



Hendry, K., Quinn, T. J., Evans, J., Scortichini, V., Miller, H., Burns, J., Cunnington, A., and Stott, D. J. (2016) Evaluation of delirium screening tools in geriatric medical inpatients: a diagnostic test accuracy study. *Age and Ageing*, 45(6), pp. 832-837. (doi:[10.1093/ageing/afw130](https://doi.org/10.1093/ageing/afw130))

This is a pre-copyedited, author-produced version of an article accepted for publication in *Age and Ageing* following peer review. The version of record Hendry, K., Quinn, T. J., Evans, J., Scortichini, V., Miller, H., Burns, J., Cunnington, A., and Stott, D. J. (2016) Evaluation of delirium screening tools in geriatric medical inpatients: a diagnostic test accuracy study. *Age and Ageing*, 45(6), pp. 832-837. is available online at: [10.1093/ageing/afw130](https://doi.org/10.1093/ageing/afw130)

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Deposited on: 26 April 2017

Introduction

Delirium is a common and serious acute neuropsychiatric disorder which affects up to 50% of hospitalised patients aged over 65 at some stage during their in-patient stay [1]. The negative outcomes associated with delirium include increased mortality, longer hospitalisation and increased risk of subsequent long-term cognitive impairment [2].

Evidence suggests that delirium is under-recognised in older hospitalised patients and this poses an obstacle to good quality patient care [3-4]. Delirium is missed in as many as two thirds of cases and this may be due to perceived lack of importance, over reliance on subjective clinical judgement and a lack of validated delirium screening tools for use in this population [5]. An ideal screening tool for delirium should be brief, require little or no training, and be appropriate to the clinical setting it is used in. It should prioritise high sensitivity over specificity, reliably detecting those with delirium and also have acceptable specificity, accurately identifying those without delirium as screen negative[6].

Published guidance recommends that all older adults admitted as an emergency to hospital should be assessed for possible dementia and delirium [7]. However, there is no consensus on how this assessment should be performed. So, it is currently unclear what clinicians should do as a first step in identification of delirium in older, hospitalised patients.

This project aimed to evaluate the test accuracy of routinely used brief cognitive assessment tools for detection of clinical diagnosis of delirium.

Methods

We used routine health-care data collected as part of a departmental audit and service improvement initiative looking at delirium assessment. Approval to access, collect and analyse NHS data for this study was obtained from the Caldicott Guardian. The components of the cognitive tests which we used were all recommended for routine clinical use in the assessment of older people in the Rehabilitation and Assessment Directorate of Glasgow and Greater Clyde. In reporting our project, we followed best practice guidance as described

in the dementia specific extension to STAndards for the Reporting of Diagnostic accuracy studies [8].

Participants

We gathered data from a consecutive cohort of non-elective elderly-care hospital in-patients within an urban teaching hospital. In-patients aged ≥ 65 years admitted under the care of 6 senior elderly care physicians were eligible. We included all admissions to specific single sex wards (4 female, 1 male) within the geriatric assessment unit (GAU). The GAU admits older adults for comprehensive geriatric assessment following initial triage in an acute medical unit.

Assessments

Direct patient screening and clinician assessment of delirium was performed once per patient.

Index Tests: Routine cognitive assessments were administered and collated by a single observer (KH), blinded to the clinical delirium and dementia assessment. We aimed to complete patient screening within 2 hours of clinician assessment.

Routine cognitive assessments as recommended for clinical practice were the components of Hodkinson's AMT (the AMT-10 which includes the AMT/-4) [9-10], the bCAM [11], 4AT [12], which includes reciting of months of the year backwards (MOTYB), and the SQiD [13]. This comprised a total of 14 items in direct patient assessment, 3 items for nurse observations, and a question for relatives or informal carers. The order of testing was fixed.

Details of the cognitive assessments performed are provided as supplementary information in on-line appendix 1.

Patient test duration was timed using a stop-watch. Following patient assessment, any barriers to the patient's ability to complete any part or all of the cognitive assessment

procedure was recorded such as hearing impairment, dysphasia, and medical instability. A headset with amplifier was also made available to patients with hearing impairments.

Informant data included information from the on-duty nurse responsible for the relevant patient, collected as soon as possible after patient testing, informant data were also gathered by the ward nurse from a relative or close friend of the patient using a paper form asking the SQiD single questions. Informants were not contacted by telephone as this was not deemed usual practice.

We obtained clinical and demographic information from patient case-notes following assessment. This included age, sex, date of admission, main symptom(s) at presentation, and barriers to communication (including deafness, visual impairment, and dysphasia).

Information obtained from direct patient testing was fed back to the relevant clinician to inform the patient care process.

Training of the researcher (KH) included completion of an MSc with a focus on delirium assessment in intensive care unit. Further training in Glasgow included direct observation and feedback from an experienced clinician (DJS).

Reference Standard: The reference standard of delirium was a clinical diagnosis by one of six experienced elderly care physicians all with an interest in cognitive assessment and delirium. Clinical assessment was performed as part of routine clinical care on twice weekly consultant ward rounds. Clinical diagnosis was carried out using an operationalised format of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM 5) criteria for diagnosis of delirium [15] whereby clinicians completed a checklist for each patient which listed each diagnostic criteria. This initial assessment was blinded to index test results. Patients were classified as i) definite delirium (meeting all DSM 5 criteria), ii) possible delirium (don't know for one or more of DSM5 criteria, with all other criteria met), iii) no delirium (failing to meet one or more of DSM 5 criteria not met).

Clinicians also assessed patients for clinical diagnosis of dementia, accepting this label if patients had prior diagnosis of dementia, or if they met DSMIV criteria for a new diagnosis

of dementia [16]); possible new dementia was recorded if there was uncertainty for one or more of the DSMIV criteria; with all other criteria met); absence of dementia was recorded if patients failed to meet one or more of the DSM IV criteria.

Statistical Methods

Subjects were categorised according to delirium diagnosis (definite, possible, no delirium). Differences in clinical and demographic features between the three groups of patients were described using Kruskal-Wallis H test analyses. Where data suggested a between group difference, we used Mann Whitney U analysis to confirm differences between two groups.

We described test accuracy statistics of sensitivity, specificity, positive and negative predictive values and corresponding 95% confidence intervals; comparing the routine cognitive index tests (AMT-10, AMT-4, 4AT, bCAM, MOTYB and SQiD) against the reference standard of consultant elderly care physician diagnosis of delirium (DSM 5). For the 4AT, a pre-determined threshold of $\leq 4/12$ was used as suggested in reference materials. The bCAM and SQiD were both dichotomised as positive or negative outcomes.

Receiver operating characteristic (ROC) analyses were carried out separately on all index tests, comparing to reference standard DSM5 delirium diagnosis. ROC analyses were used to select optimal cut-point for screening tests which did not have an agreed cut-point specifically for delirium based on existing literature (AMT-10/-4). Data were analysed separately for delirium only diagnosis (table 2) and a composite of delirium and possible delirium diagnosis (table 3).

All analyses were performed using SPSS for Windows (version 22.0; SPSS, Armonk NY, IBM Corp.)

Results

We assessed 500 patients over an 8 month period. Clinician assessment for delirium was completed in 474/500 patients (94.8%), with 8/500 (1.6%) not assessable and 18/500 (3.6%)

patients not seen by study clinician during the assessment period. Patients were 433/500 (87%) female; mean age 83.1 years (SD= 6.7) (Table 1). Patients were tested a median of 2 days after admission (IQR=0-4).

Reference standards:

Using DSM5 delirium criteria, 93/500 (18.6%) patients had definite delirium, 104/500 (20.8%) possible delirium and 277/500 (55.4%) no delirium. See figure 1 in supplementary materials.

A total of 140/500 (28%) of patients had a prior diagnosis of dementia and 22/500 (4%) received a new diagnosis of dementia (DSMIV criteria).

Index tests:

Figure 1 in online supplementary materials outlines total numbers of patients able to complete each index test as well as barriers faced for each test.

Index test assessment took place at a mediantime of 50 minutes (IQR=25-70) from clinician delirium assessment. Index test assessment took a median time of 4 (IQR=4-5) minutes. We were able to obtain a total score as well as a reference standard assessment in 434 patients on the 4AT; 408 patients on the AMT-4/-10; 406 patients on the months of the year backwards; 387 patients on the bCAM. Data was obtained from relatives or carers for 141/500 (28.2%) patients using the SQiD. Median patient score on the AMT-10 for those diagnosed as definite delirium was 3(IQR=2-5); for possible delirium 5 (IQR=4-6); for no delirium 7 (IQR=3-9); a lower score indicates greater impairment. Median patient score on the 4AT for those diagnosed as definite delirium was 7 (IQR=6-7); for possible delirium 4 (IQR=2-7); for no delirium 1 (IQR=0-3) with a higher score indicating greater impairment.

Sensitivity of screening assessments for definite delirium ranged from 92.7% (95% CI= 84.8-97.3) (AMT-4 \leq 3/4) to 70.3% (95% CI= 58.5-80.3) (bCAM). Specificity for definite delirium ranged from 91.4% (95% CI=87.7-94.3) (bCAM) to 49.7 (95% CI=44.1-55.3) (MOTYB \leq 5/12). ROC curves for patients with definite delirium are displayed in supplementary materials figure 2.

Discussion

We found that brief cognitive tests, including AMT10, AMT4, MOTYB and 4AT, had good sensitivity for detecting definite delirium, with sensitivity of these tests above 86%. However the specificity of these assessments for definite delirium was less good, ranging from 50 to 70%. These figures are reflected in the negative and positive predictive values, with good negative predictive value (over 95%) but poor positive predictive value (40% or less).

Amongst these assessments using the full AMT-10 seemed to carry no advantage over the subset of questions in the AMT-4, with very similar diagnostic performance characteristics.

The performance of the bCAM as a screening test for delirium appeared to be less good, with poor sensitivity, missing around 3 in 10 patients with delirium. However it had good specificity at over 90%. Therefore the bCAM might have a role as an assessment to detect patients with definite delirium for research studies (few false positives), but it appears not to be appropriate as a clinical screening test for the acute medical condition of delirium (too many false negatives).

The above brief cognitive assessments appeared to be feasible in this cohort, although common barriers to assessment (severe illness, depressed conscious level, inability to respond to instruction) prevented direct assessment of cognition in around 1/5 cases. The informant-based SQiD showed promise as a screening assessment, with high sensitivity and good negative predictive value, however it proved difficult to obtain these data with informant responses obtained in less than 30%.

The 4AT was found to be the most feasible tool with the highest patient completion rate. This is due to the patients receiving a maximum score of 2 on each of the two direct cognitive testing components (MOTYB and AMT 4) if they are unable to attempt these components of the test, rather than being deemed non-assessable. The bCAM was not found to be feasible within this cohort and this appears to be due the tool relying on the patient being able to complete the direct cognitive testing components and in cases where this did not happen, it was not possible to complete assessment with the bCAM.

This study showed that there was often uncertainty in the diagnosis of delirium, even by experienced clinicians with an interest in cognitive impairment. Diagnostic uncertainty is a major issue which is generally under-recognised within the current literature, where there is often a focus on making a definite yes or no delirium diagnosis.

Our findings are generally consistent with the published literature. The prevalence of delirium was in line with other recent reports of older hospital inpatients. A meta-analysis of 42 studies reported delirium prevalence in medical in-patients to be 10-31% [17].

Some investigators have reported better performance of the 4AT; this assessment has been reported to have very high sensitivity (100%) and good specificity (82%) within the acute stroke unit setting [18]. However, this was in a smaller patient sample (n=108) than our study. Furthermore, this study was within a different patient setting, used a different diagnostic criteria (the CAM based on DSM III criteria) and demonstrated a lower delirium prevalence of 11%. The 4AT was also investigated as a delirium assessment tool in a consecutive sample within acute care in Italy (n=236) [12]. In this study, the 4AT was found to have a sensitivity of 90% and specificity of 84%. We found a similar sensitivity although specificity in our study was not as good. This study demonstrated a lower delirium prevalence of 12% and did not compare the 4AT with other brief cognitive assessments.

There is limited validation data published on the bCAM. It has been tested in an emergency department sample of 406 patients with a lower prevalence of 12% delirium; they found similar test accuracy to our data with poor sensitivity and a missed delirium diagnosis in around 1 in 5 patients, but claimed excellent specificity of 97% [11].

Our study has confirmed that no single screening tool is 'perfect' in the detection of delirium. In clinical practice, delirium can signify important underlying illness and so sensitivity (ensuring all cases are correctly diagnosed) is important. Our data suggest that simple and brief screening tests such as the AMT-4, or months of the year backwards are sensitive tools in the screening for delirium. However these brief cognitive assessments are conceptually simple and lack content validity for delirium diagnosis. They do not formally assess the separate components of the syndrome such as defined by the DSM5. For example, there is no measure in these assessments of the patient's level of arousal, fluctuation or if the patient's cognitive functioning represents a change from baseline. However, a comprehensive assessment may not be necessary initially and the tools could be used to "triage" those patients who need a more detailed delirium assessment. The simplicity of assessment and scoring makes these tests suitable for use by a non-specialist.

Results are strengthened by a relatively large, consecutive patient sample. We employed a blinded assessment methodology with separate individuals carrying out a range of index tests compared to a reference standard. Our reference standard mirrors clinical practice with experienced geriatricians using a standardised process of applying DSM 5 criteria for the diagnosis of delirium (appendix 1).

We acknowledge the limitations of this study. The index tests were combined to form a short program of questions performed in a fixed order of testing. Individual screening assessments may perform differently if used in isolation and there is the risk of potential contamination of results between different screening questions. Our project was designed to describe clinical practice in a single site, an urban teaching hospital in an area of high socio-economic deprivation, with high proportion of patients with underlying dementia. Results may not be generalizable to other health care contexts. Due to the allocation of single sex wards within the geriatric assessment unit, our evaluation included a low proportion of male participants.

Our data were gathered at a single point in time soon after admission and this may have artificially increased the diagnostic uncertainty of clinicians. In clinical practice patients are usually observed over a period, and this cumulative information 'feeds in' to determining whether or not delirium is present. Furthermore, while a small proportion of patients were identified as 'too drowsy' to be assessed for delirium, it may have been the case that these patients were 'unassessable' due to delirium. A revision to the DSM 5 delirium diagnostic criteria states that reduced level of consciousness is fundamental and patients must not be excluded due to not being able to complete direct cognitive testing [19].

We used ROC analyses to determine the optimal cut-points for the AMT-10 and AMT-4 due to the lack of existing research into optimal cut-points on these tests as screening tools for delirium. The approach may have exaggerated test performance compared to those tests where a cut-point is already established (4AT, MOTYB).

Conclusions:

The most brief, simple assessments in this study, the AMT-4 and months of the year backwards, were found to have good sensitivity for underlying delirium in a population with

a high prevalence of underlying dementia. The 4AT was found to have a slightly lower sensitivity, but higher specificity than these more simplified screening tools. The bCAM had poor sensitivity for definite delirium within this study, although it was highly specific; it seems less suited as a screening tool than the other assessments. Finally, systematic gathering of informant information such as using the SQiD was shown to have potential as a screening test, however further work is required on ways to more effectively capture this information. The results of this evaluation suggest that a two-stage approach for identification of delirium is appropriate using a highly sensitive brief delirium screening tool (such as AMT 4, MOTYB or 4AT) followed by more detailed clinician assessment of patients identified by the first stage.

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Figure 1. Testing procedure separated by informant assessment and direct-patient testing.

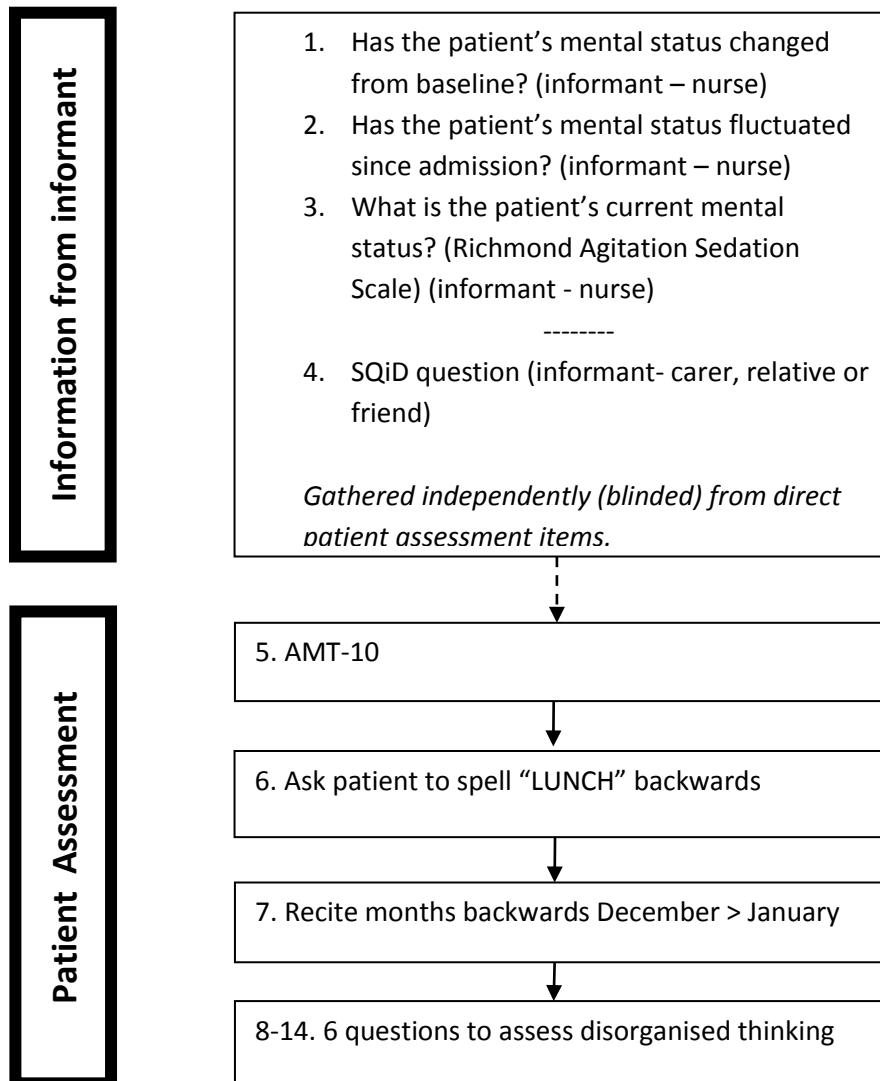


Table 1. Summary of characteristics of patients by delirium diagnosis (DSM 5 criteria).

	All patients (n= 500)[†]	Patients with delirium (n= 93)	Patients with possible delirium (n= 104)	Patients with no delirium (n= 277)
Mean age (years)	83.1 (SD=6.7)	83.9 (SD=6.1)	83.3 (SD=7.1)	83.0 (SD=6.8)
Male n (%)	67 (13)	18 (21)	9 (9)	34 (13)
Hearing impairment (%)	93 (18.6)	15 (16.1)	21 (20.2)	50 (18.1)
Sight impairment (%)	139 (27.8)	26 (28.0)	26 (25.0)	79 (28.5)
Alcohol dependence (%)	14 (2.8)	2 (2.2)	5 (4.8)	7 (2.5)
Main symptom at presentation;				
Confusion only (%)	102 (20.4)	26 (28.0) *	29 (27.9)	42 (15.2) *
Immobility only (%)	46 (9.2)	4 (4.3)	12 (11.5)	27 (9.7)
Falls only (%)	104 (20.8)	14 (15.1)	19 (18.2)	67 (24.2)
Combined confusion, mobility &/or immobility (%)	99 (19.8)	30 (32.3)	17 (16.3)	44 (15.9)
Other (%)	149 (29.8)	19 (20.3)	27 (26.1)	97 (35.0)
Cognitive assessments				
AMT-10 median (IQR)	6 (4-8)	3 (2-5)	5 (4-6)	7 (3-9)
AMT-10 n testable (%)	422 (84.4)	82 (88.2)	79 (76.0)	247 (89.2)
Prior/new dementia diagnosis n (%)	162 (32.4)	33 (35.5)	52 (50)	76 (27.4)

[†] 8 (1.6%) patients were not assessable for delirium and 18 (3.6%) patients were not assessed by elderly care physicians *p<0.001 Mann-Whitney U test; definite delirium compared to no delirium.

Table 2. Diagnostic test accuracy for delirium of Abbreviated Mental Test (AMT-10, AMT-4), 4 A's Test (4AT), brief Confusion Assessment Method (bCAM), months of the year backwards and Single Question in Delirium (SQiD) in study cohort of 500 patients. Patients with a definite delirium diagnosis (n=93) classified as positive for delirium compared to all other patients..

	Area under the curve (AUC)	Sensitivity % (n)	Specificity % (n)	Positive Predictive Value % (n)	Negative Predictive Value % (n)
AMT-10 (score $\leq 4/10$) n = 408	0.80	86.6 (71/82) 95% CI 77.3-93.1	63.5 (207/326) 95% CI 58.0-68.7	37.4 (71/190) 95% CI 30.5-44.7	95.0 (207/218) 95% CI 91.2-97.5
AMT-4 (score $\leq 3/4$) n = 408	0.80	92.7 (76/82) 95% CI 84.8-97.3	53.7 (175/326) 95% CI 48.1-59.2	33.5 (76/227) 95% CI 27.4-40.0	96.7 (175/181) 95% CI 92.9-98.8
4AT (score $\geq 4/12$) n = 434	0.84	86.7 (72/83) 95% CI 77.5-93.2	69.5 (244/351) 95% CI 64.4-74.3	40.2 (72/179) 95% CI 33.0-47.8	95.7 (244/255) 95% CI 92.4-97.8
bCAM n = 387	0.81	70.3 (52/74) 95% CI 58.5-80.3	91.4 (287/314) 95% CI 87.7-94.3	65.8 (52/79) 95% CI 54.3-76.1	92.9 (287/309) 95% CI 89.4-95.5
Months of the year backwards (score $\leq 5/12$) n = 406	0.76	91.3 (73/80) 95% CI 82.8-96.4	49.7 (162/326) 95% CI 44.1-55.3	30.8 (73/237) 95% CI 25.0-37.1	95.9 (162/169) 95% CI 91.7-98.3
SQiD n = 141	0.77	91.4 (32/35) 95% CI 76.9-98.2	61.3 (65/106) 95% CI 51.4-70.6	43.8 (32/73) 95% CI 32.2-56.0	95.6 (65/68) 95% CI 87.6-99.1

Supplementary materials

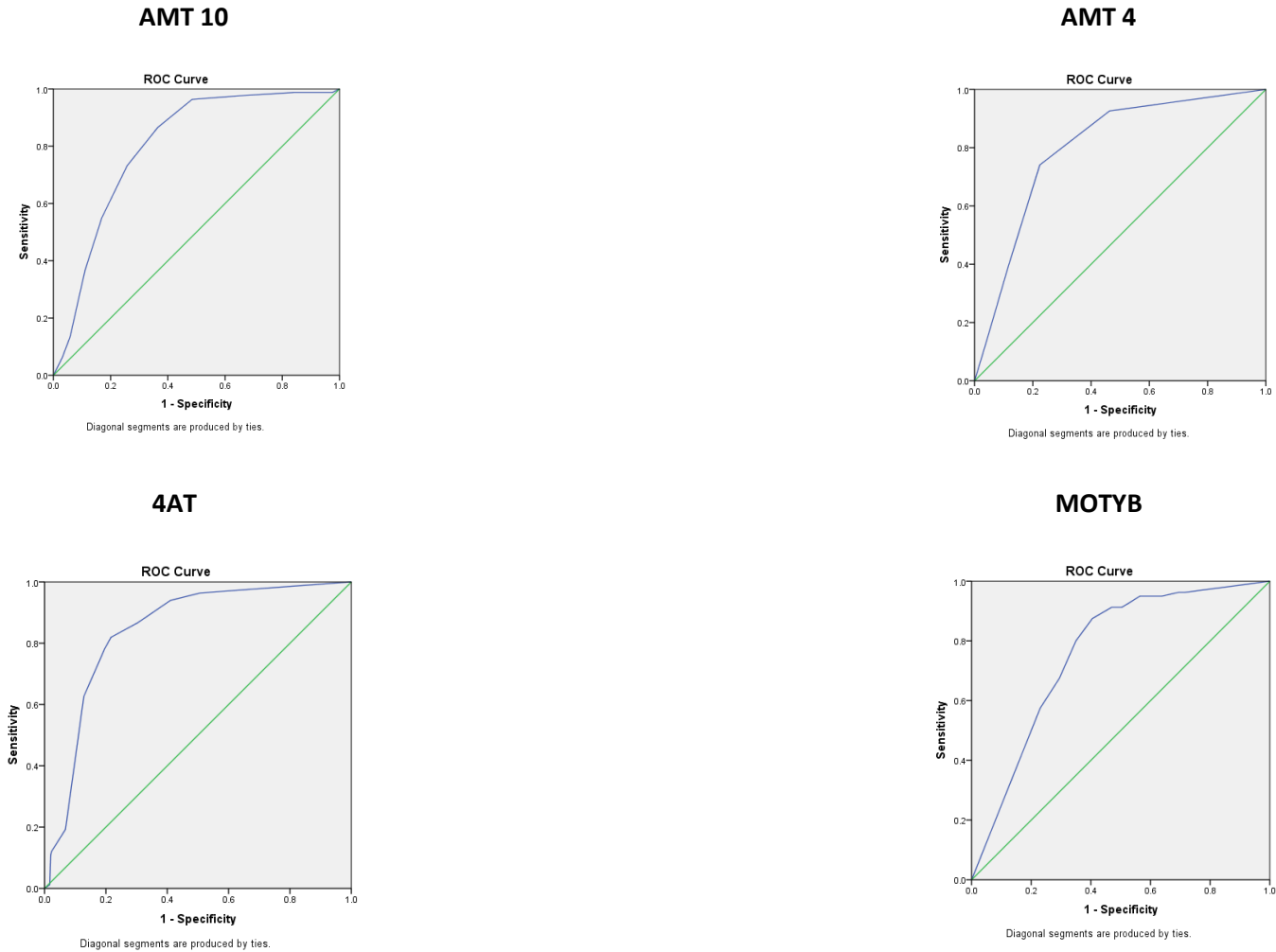


Figure 2. ROC curves showing index test performance for patients with definite delirium compared to all other patients. Index tests illustrated are those which use a continuous scale- AMT 10, AMT 4, MOTYB and 4AT. See table 2 for patient numbers for individual tests.

Appendix 1. Description of each screening test for delirium analysed within this evaluation.

AMT 10/4 [9-10]

The AMT10 is a ten item tool developed for the assessment of cognitive impairment. Patients gain a point for every correct answer,. A shorter version of this tool includes four of the ten AMT 10 questions, namely the AMT 4 which is scored out of a maximum of 4 points. A lower score on the AMT 4 and AMT 10 indicated increased impairment.

4AT [12]

This is a brief screening tool designed for the detection of possible delirium. This tool has 4 separate domains which measure alertness, AMT 4, attention (MOTYB) and acute change/fluctuating course. The tool has a maximum score of twelve with a higher score indicating increased impairment.

bCAM [11]

This is a two stage screening method for delirium. In the first stage the patients level of consciousness (direct observation) and inattention (Spelling 'lunch' backwards) are assessed. Patients with disturbed consciousness or more than one spelling error proceed to a second stage including assessment of inattention (MOTYB) and disorganised thinking assessed through direct patient testing (6 short questions). This tool is intended to be a short and pragmatic operationalisation of the Confusion Assessment Method, a method of delirium diagnosis which uses DSM IV criteria.

SQid [13]

A single screening question for delirium to be directed at a relative, carer or close friend of the patient. The question asks; "Has your friend/relative been more confused lately?" with a dichotomised response method, yes or no.

MOTYB

This is a brief test of inattention which asks the patient to recite the months of the year backwards starting at December and ending at January. We determined the patient's score out of a maximum possible 12 dependent on how many months they could recite backwards in the correct order. A validation study evaluating MOTYB as a screening test in general in-patient wards cited a optimal threshold of ≤ 5 out of 12 for detection of delirium [14].

Appendix 2. Operationalised DSM 5 delirium diagnostic criteria and DSM IV Dementia diagnostic criteria checklists used in this study.

DSM-V Delirium criteria / exclusions

- a) A disturbance in;**
- i) Attention- reduced ability to direct, focus, sustain, and shift attention **yes / no / don't know**
 - ii) Awareness (reduced orientation to the environment) **yes / no / don't know**
- b) The disturbance;**
- i) Develops over a short period of time (usually hours to a few days) **yes / no / don't know**
 - ii) Represents a change from baseline attention & awareness **yes / no / don't know**
 - iii) Tends to fluctuate in severity during the course of the day **yes / no / don't know**
- c) An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception).** **yes / no / don't know**
- d) Exclusions- The disturbance in criteria A and C are;**
- i) Better explained by another pre-existing, established, or evolving neurocognitive disorder **yes / no / don't know**
 - ii) Occur in the context of a severely reduced level of arousal such as coma. **yes / no / don't know**
- e) There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.** **yes / no**

INITIAL DIAGNOSIS: Delirium - all items a, b, c and e 'yes', plus d 'no'

No delirium - if any 'no' in a,b,c,or e or yes in d

Possible delirium - if any 'don't know' in a-d or 'no' in e.

REVISED DIAGNOSIS: Date: Delirium / Possible Delirium / No Delirium

DSM-IV Dementia criteria / exclusions

If prior diagnosis of dementia, please go to the diagnosis section below.

- a) Memory impairment** **yes / no / don't know**
- b) At least one of the following;** **yes / no / don't know**
 Aphasia Apraxia Agnosia
 Disturbances in executive functioning
- c) The cognitive impairments must be severe enough to cause impairment in social and occupational functioning.** **yes / no / don't know**
- d) The decline must represent a decline from a previously higher level of functioning.** **yes / no / don't know**
- e) Exclusion - The cognitive deficits occur exclusively during the course of a delirium.** **yes / no / don't know**

INITIAL DIAGNOSIS:

Dementia- prior diagnosis Dementia- a-d all 'yes' plus e 'no'

Possible Dementia- if any 'don't know' plus other responses all consistent with dementia as above

No Dementia- if any a-d 'no' or e 'yes'

REVISED DIAGNOSIS: Date: Dementia / Possible Dementia/ No Dementia

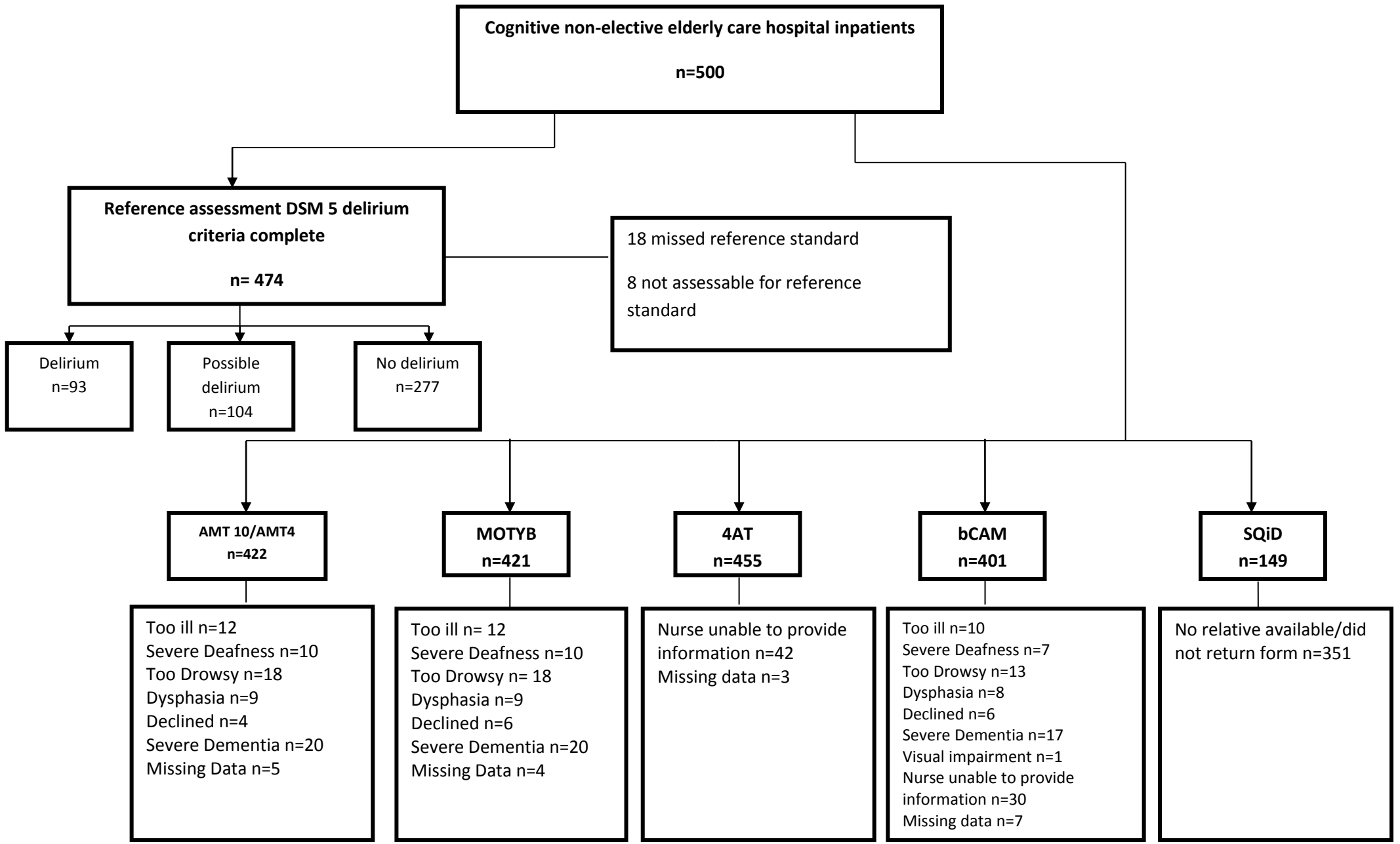


Figure 1. Flowchart illustrating the number of patients who received the DSM 5 delirium reference standard as well as numbers who completed each index test and reasons for those who did not.