INTRODUCTION
Folstein and colleagues published the Mini Mental State examination (MMSE) for brief quantitative assessment of cognitive function 30 years ago (Folstein et al. 1975). Since then it has been translated into many languages and has become the most widely used brief test of cognition in clinical and research settings, with adequate validation. The aim of the examination is:
• screen for cognitive impairment
• assess the severity of any impairment
• monitor change by serial testing

It relies heavily on verbal cognitive function at the expense of nondominant hemisphere skills and is vulnerable to the vagaries of scoring by different observers. Nevertheless, it has stood the test of time and provides a common and widely understood tool to measure global cognitive function.

STRUCTURE
The MMSE is a collection of questions that test various cognitive domains including orientation to time and place, repetition, verbal recall, attention and calculation, language and visual construction. The test takes 5–10 min to administer and the total test score ranges from 0 (impaired) to 30 (normal).

REQUIREMENTS FOR PERFORMING THE MMSE
• Privacy in a quiet, well-lit room with no distractions.
• Pen or pencil, watch, and a blank piece of paper.
• The subject is conscious and alert.
• The subject has sufficient knowledge of English and literacy skills to be able to cooperate with test items (a translated version of the MMSE administered by a trained translator may be used where available).
• The subject has adequate hearing, vision, articulation and dominant limb ability to perform the MMSE tasks other than those thought to be related to cognitive impairment. Hearing and visual aids should be worn if needed.
• Consistency in the examiner’s way of administering and scoring the MMSE to minimize variability.

HOW TO CONDUCT THE MMSE
The tester needs to establish rapport with the subject in order to put him or her at ease, and obtain cooperation. A simple explanation of the purpose and structure of the test is provided first. The subject is then asked to answer the questions to the best of their ability and to guess...
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if unsure. If next of kin are present, it is important to ask them not to assist the subject, unless for help with translation when required. The test is not timed, but it is sensible to assume a score of zero if the subject does not come up with an answer after 10–20 s. Whenever possible, record the patient’s exact response, and why he or she was not able to perform a task.

MMSE SUBTESTS
The MMSE test items are classified under the following headings:

Orientation to time
Ask the subject in turn, ‘what is the (year) (season) (month) (date) (day)?’ One should allow for seasonal transitions in the 2-week period spanning any seasonal change. In countries where other seasonal divisions are used, these can be accepted as alternatives, e.g. monsoon season.

Give one point for each correct answer to a maximum score of 5.

Orientation to place
Ask the subject in turn about the state/country, city/county, area of city/town, building/street name, floor of building/house number or type of room if in subject’s house. The set of questions will vary depending on whether the test is conducted in a large city or a small town, and whether in a hospital or the subject’s home.

Give one point for each correct answer to a maximum score of 5.

Repetition/registration
Ask the subject to listen carefully because you will ask him or her to repeat after you three words. Speak loudly and clearly and pause for 1 second after each word. Three unrelated words are used, most commonly ‘apple, penny, table’.

Give one point for each correct answer to a maximum score of 3, irrespective of recalled word order. Phonemic or paraphasic errors should be penalized. If the subject is not able to repeat all three words on the first trial, repeat them again up to fivetimes until he or she is able to say them all back to you. But the performance on only the first repetition is included in the total MMSE score.

Attention and calculation
Ask the subject to take away 7 from 100. Ask him or her to take away another 7 and continue to a total of 5 subtractions. An answer is considered correct if it is exactly 7 less than the previous answer.

Give one point for each correct answer to a maximum score of 5.

If a subject does not attempt the test or does not get a full score, then he or she is asked to spell WORLD, first forwards correcting any mistakes and then backwards. One point is given for each letter spelled in the correct order backwards to a maximum score of 5. If more or less than 5 letters are given, then one point is deducted for each extra or missing letter.

Only use the best score of either the serial 7 s or spelling WORLD backwards in the total MMSE score.

Recall
Ask the subject to recall the three words you earlier asked him or her to remember, without prompting or giving any clues.

Give one point for each correct answer to a maximum score of 3, irrespective of recalled word order.
Naming
Point to a pen or pencil, and a watch, in turn and ask the subject to name them. Glasses or keys are possible substitutes.
Give one point for each correct answer to a maximum score of 2.

Repetition
Ask the subject to listen carefully and repeat what you are about to say. Say ‘no ifs ands or buts’ making sure all the ‘s’ letters are clearly articulated and pausing for a second after each word.
Score zero unless all the letters are clearly articulated in the correct order. A maximum score of one point is given.

Comprehension
Ask the subject to listen carefully and do what you are about to ask. Say clearly and loudly ‘take this paper with your right hand, fold it in half and put it on the floor’ (Fig. 1). Do not remind the subject what to do next if he or she forgets or does not understand what is required.
Score one point for each step performed correctly. If the right hand is disabled, then ask the subject to take the paper with his or her left hand.

Reading
Show the subject a blank piece of paper with ‘CLOSE YOUR EYES’ clearly written. Ask the subject to read and then do what the sentence says. Make sure that there is sufficient lighting and the subject is wearing his or her reading glasses if required. Provide the command in the subject’s first language if he or she cannot read English.
Only give one point if the patient closes his or her eyes.

Writing
Ask the subject to write a sentence on a blank piece of paper. Again make sure there is sufficient lighting, and reading glasses are worn if needed. If the subject does not respond then prompt him or her to write something about the weather or a pet.
Only give a score of one point if he or she writes a comprehensible sentence containing a subject and verb. Ignore minor spelling, grammatical or punctuation errors. Ignore quality of handwriting including tremor, letter size and linearity. Examples of acceptable and unacceptable sentences are shown in Fig. 2.

Drawing
Show the subject two clearly drawn intersecting pentagons, with each side about 2 cm long. Ask him or her to copy the diagram on a blank piece of paper.
A score of one point is given only if two five-sided figures are drawn overlapping to form a four-sided embedded figure. Scaling, side length, rotation, and tremor are ignored. Examples of acceptable and unacceptable drawings are shown in Fig. 3.

ALLOWANCE FOR SCORING
It is important to remember that the purpose of the MMSE is to test cognitive function, not any noncognitive disability. This has an impact on whether to modify the test items or allow for any inability to cooperate despite intact cognitive function. Examples include visual or hearing impairment, aphonia or dysarthria, and dominant limb disability. However, if the task cannot be performed due to possible cognitive dysfunction then the subject must be scored accordingly.
One should also consider the exact domain of cognition that is being tested. An aphasic subject who fails on tests of repetition, may still be orientated in time and place and be able to recall the 3 words if allowed to write his or her responses. In this case it is more valid to document the written rather than the verbal response.
Overall, it is important to document why a subject cannot perform a task, particularly if the cause is thought not to be due to an underlying cognitive deficit, and to record any minor modifications to the test items used. Although cut-off scores for dementia may not be applicable in such subjects, one could still monitor change with time on repeat testing – provided consistency in testing and scoring is maintained.

FACTORS THAT INFLUENCE MMSE SCORE
Age
MMSE scores tend to decline with increasing age, particularly over the age of 65 years – even after controlling for education. In addition, the range of scores tends to get wider with age (Crum...
et al. 1993). Although decline in performance on the MMSE may reflect normal ageing, it is worth noting that increasing age is of course associated with increasing risk of dementia.

**Education**

With increasing educational level, the MMSE scores tend to increase and the range of scores to narrow (Crum et al. 1993). Thus, education introduces a bias resulting in a false positive diagnosis of dementia in less educated subjects. Conversely, high education level may mask mild cognitive impairment and result in a false negative diagnosis. Education does not seem to affect the rate of change of MMSE scores in either cognitively normal or dementia subjects, and so repeat MMSE testing is not confounded (Helkala et al. 2002).

**Gender**

There seems to be no significant difference in MMSE scores between men and women. However, in one study men tended to make more mistakes on spelling and other language tasks whereas women were more likely to err on serial subtractions (Jones & Gallo 2002). Nonetheless, the consensus is that gender is not a determinant of MMSE performance (Tombaugh & McIntyre 1992).

**Socioeconomic status**

Subjects from lower socioeconomic classes tend to have a lower MMSE score (Brayne & Calloway 1990; O’Connor et al. 1989). This may be in part be because of and so confounded by poor education. Other possible explanations could be developmental
cognitive limitations predisposing to lower socioeconomic attainment, or vice versa, lower socioeconomic status associated with a higher risk of developing dementia.

Culture, language and ethnicity
There is some suggestion that MMSE scores are affected by race and ethnicity. MMSE scores are reported to be lower in older black and other ethnic minority groups (Parker & Philip 2004; Espino et al. 2001). However, most of the difference is thought to reflect lower educational level, socioeconomic status, type of neighbourhood, and reduced English language fluency in immigrants compared to the indigenous white population.

Test location
Subjects tend to perform better at home than in hospital, probably due to better orientation and reduced anxiety. Therefore, it is important to maintain consistency in the test location on repeat testing in order to reduce variability in MMSE performance.

Test repetition
Non-demented subjects typically improve their performance if the test is re-administered within a two-month interval. However, this effect is less prominent in patients with dementia where learning is defective and counterbalanced by disease progression with time (Hékala et al. 2002; Galasko et al. 1993). Repeat presentation of the MMSE within a short interval (under two months) improves the accuracy of the MMSE as a screening tool for early dementia (Hékala et al. 2002). In order to reduce the bias of learning, one can use different words for the recall task, and different common objects to name on each testing occasion. However, there are no parallel forms for the other components of the MMSE.

TEST PERFORMANCE
Internal consistency between the test domains
There seems to be a good degree of homogeneity (internal consistency) between the various test items of the MMSE which suggests that the test is reliable. However, as the MMSE is meant to measure different cognitive domains, some degree of heterogeneity would be desirable. The degree of internal consistency depends on several factors. It tends to be higher in hospital-based studies compared with community-based studies, and among subjects with lower education than those with higher education. The use of serial sevens alone as opposed to the combination with spelling WORLD backwards yields a higher level of internal consistency (Espino et al. 2004).

Test-retest reliability
For a test-retest interval of 2 months or less, the correlation coefficient between each subject’s baseline and repeat MMSE scores is around 0.9 (Folstein et al. 1975; Tombbaugh & McIntyre 1992) in both normal and demented subjects, suggesting good test-retest reliability. The change in score is partly due to improvement in performance as a result of practice. With a test-retest interval of about 2 years, the correlation coefficient is less but still acceptable at 0.8 in nondemented subjects (Hopp et al. 1997). Repeat MMSE testing over a 5-year period in normal subjects over the age of 65 years shows a slight improvement in the first year, probably reflecting a practice effect, followed by slight decline over the following 4 years (Jacmin-Gadda et al. 1997).

Inter-rater reliability
Folstein et al. found a high inter-rater reliability coefficient of 0.8 (Folstein et al. 1975). However, this has subsequently been found to be significantly lower (Bowie et al. 1999), mostly due to variability in the scoring criteria and the version of the attention test used, i.e., whether serial 7’s alone, spelling WORLD backwards alone, or both (Davey & Jamieson 2004).

Validity
The sensitivity and specificity of the MMSE in differentiating dementia from normality depends on the cut off score, pattern of cognitive impairment present, disease severity, and subject characteristics such as age, education, cultural influence, language fluency, and test location. Using a cut-off score of below 24, the MMSE is 87% sensitive and 82% specific in detecting dementia and delirium among inpatients on a general medical ward (Anthony et al. 1982). A higher cut-off score increases sensitivity of detecting mild dementia, particularly in young educated individuals, but reduces the specificity and increases the false positive diagnosis of dementia in older uneducated individuals and in those belonging to ethnic minority groups. The MMSE is more specific and sensitive in detecting moderate to severe dementia than mild forms of dementia, and in detecting cognitive deficits related to language and memory rather than frontal executive dysfunction.

Several approaches have been used to improve the validity of the MMSE. One is to generate population-based normative data to provide different cut-off scores, stratified according to age and education level (Crum et al. 1993). However, it is doubtful if such adjustments improve the accuracy of the MMSE (Jones & Gallo 2002). Another approach is to use modified forms of the MMSE to minimize educational and cultural bias (Xu et al. 2003). Modifications to the MMSE have also been suggested in order to improve the accuracy of differentiating Alzheimer’s disease from normality, including the use of differential weighting of different test items (Galasko et al. 1990), adding extra test items such as word fluency (Galasko et al. 1990), date and place of birth, similarities and delayed recall of words (Teng & Chui 1987), and taking into account an informant rating score (Tierney et al. 2003). Although these modifications tend to produce subtle improvements, they prolong the testing time and are not as popular as the original MMSE.

PATTERNS OF COGNITIVE DECLINE IN DEMENTIA SYNDROMES
Patients with Alzheimer’s disease tend to perform worst on recall of three words and orientation to time (Galasko et al. 1990; Jefferson et al. 2002), whereas patients with vascular dementia, Parkinson’s disease and dementia with Lewy bodies tend to perform worst on attention, obeying a three-step command, writing a
SUMMARY

- Despite its limitations, the M M S E is the most widely used brief test of cognitive function.
- Clinically, it provides a baseline framework to structure the bedside cognitive assessment.
- It provides an objective record to monitor disease progression and response to treatment.
- It gives an estimate of disease severity that is meaningful for communication among different health care workers.
- Although modified versions of the M M S E do exist, the original M M S E is still the most popular form.
- The utility of the M M S E in clinical practice can be improved by bearing in mind patient characteristics that may affect performance (age, education, culture, ethnicity, hearing or visual impairment and any other relevant physical disabilities), and by using a standardized scoring scheme within and between physicians.

sentence and copying intersecting pentagons, suggesting impairment of working memory and motor, constructional and visuo-perceptual skills (Jefferson et al. 2002; Ala et al. 2002). Patients with fronto-temporal dementia tend to have higher M M S E scores in comparison to Alzheimer patients at initial presentation, and slower annual rates of decline (0.9 points vs. 2.0, respectively). This reflects the fact that the M M S E is geared more towards detecting impairments of orientation, memory and language than the executive dysfunction typical of fronto-temporal dementia.

MMSE AND THE USE OF CHOLINESTERASE INHIBITORS

Cholinesterase inhibitors such as donepezil, rivastigmine and galantamine have emerged as modestly useful agents for the symptomatic treatment of mild to moderate Alzheimer’s disease (Lanctot et al. 2003; Seltzer et al. 2004). Their cost implications, and the high disease prevalence in the elderly, have reinforced the need for brief and reliable tools for assessing eligibility for treatment, monitoring drug efficacy, and withdrawing treatment – such as the M M S E.

REFERENCES
