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Findings from a validation study

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The 4AT, a rapid delirium detection tool, in hospice inpatient units: findings from a validation study

Authors

Arnold Elizabeth (EA) ¹

Finucane Anne M (AMF) ^{1,2}

Taylor Stacey (ST)¹

Spiller Juliet A (JAS) ¹

O'Rourke Siobhan (SO)³

Spenceley Julie (JSp) ³

Carduff Emma (EC) ³

Tieges Zoë (ZT) ^{4,5}

MacLulich Alasdair MJ (AMJM) ⁴

Corresponding author – Elizabeth Arnold (liz.arnold@mariecurie.org.uk)

¹ Marie Curie Hospice Edinburgh, 45 Frogston Road West, Edinburgh EH110 7DR, UK

² Clinical Psychology, University of Edinburgh, Doorway 6, Edinburgh, EH8 9AG, UK

³ Marie Curie Hospice Glasgow, 133 Balornock Road, Glasgow, G21 3US, UK

⁴ Edinburgh Delirium Research Group, Ageing and Health, Usher Institute, University of Edinburgh, Room S1642, Royal Infirmary of Edinburgh, Edinburgh, EH16 4SB, UK

⁵ Department of Computing, School of Computing, Engineering and Built Environment, Glasgow Caledonian University, Scotland, UK.

ABSTRACT (250/250)

Background: Delirium is a serious neuropsychiatric syndrome with adverse outcomes, which is common but often undiagnosed in terminally ill people. The 4 'A's test or 4AT (www.the4AT.com), a brief delirium detection tool, is widely used in general settings, but validation studies in terminally ill people are lacking.

Aim: To determine the diagnostic accuracy of the 4AT in detecting delirium in terminally ill people, who are hospice inpatients.

Design: A diagnostic test accuracy study in which participants underwent the 4AT and a reference standard based on the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders. The reference standard was informed by Delirium Rating Scale Revised-98 and tests assessing arousal and attention. Assessments were conducted in random order by pairs of independent raters, blinded to the results of the other assessment.

Setting/participants: Two hospice inpatient units in Scotland, UK. Participants were 148 hospice inpatients aged ≥ 18 .

Results: 137/148 participants completed both assessments. Three participants had an indeterminate reference standard diagnosis and were excluded, yielding a final sample of 134. Mean age was 70.3 (SD 10.6) years. 33% (44/134) had reference standard delirium. The 4AT had a sensitivity of 89% (95% CI 79-98%) and a specificity of 94% (95% CI 90-99%). The area under the receiver operating characteristic curve was 0.97 (95% CI 0.94-1).

Conclusion: The results of this validation study support use of the 4AT as a delirium detection tool in hospice inpatients, and adds to the literature evaluating methods of delirium detection in palliative care settings.

Trial registry: ISCRTN 97417474

Key Statements

What is already known about this topic?

- Delirium is a serious neuropsychiatric syndrome with adverse outcomes, which is common but often undiagnosed in terminally ill people.
- The 4AT is a brief delirium detection tool, which is widely used in general settings, but validation studies in the terminally ill are lacking.

What this paper adds

- This study adds to the small literature evaluating methods of delirium detection in terminally ill people and is the first validation study of the 4AT in a hospice inpatient setting.
- The 4AT had a sensitivity of 89% and specificity of 94% for delirium detection, as assessed by the DSM-5 delirium reference standard, in this study of terminally ill people in hospice inpatient units.
- These findings support the use of the 4AT as a validated delirium detection tool in hospice inpatient settings.

Implications for practice, theory or policy

- The simplicity and brevity of the 4AT, functionality to assess non-verbal patients, and that it requires no training prior to use are advantages in clinical practice.
- Implementation studies are essential to support routine delirium assessment of terminally ill people.
- Further research evaluating 4AT use in community settings is needed, specifically homes and care homes, where delirium assessment presents different challenges.

Background

Delirium is a serious and distressing neuropsychiatric condition(1), which is common in terminally ill people. Recent studies suggest delirium is present in over a quarter of patients admitted to hospices, and that prevalence increases towards the end of life.(2) Delirium often remains undiagnosed and hence under-treated.(3) The hypoactive subtype is common amongst terminally ill people, (2) yet this subtype has been proposed as more likely to go underdiagnosed (4, 5), perhaps due to overlapping symptoms with depression, dementia and fatigue. (4, 6)

Delirium may be reversible, but its development may also signal the patient is approaching end of life.(7) Earlier detection facilitates more timely management, which may result in better patient outcomes.(8) Palliative and generic delirium guidance recommends routine delirium screening, including detection tool use, on admission to hospitals and other care settings, or if delirium is suspected.(9-14) A UK survey in 2019 reported that only a third of palliative medicine specialists used delirium screening tools, with more relying on clinical judgement alone.(15) Yet there is increasing awareness that clinical judgement alone risks delirium going under-diagnosed.(5, 16)

Many delirium detection tools are available, with some designed to detect delirium at first assessment and when delirium is suspected. Other tools monitor for new onset delirium in inpatients, measure delirium severity, or are primarily used for research purposes. (8) A systematic review and meta-analysis in 2021 reported the characteristics and performance of 14 delirium detection tools used in palliative care. (17) These were the Bedside Confusion Scale, the Communication Capacity Scale, Clinical Assessment of Confusion (versions A and B), the Confusion Assessment Method (CAM) and brief Confusion Assessment Method (bCAM), the Delirium Observation Screening Scale (DOS), the Delirium Rating Scale (DRS) and the revised version (DRS-R-98), the Memorial Delirium Assessment Scale (MDAS), the Single Question in Delirium (SQiD), the Neelon and Champagne Confusion Scale (NEECHAM), the Nursing Delirium Screening Scale (Nu-DESC) and the Visual Analogue Scale for Acute

Confusion (VASAC). Of the 14 tools examined, 12 were assessed in only one study. Sample sizes ranged from 19 to 2343, though most studies had relatively small samples. The review concluded it was difficult to make recommendations given the heterogeneity of the studies, and that choice of tool may depend on the population, setting and expertise of healthcare professionals. The CAM and the MDAS were proposed for assessing delirium amongst patients able to co-operate with cognitive testing. Alternatively, the DOS and Nu-DESC, which are solely dependent on the assessor's observations, were deemed suitable for non-verbal patients approaching the end of life.(17) A subsequent study, not included in the 2021 review, compared the performance of the SQiD and short CAM to psychiatrist interview amongst oncology patients - this reported high levels of specificity (87% and 100% respectively), but lower sensitivity levels (44% and 26%).(18) The challenges of providing adequate training to use the CAM were acknowledged, as this and previous studies have reported accuracy may be dependent on user expertise.(19, 20)

Despite the range of delirium detection tools assessed, the 4AT (www.the4AT.com) remains unvalidated in palliative care populations. Whilst the CAM is recommended for use by American and Canadian delirium guidance (21, 22), the 4AT is recommended as the main delirium assessment tool in non-ICU settings by the UK National Institute of Health and Care Excellence (NICE) and the Scottish Intercollegiate Guidelines Network (SIGN) (23, 24), as well as Australian guidance.(25)

The 4AT is a short bedside test widely used by healthcare professionals in routine clinical practice to determine if patients may have delirium.(26) (Figure 1) It incorporates 4 items (the 4 'A's) to score from 0-12, including an observational measure of Alertness, the Abbreviated Mental Test-4, an Attention score (participant asked to say the months of the year in backwards order), and evidence of Acute change or fluctuation in alertness, cognition or mental function arising over the preceding 2 weeks and still evident in the last 24 hours. The 4AT has some advantages over other detection tools,

in that it requires no training prior to use, is simple and quick to administer, and can be used with non-verbal patients, who are either very agitated or drowsy. Whilst unvalidated in palliative care populations, the 4AT has been extensively validated in other populations, with 25 studies involving over 5,000 patients.⁽²⁶⁾ A systematic review and meta-analysis of 17 studies of elderly adults (≥ 65 years) published in 2021 reported pooled sensitivity of 88% (95% CI 80-93%) and specificity of 88% (95% CI 82-92%).⁽²⁷⁾

Figure 1: The 4AT (26)

The 4AT: Assessment test for Delirium and Cognitive impairment

[1] ALERTNESS **CIRCLE**

This includes patients who may be markedly drowsy (e.g. difficult to rouse and/or obviously sleepy during assessment) or agitated/hyperactive. Observe the patient. If asleep, attempt to wake with speech or gentle touch on shoulder. Ask the patient to state their name and address to assist rating.

Normal (fully alert, but not agitated, throughout assessment)	0
Mild sleepiness for <10 seconds after waking, then normal	0
Clearly abnormal	4

[2] AMT4

Age date of birth place (name of the hospital or building) current year

No mistakes	0
1 mistake	1
2 or more mistakes/untestable	2

[3] ATTENTION

*Ask the patient: "Please tell me the months of the year in backwards order, starting at December."
To assist initial understanding one prompt of "what is the month before December?" is permitted.*

Months of the year backwards

Achieves 7 months or more correctly	0
Starts but scores <7 months / refuses to start	1
Untestable (cannot start because unwell, drowsy, inattentive)	2

[4] ACUTE CHANGE OR FLUCTUATING COURSE

Evidence of significant change or fluctuation in: alertness, cognition, other mental function (e.g. paranoia, hallucinations) arising over the last 2 weeks and still evident in last 24hrs

No	0
Yes	4

4AT SCORE

4 or above: possible delirium +/- cognitive impairment
 1-3: possible cognitive impairment
 0: delirium or severe cognitive impairment unlikely (but delirium still possible if [4] information incomplete)

GUIDANCE NOTES **Version 1.2. Information and download:**

www.the4AT.com

The 4AT is a screening instrument designed for rapid initial assessment of delirium and cognitive impairment. A score of 4 or more *suggests* delirium but is not diagnostic: more detailed assessment of mental status may be required to reach a diagnosis. A score of 1-3 suggests cognitive impairment and more detailed cognitive testing and informant history-taking are required. A score of 0 does not definitively exclude delirium or cognitive impairment: more detailed testing may be required depending on the clinical context.

Items 1-3 are rated solely on observation of the patient at the time of assessment.
Item 4 requires information from one or more source(s), e.g. your own knowledge of the patient, other staff who know the patient (e.g. ward nurses), GP letter, case notes, carers. The tester should take account of communication difficulties (hearing impairment, dysphasia, lack of common language) when carrying out the test and interpreting the score.

Alertness: Altered level of alertness is very likely to be delirium in general hospital settings. If the patient shows significant altered alertness during the bedside assessment, score 4 for this item. **AMT4 (Abbreviated Mental Test - 4):** This score can be extracted from items in the AMT10 if the latter is done immediately before. **Acute Change or Fluctuating Course:** Fluctuation can occur without delirium in some cases of dementia, but marked fluctuation usually indicates delirium. To help elicit any hallucinations and/or paranoid thoughts ask the patient questions such as, "Are you concerned about anything going on here?"; "Do you feel frightened by anything or anyone?"; "Have you been seeing or hearing anything unusual?"

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Aim

The aim of the study was to determine the accuracy of the 4AT in detecting delirium amongst terminally ill people, in hospice inpatient settings, in terms of sensitivity and specificity.

Methods

Design

We conducted a test validation study comparing the accuracy of the 4AT against a reference standard assessment, based on the diagnostic criteria of the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).(1) (Figure 2) The study was registered on the ISCRTN (ISRCTN97417474 – 21/2/20), and full methodology is available in the protocol paper. (28)

Sites

The sites were two hospice inpatient units in Scotland, UK. Approval was gained for a third site, which later withdrew from the study. In the UK, hospices are part of specialist palliative care services, which provide care to terminally ill people with complex needs, that cannot be met by generalist services.

Figure 2: Study Overview Flow Chart – this chart has been adapted from Shenkin *et al* 2018 (29) (<http://creativecommons.org/licenses/by/4.0/>)

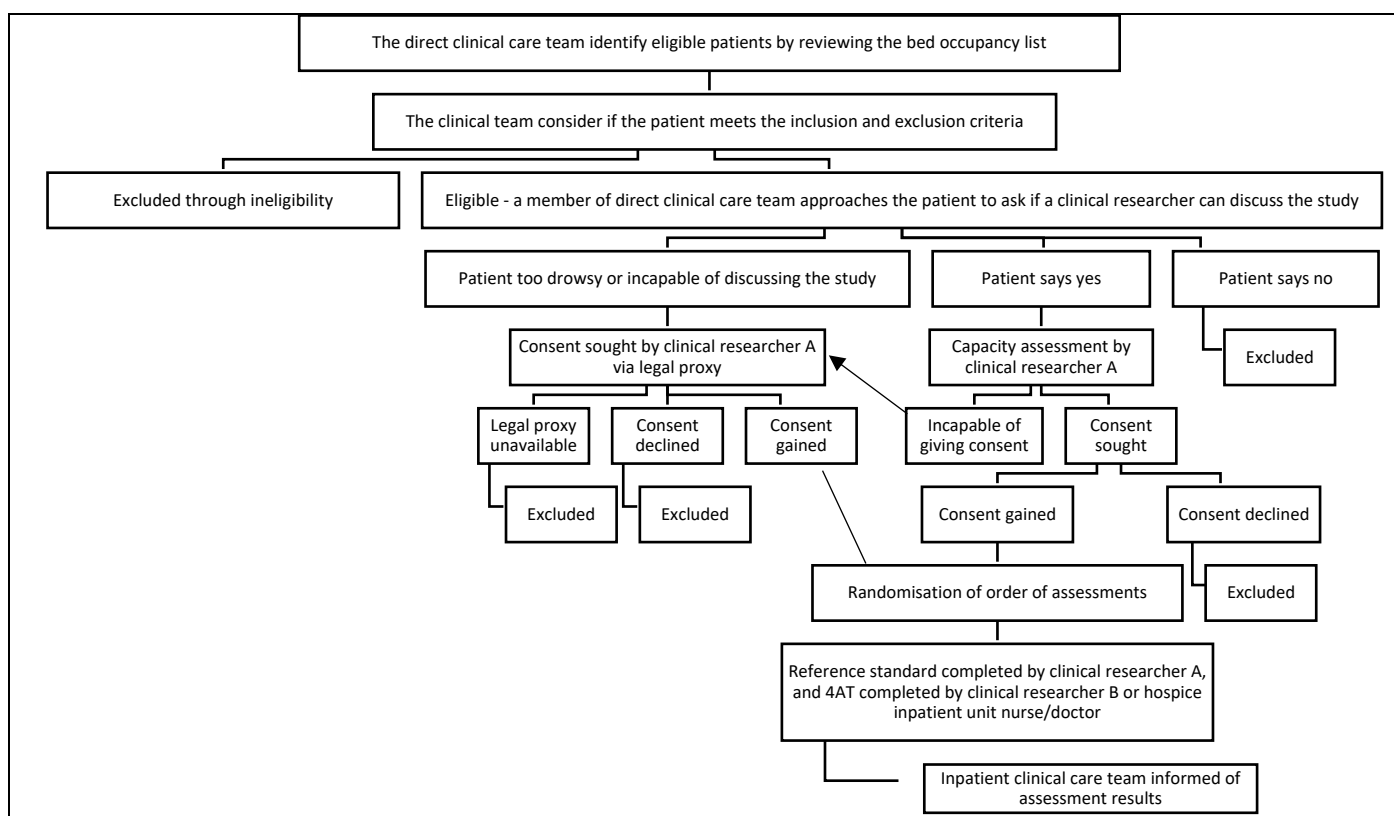


Table 1. Inclusion and exclusion criteria

Inclusion criteria
Aged 18 years or over
Admitted acutely to the hospice inpatient unit
Exclusion criteria
Acute life-threatening illness requiring time critical intervention (e.g. suspected spinal cord compression)
High level of patient and family distress, as judged by the clinical team
Severe dysphasia
Combined hearing and visual impairment which would limit participation in the study's tests
Being unable to communicate in English
Coma

Population

Sample size and recruitment

Based on a sensitivity/specificity of 0.85 and a minimal acceptable lower confidence level of 0.75, we estimated a sample size of 176 participants would be required to complete the study assessments.

(30) To achieve this, and given the likelihood of withdrawals, we sought to recruit approximately 240 participants.(28)

Recruitment began in October 2019 but halted at the start of the Covid-19 pandemic in March 2020, before restarting between July 2021 and April 2022. People admitted to the hospice inpatient units were eligible to participate, and the study inclusion and exclusion criteria are shown in Table 1. Those who fulfilled the eligibility criteria, were approached by their direct clinical team, which may have included the clinical researchers (hospice nurses SO, ST and doctors JSp, EA). Eligible patients, who were interested, received verbal and written information about the study from researchers. People deemed to have capacity to consent by the researchers were invited to sign the consent form. If the researcher assessed the person as lacking capacity to consent, their legal proxy (Welfare Attorney, Guardian or nearest relative, approached in that order) was asked on their behalf, as permitted by the Adults with Incapacity (Scotland) Act 2000.(31) The clinical researchers had allocated research time, but the study was also conducted alongside their usual clinical practice, which influenced the timing of the initial approach and recruitment.

Assessments

Participants underwent the 4AT and a reference standard assessment within a 3-hour period.

Assessments were conducted in random order by pairs of independent assessors, who were blinded to the results of the other assessment. Unblinding occurred immediately following completion of both assessments. Participants' involvement in the study was solely for the duration of the two assessments, within the 3-hour time period.

4AT assessment

The 4AT was completed by a clinical researcher or a hospice inpatient unit nurse or doctor. All had received generic delirium education (undergraduate and/or as continuing professional development) prior to the study – however only the clinical researchers completed study-specific delirium assessment training.(26) The 4AT incorporates 4 items to score from 0-12. (Figure 1)(26) For the purposes of this study, a score of more than 3 was considered ‘delirium present’, whereas scores of 0-3 were designated ‘delirium absent’.(32)

Reference standard assessment

The reference standard assessment was completed by the clinical researcher, who had completed the consent process with the participant. The reference standard was centred on the delirium diagnostic criteria in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (1) and described in more detail in the protocol paper. (28) The battery of tests assessing attention and cognition were supplemented by collateral history from family members, carers or other staff members (other than the 4AT assessor). (Supplementary file 1) Following the reference standard assessment, the participant was allocated to one of 4 categories: ‘delirium present’, ‘delirium absent’, ‘possible delirium’ (some DSM-5 delirium criteria were positive, but not all, due to missing information) or ‘undetermined’ (some, but not all, DSM-5 delirium criteria were positive).

The reference standard assessors discussed all ‘possible delirium’ or ‘undetermined’ cases with an expert panel (JAS, ZT and AMJM), as well as other cases where there was uncertainty regarding final group allocation. The expert panellists were blinded to the initial assessment outcomes, until this final allocation was complete.

Data collection

The following data were collected for each participant: age, sex, primary diagnosis (including cancer type if relevant), Australia-modified Karnofsky Performance scale, presence of dementia or learning disability, medication use (specifically opioids, antipsychotics and benzodiazepines), outcome of hospice admission (discharge or death).

Outcomes

We reported the sensitivity and specificity of the 4AT compared to the reference standard delirium assessment for individual and combined sites. Sensitivity was defined as the proportion accurately identified as having delirium, and specificity as the proportion accurately identified as being without delirium. We also reported the area under the receiver operating characteristic curve (AUROC) and its 95% confidence interval. The AUROC is a measure of the performance of the test, ranging between 0-1, with a higher score indicating a more accurate test.⁽³³⁾ Further secondary analyses were completed whereby the indeterminate cases ('possible delirium' and 'undetermined'), pre- and post-expert panel, were either assumed to have delirium or not have delirium. IBM SPSS version 27 was used to support the analysis.

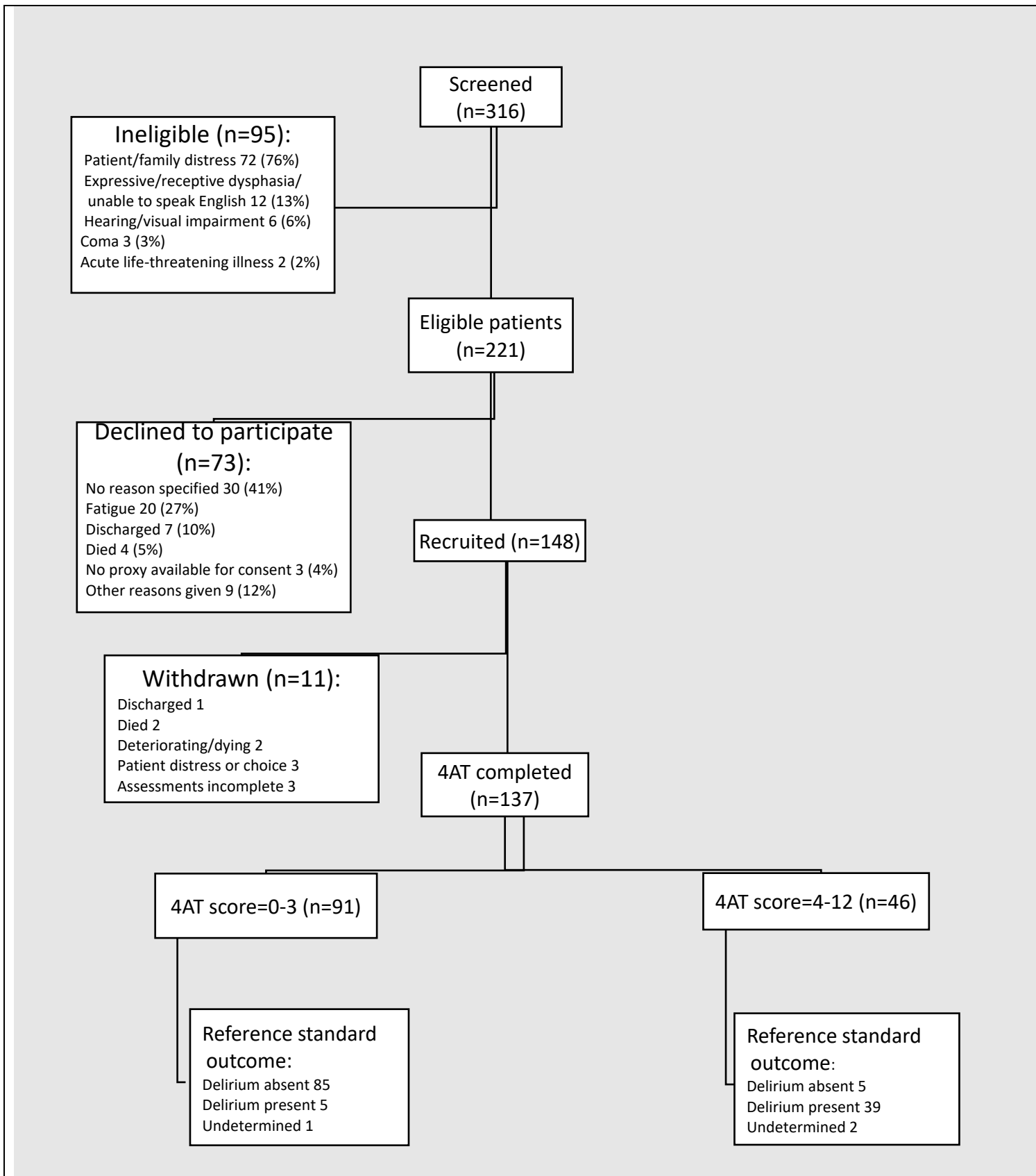
Results

Three hundred and sixteen patients were screened to participate in the study, with over two-thirds (70%, 221/316) being eligible to participate (Figure 3). Of the 221 patients eligible to participate, 67% (148/221) were recruited, with 137 (93%) completing both the assessments. Eleven withdrew between recruitment and data collection. (Figure 3)

Sixteen (12%) of the 137 participants, who completed the assessments, were discussed with the expert panel - twelve of these cases (12/16) originally had a 'possible delirium' or 'undetermined' diagnosis. Following the expert panel, 134/137 participants (98%) had a definitive diagnosis of either

'delirium present' or 'delirium absent'. The 3 participants with 'undetermined' diagnoses were excluded from the primary analysis, yielding a final sample of 134.

Figure 3: Standards for Reporting Diagnostic Accuracy diagram (STARD) showing summary of eligibility, participation and outcomes, final reference standard delirium status.



Note: During the study, it became apparent a proportion of ineligible patients had been inaccurately allocated to the category 'coma', when the reason was more appropriately described as patient and/or family distress associated with the dying phase. Where there was sufficient information, these cases were retrospectively reallocated from coma to 'patients and/or family distress'. The proportion of reasons given for exclusion were affected, but not the analysis of the main results.

Characteristics of participants

The mean age was 70.3 (S.D. 10.6) years and 50% (67/134) were female. Table 2 shows the clinical and demographic features of the 134 participants, who completed the assessments, both as a whole group and as subgroups (delirium present or delirium absent) determined by their reference standard delirium final status. The median and mode Australia-modified Karnofsky Performance Status (KPS) score was 50% - this score reflects patients in need of considerable assistance and frequent medical care.⁽³⁴⁾

Most participants (94%, 124/132) had a primary diagnosis of malignancy, with only 6% (8/132) having non-malignant disease. Of those whose cancer type was specified (85%, 105/124), approximately a third had lung cancer (34%), another third had cancer of gastrointestinal origin (32%), 8% had prostate cancer, 7% gynaecological, 6% breast and 5% urological cancers. The prevalence of dementia was 6% (8/134) as documented in their medical case notes or from informant history, with an additional 2% (3/134) of participants having a history of cognitive impairment ranging between months to 2 years. The reason for hospice admission was symptom control and/or end of life care for 88% and end of life care alone for 10%. At least half of participants (52%) died during their hospice admission.

Table 2: Clinical and demographic characteristics of participants by final reference standard delirium status (n=134)

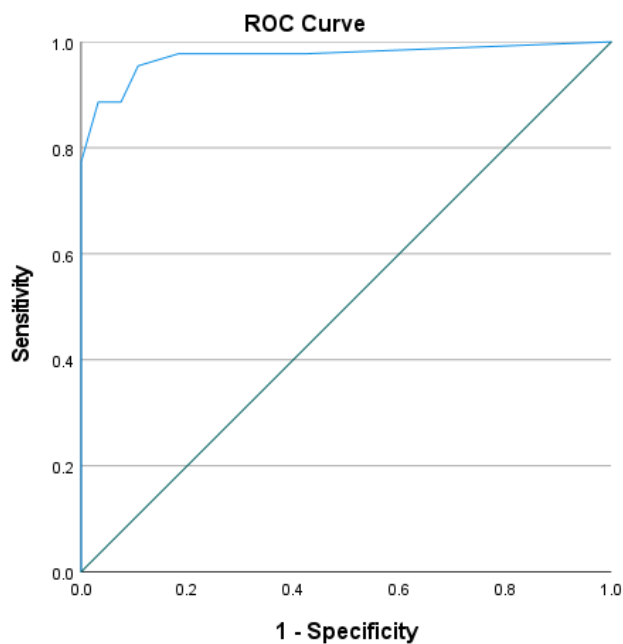
		All participants n=134	Delirium absent n=90	Delirium present n=44
Age in years: Mean (SD)		70.3 (10.6)	68.7 (10.6)	73.5 (10.0)
Cancer diagnosis (n=132) Data missing for 2 participants		124 (94%)	85 (94%)	39 (89%)
Gender	Female	67 (50%)	44 (49%)	23 (52%)
	Male	67 (50%)	46 (51%)	21 (48%)
Australia-Modified Karnofsky Performance Status score % (N=131): median (mode) Data missing for 3 participants		50% (50%)	50% (50%)	40% (30%)
Participant using medication <24 hours of delirium assessments	Opioids	122 (91%)	85 (94%)	37 (84%)
	Antipsychotics Indication for use was unspecified (may have been as antiemetic or to palliate agitated delirium symptoms)	43 (32%)	17 (19%)	26 (59%)
	Benzodiazepines	71 (53%)	48 (53%)	23 (52%)
Participants using sedative medication - regularly and/or <4 hours of assessment. (e.g. antipsychotics / benzodiazepines)		52 (39%)	31 (34%)	21 (48%)
Participant outcome	Discharge	47 (35%)	39 (43%)	8 (18%)
	Death	69 (51%)	36 (40%)	33 (75%)
	Unknown	18 (13%)	15 (17%)	3 (7%)

Diagnostic test accuracy of the 4AT

Primary analysis

The sensitivity of the 4AT using the standard cut-off score of >3 was 89% (95% CI 79-98%) and the specificity was 94% (95% CI 90-99%) The area under the receiver operating characteristic curve was 0.97(95% CI 94-100%). (Figure 4)

Figure 4: Receiver operating characteristic curve for 4AT diagnostic accuracy.



Subgroup analysis for the two sites

4AT sensitivity was 88% and specificity 92% at hospice site B (n=86) and 90% and 97% respectively at hospice site A (n=48). (Table 3)

Table 3: Results of assessments for individual sites: Site A (n=48) and Site B (n=86)

		Site A		Site B	
		Delirium absent	Delirium Present	Delirium absent	Delirium present
4AT outcome	Score 0-3(Delirium absent)	37	1	48	4
	Score 4-12(Delirium present)	1	9	4	30
	Total	38	10	52	34
	Sensitivity	90%		88%	
	Specificity	97%		92%	

Secondary analyses

Pre-expert panel: Table 4 shows the assessment results, pre-expert panel. Using the reference standard assessors' initial DSM-5 outcomes, 'delirium present' / 'delirium absent', (excluding 12 cases of 'undetermined' and 'possible delirium'), the 4AT sensitivity score was 93% and specificity 95%.

Alternatively, inclusion of these 12 cases, assuming delirium was present for all 12 cases, sensitivity was lower at 79%, but the specificity result was similar at 95%, compared to the primary analysis. If delirium was assumed to be absent for these 12 cases, the sensitivity of the 4AT was 93% and specificity 92%.

Table 4: Results of pre-expert panel outcomes for the reference standard assessment

		Reference standard assessment outcome, pre-expert panel		
		Delirium absent	Delirium present	Possible delirium or undetermined
4AT outcome	Score 0-3: Delirium absent	80	3	8
	Score 4-12: Delirium present	4	38	4
Total		84	41	12

Post-expert panel: Assuming the 3 ‘undetermined’ cases excluded from the primary analysis had delirium, resulted in sensitivity of 87% and specificity of 94% for the 137 participants. Conversely if the 3 ‘undetermined’ cases did not have delirium, resulted in overall sensitivity of 89%, and a specificity of 92%.

Discussion

We found that the 4AT had a sensitivity of 89% and specificity of 94% for delirium detection, as assessed independently by the DSM-5 delirium reference standard assessment in hospice inpatients. The area under the receiver operating characteristic curve was high at 0.97. Our findings indicate that the 4AT is a valid tool for detecting delirium in hospice inpatients.

The sensitivity of the 4AT for delirium detection in this hospice study is comparable to that reported in the 2021 systematic review and meta-analysis of 17 studies in older adults (aged ≥ 65 years), with a reported pooled sensitivity of 88%.⁽²⁷⁾ The specificity result here was higher (94% versus 88%), which may have been due to the hospice population being younger (28% of participants were under

the age of 65 years), more homogeneous in terms of their primary diagnosis (93% had a cancer diagnosis), with lower prevalence of dementia (6%). Studies included in the 2021 systematic review of older adults (35) reported lower specificity scores for the 4AT amongst populations with higher prevalence of dementia.(32, 36, 37)

The sensitivity and specificity results of the 4AT from this hospice study are also comparable with studies of other delirium detection tools in palliative populations, including the Confusion Assessment Method and its shorter variants, the Memorial Delirium Assessment Scale and Delirium Observation Screening Scale. (17, 18)

Strengths and weaknesses

This study had several strengths. We used a comprehensive process to inform the reference standard assessments, which improves replicability and transparency. The prevalence of delirium in this study as detected by the reference standards was 33%, which suggests the sample is reflective of hospice inpatient units described elsewhere in the literature.(2) Reference standard and index (4AT) assessments were conducted independently. Indeterminate cases were managed using an explicit process with an expert panel blinded to 4AT scores. A further strength of the study was that it was conducted across two sites, with assessments completed by nurses and doctors working within the units, which may have supported the relatively high levels of recruitment and assessment completion. Despite Covid pandemic restrictions, limited visiting continued, thus permitting relatively easy access to family members, who provided collateral history to support the accuracy of delirium assessments. The secondary analyses were also supportive of the primary analysis – the sensitivity and specificity results were higher for site A (90% and 97% respectively) compared to site B (88% and 92% respectively), although the prevalence of delirium was lower at site B (21%) compared to site A (39%). The variation in delirium prevalence between sites is unclear, but may have been due to

differences in clinical researchers' availability and/or timing of assessments following admission, although we do not have the data to support this.

Limitations of this study should be acknowledged. Most participants had cancer as their primary diagnosis, so results may not be generalisable to those with advanced non-malignant disease or more heterogenous palliative populations. Furthermore, although the 4AT can be used to assess patients unable to communicate, the study's eligibility criteria excluded terminally ill people unable to speak English or with severe dysphasia according to their primary diagnosis. Hence some with cerebral malignancies or neurological diseases, who may be more challenging to assess for delirium, will have been excluded from participation. Related to this point, 'patient and/or family distress' was the most frequent exclusion criterion, particularly for those entering the very terminal phase of their illness (last days or week of life). Previous studies have shown that the prevalence of delirium increases toward the end of life(2), yet delirium detection tool use may be more complex during the dying phase of the patient's illness.

Recruitment bias may have been present, with those at moderate risk of delirium potentially being more challenging to recruit, compared to those at low or high risk. That is, those at moderate risk may have been more readily viewed as ineligible due to distress or other issues. In contrast, those at low risk of delirium may have been more easily judged as eligible due to having capacity, while those at high risk of delirium could be approached for consent via their legal proxy. Spectrum bias in delirium studies is an inherent challenge in studies requiring patient or proxy consent. Lower 4AT completion rates may be found in routine clinical practice. Use of the 4AT, including completion rates and scores across the severity spectrum, should be further evaluated using observational data from clinical practice. The target recruitment rate of 240 participants was not achieved despite the extended

recruitment period, however the numbers completing the study remain comparable with other delirium detection tool validation studies in hospice or palliative inpatient populations.(17)

Implications for practice

Our findings support the use of the 4AT for delirium detection in hospice inpatient settings. The simplicity and brevity of the 4AT, and functionality to assess non-verbal patients are advantages in clinical practice. Delirium prevalence increases during patients' hospice stay, so it would seem appropriate to consider further 4AT use during the patient's admission, whenever delirium is suspected. (2, 38) Whilst the 4AT does not require special training prior to use, adequate knowledge about the condition delirium is important in detection tool use (39), thus staff training in understanding delirium, its detection and management is recommended

Further research

Implementation studies are essential to support routine delirium assessment for terminally ill patients in clinical practice. Barriers to adoption of the 4AT and other tool use have been described in other settings(40) and need to be examined and addressed regarding terminally ill populations. This could be achieved, by examining completion rates and positive score rates in routine practice, as has been done in other settings.(41) Further research evaluating 4AT use amongst terminally ill people in community settings is needed, specifically home and care homes, where delirium assessment presents different challenges.(42)

Conclusion

The 4AT is a short delirium detection tool that can be used to identify delirium in terminally ill people receiving palliative care in hospice inpatient settings. Embedding the 4AT within standard clinical assessment is recommended.

Declarations

Ethics Approval and consent to participate: Approval was granted by NHS Scotland A Research Ethics Committee (reference 19/SS/0091) on 15/10/19 and Marie Curie Research Governance committee.

Funding: This study was funded by a Marie Curie Small Research Grant (www.mariecurie.org.uk). Marie Curie UK played no role in the study design, collection, analysis, interpretation of data, and in writing the manuscript.

Conflict of Interests: The Chief Investigator AMJM led the design of the 4AT, with others, in 2011. The 4AT is free to download and use, and there are no current or future financial conflicts of interest. This study was presented at the Marie Curie Research Conference and the American Delirium Society Conference.⁽⁴³⁾

Authors' Contributions: JAS, AF and AMJM conceived the idea for the study. JAS, AF, AMJM, ZT, EM and EA were involved in the study design. ST, SO, JSp and EA were involved in data collection. All except ST and SF were involved in data analysis and interpretation. All were involved in manuscript preparation and final draft approval. Authors fulfil the criteria for ICMJE authorship.

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Data availability Supplementary files: ISCRTN registry

Supplementary file 1 – reference standard assessment

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References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth ed: Washington, DC : American Psychiatric Publishing; 2013.

2. Watt CL, Momoli F, Ansari MT, Sikora L, Bush SH, Hosie A, et al. The incidence and prevalence of delirium across palliative care settings: A systematic review. *Palliative medicine*. 2019;33(8):865-77.
3. Fang C-K, Chen H-W, Liu S-I, Lin C-J, Tsai L-Y, Lai Y-L. Prevalence, Detection and Treatment of Delirium in Terminal Cancer Inpatients: A Prospective Survey. *Japanese Journal of Clinical Oncology*. 2008;38(1):56-63.
4. Spiller JA, Keen JC. Hypoactive delirium: assessing the extent of the problem for inpatient specialist palliative care. *Palliative Medicine*. 2006;20(1):17-23.
5. Rainsford S, Rosenberg J, Bullen T. Delirium in Advanced Cancer: Screening for the Incidence on Admission to an Inpatient Hospice Unit. *Journal of Palliative Medicine*. 2014;17(9):1045-8.
6. Downing LJ, Caprio TV, Lyness JM. Geriatric psychiatry review: differential diagnosis and treatment of the 3 D's-delirium, dementia, and depression. *Current psychiatry reports*. 2013;15:1-10.
7. Bramati P, Bruera E. Delirium in Palliative Care. *Cancers (Basel)*. 2021;13(23).
8. Wilson JE, Mart MF, Cunningham C, Shehabi Y, Girard TD, MacLulich AMJ, et al. Delirium. *Nature Reviews Disease Primers*. 2020;6(1):90.
9. Scottish Palliative Care Guidelines. 2020. <https://www.palliativecareguidelines.scot.nhs.uk/guidelines/symptom-control/delirium.aspx>. Accessed 25 January 2023.
10. Scottish Intercollegiate Guidelines Network. SIGN 157. Risk Reduction and Management of Delirium. 2019. <https://www.sign.ac.uk/media/1423/sign157.pdf>. Accessed 25 January 2023.
11. National Institute for Health and Care Excellence. Delirium: Prevention, diagnosis and management in hospital and long-term care. Clinical Guideline (CG103). 2010 (Updated: January 2023). <https://www.nice.org.uk/guidance/cg103>. Accessed 25 January 2023.
12. Australian Commission on Safety and Quality in Health Care. Delirium Clinical Care Standard (Revised 2021) https://www.safetyandquality.gov.au/sites/default/files/2021-11/delirium_clinical_care_standard_2021.pdf Accessed 25 January 2023.
13. Canadian Coalition for Seniors' Mental Health. Guideline on the Assessment and Treatment of Delirium in Older Adults at End of Life. Adapted from the CCSMH National Guidelines for Seniors' Mental Health. 2010. (Updated 2019) https://ccsmh.ca/wp-content/uploads/2016/03/NatlGuideline_DeliriumEOLC.pdf. Accessed 25 January 2023.
14. Bush SH, Lawlor PG, Ryan K, Centeno C, Lucchesi M, Kanji S, et al. Delirium in adult cancer patients: ESMO Clinical Practice Guidelines. *Ann Oncol*. 2018;29(Suppl 4):iv143-iv65.
15. Woodhouse R, Siddiqi N, Boland JW, Featherstone I, Johnson MJ. Delirium screening practice in specialist palliative care units: a survey. *BMJ Supportive & Palliative Care*. 2020;bmjpspcare-2020-002251.
16. de la Cruz M, Fan J, Yennu S, Tanco K, Shin S, Wu J, et al. The frequency of missed delirium in patients referred to palliative care in a comprehensive cancer center. *Supportive Care in Cancer*. 2015;23(8):2427-33.
17. Watt CL, Scott M, Webber C, Sikora L, Bush SH, Kabir M, et al. Delirium screening tools validated in the context of palliative care: A systematic review. *Palliat Med*. 2021;35(4):683-96.
18. Sands MB, Sharma S, Carpenter L, Hartshorn A, Lee JT, Lujic S, et al. "SQiD, the Single Question in Delirium; can a single question help clinicians to detect delirium in hospitalised cancer patients?" running heading Single Question in Delirium" (Bcan-D-20-01665). *BMC Cancer*. 2021;21(1):75.
19. Sands MB, Dantoc BP, Hartshorn A, Ryan CJ, Lujic S. Single question in delirium (SQiD): testing its efficacy against psychiatrist interview, the confusion assessment method and the memorial delirium assessment scale. *Palliative medicine*. 2010;24(6):561-5.
20. Ryan K, Leonard M, Guerin S, Donnelly S, Conroy M, Meagher D. Validation of the confusion assessment method in the palliative care setting. *Palliative Medicine*. 2009;23(1):40-5.
21. American Delirium Society. <https://americandeliriumsociety.org/healthcare-professionals/ags-cocare-cam-and-help-tools/> accessed 3/11/23.
22. Canadian Coalition for Seniors' Mental Health. Canadian Coalition for Seniors' Health. Guideline on the Assessment and Treatment of Delirium in Older Adults at End of Life. Adapted from the CCSMH National Guidelines for Seniors' Mental Health. 2010. (Updated 2021) <https://ccsmh.ca/projects/delirium/> Accessed 25 January 2023. [
23. Scottish Intercollegiate Guidelines Network. Scottish Intercollegiate Guidelines Network. SIGN 157. Risk Reduction and Management of Delirium. 2019. <https://www.sign.ac.uk/media/1423/sign157.pdf>. Accessed 25 January 2023. [

24. National Institute for Health and Care Excellence. National Institute for Health and Care Excellence. Delirium: Prevention, diagnosis and management in hospital and long-term care. Clinical Guideline (CG103). 2010 (Updated: January 2023). <https://www.nice.org.uk/guidance/cg103>. Accessed 25 January 2023. [
25. Australian Commission on Safety and Quality in Health Care. Australian Commission on Safety and Quality in Health Care. Delirium Clinical Care Standard (Revised 2021) https://www.safetyandquality.gov.au/sites/default/files/2021-11/delirium_clinical_care_standard_2021.pdf Accessed 25 January 2023. [
26. 4AT Rapid Clinical Test for Delirium. <https://www.the4at.com>. Accessed 15 January 2023.
27. Tiegies Z, Maclullich AMJ, 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*. 2020.
28. Arnold E, Finucane AM, Spiller JA, Tiegies Z, MacLullich AMJ. Validation of the 4AT tool for delirium assessment in specialist palliative care settings: protocol of a prospective diagnostic test accuracy. *ARMC Open Research*. 2021;3:16. <https://doi.org/10.12688/armcopenres.12973.1>.
29. Shenkin SD, Fox C, Godfrey M, Siddiqi N, Goodacre S, Young J, et al. Protocol for validation of the 4AT, a rapid screening tool for delirium: a multicentre prospective diagnostic test accuracy study. *BMJ Open*. 2018;8(2):e015572.
30. Flahault A, Cadilhac M, Thomas G. Sample size calculation should be performed for design accuracy in diagnostic test studies. *Journal of Clinical Epidemiology*. 2005;58(8):859-62.
31. Scottish Government. Adults with Incapacity (Scotland) Act 2000. <https://www.legislation.gov.uk/asp/2000/4/contents>. Accessed 30 September 2020.
32. Bellelli G, Morandi A, Davis DHJ, 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.
33. Mandrekar JN. Receiver Operating Characteristic Curve in Diagnostic Test Assessment. *Journal of Thoracic Oncology*. 2010;5(9):1315-6.
34. Abernethy AP, Shelby-James T, Fazekas BS, Woods D, Currow DC. The Australia-modified Karnofsky Performance Status (AKPS) scale: a revised scale for contemporary palliative care clinical practice [ISRCTN81117481]. *BMC Palliative Care*. 2005;4(1):7.
35. Tiegies Z, Maclullich AMJ, 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):733-43.
36. De J, Wand APF, Smerdely PI, Hunt GE. Validating the 4A's test in screening for delirium in a culturally diverse geriatric inpatient population. *Int J Geriatr Psychiatry*. 2017;32(12):1322-9.
37. O'Sullivan D, Brady N, Manning E, O'Shea E, O'Grady S, O'Regan N, 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):61-8.
38. Arnold E, Fairfield C, Spiller JA, Finucane AM. Exploration of delirium assessment and management in a hospice inpatient unit. *International Journal of Palliative Nursing*. 2022;28(11):506-14.
39. Johansson YA, 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.
40. Alhaidari AAO, Matsis KP. Barriers to completing the 4AT for delirium and its clinical implementation in two hospitals: a mixed-methods study. *European Geriatric Medicine*. 2022;13(1):163-72.
41. Anand A, Cheng M, Ibitoye T, Maclullich AMJ, Vardy ERLC. 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):afac051.
42. Harris C, Spiller J, Finucane A. Managing delirium in terminally ill patients: perspective of palliative care nurse specialists. *British Journal of Community Nursing*. 2020;25(7):346-52.
43. Arnold E, Finucane AM, Spiller JA, O'Rourke S, Spencely J, Carduff E, et al. 55 Validation of the 4AT for delirium detection in patients receiving palliative care in a hospice inpatient setting. *BMJ Supportive & Palliative Care*. 2023;13:A23.