	Are the outputs of the integration of qualitative and quantitative components adequately interpreted?
5.4	Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?
5.5	Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?