Codex (cognitive disorders examination) for the detection of dementia and mild cognitive impairment

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Summary

Background > Dementia is a major public health problem. Rapid and simple tests, easy to use for screening of dementia and mild cognitive impairment (MCI), are required.

Aim > To examine the utility of Codex (cognitive disorders examination), a decision tree, for the detection of dementia and MCI.

Methods > Codex was administered to 105 consecutive patients attending a memory clinic over a six month period.

Results > The study showed good sensitivity (0.81) and specificity (0.81) for Codex in identifying patients with dementia. The sensitivity and specificity were 0.68 and 0.90 respectively for the detection of MCI.

Conclusion > Codex is a simple, quick and reliable test for the detection of dementia, but it is not sufficiently sensitive for the detection of MCI.
Since its publication nearly 40 years ago, the Mini-Mental State Examination (MMSE) [1] has become the most commonly used cognitive screening instrument. This has occurred despite the recognized shortcomings of the MMSE, one problem being the time required for its administration. There have been many attempted modifications of the MMSE, a number of which aim to shorten its administration time without loss of diagnostic utility [2]. In one such modification reported by Belmin et al., named the cognitive disorders examination or Codex, a two-step decision tree was developed incorporating the three-word recall and spatial orientation components from the MMSE along with a simplified clock drawing test, taking around three minutes to perform. Codex produced four diagnostic categories with differing probabilities of dementia (A = very low, B = low, C = high, D = very high). In a validation study in elderly people, taking categories C and D as indicators of dementia Belmin et al. found Codex to have high sensitivity and specificity for the diagnosis of dementia (92% and 85% respectively), a better sensitivity than the MMSE [3].

Despite these encouraging initial findings, no further validation study of the diagnostic utility of Codex appears to have been published. Therefore, a pragmatic prospective study to examine Codex screening utility in an independent patient cohort was undertaken. This involved patients attending a cognitive disorders clinic and afforded not only the opportunity to examine Codex utility in the diagnosis of dementia but also of milder forms of cognitive impairment insufficient to reach a criterion diagnosis of dementia. The mild cognitive impairment (MCI) construct has achieved a degree of consensus and may in some instances delineate a pre-dementia disorder which might be amenable to interventions effective in slowing disease progression [4], hence the importance of identifying such cases. Cognitive screening instruments which are sufficiently sensitive to identify not only cases of dementia but also of MCI are therefore considered desirable in clinical practice.

The aims of the current study were to test the diagnostic utility of Codex in screening for dementia and for cognitive impairment (dementia and MCI) in day-to-day clinical practice in a large cohort of patients with cognitive complaints of unknown etiology.

### Methods

#### Patients

Consecutive patients referred to the Cognitive Function Clinic over a six month period (February–August 2012) were administered the Folstein MMSE [1] and a simplified Clock Drawing Test (sCDT), as per the Codex study [3]. Standard diagnostic criteria for dementia (DSM-IV) and dementia subtypes (e.g. Alzheimer’s disease, frontotemporal dementia, dementia with Lewy bodies) and MCI [5] were used as in previous pragmatic diagnostic accuracy studies undertaken in this clinic [6]. Criterion diagnosis was by judgment of an experienced clinician based on diagnostic criteria. Codex category was not used in diagnosis to avoid review bias [7].

#### Analysis

Summary measures of Codex diagnostic utility were calculated as in previous diagnostic accuracy studies (sensitivity, specificity, Youden index, positive and negative predictive values, predictive summary index, diagnostic odds ratio, positive and negative likelihood ratios, positive and negative utility index, area under the receiver operating characteristic curve) [6]. The desiderata of the STARD checklist for reporting diagnostic accuracy studies [8] were observed.

#### Results

Of 105 patients seen (M:F = 59:46, 56% male; age range 31–89 years, median age 62 years, mean 61.9 ± 13.3 years), 26 were diagnosed with dementia (dementia prevalence = 24.8%) and a further 18 with MCI (cognitive impairment prevalence = 20.6%). Dementia diagnoses were Alzheimer’s disease and mixed Alzheimer’s disease/cerebrovascular disease (AD/CVD; 18), dementia with Lewy bodies (DLB; 4), frontotemporal dementia (FTD; 2), and progressive supranuclear palsy (PSP; 2). All patients completed the MMSE and sCDT and could therefore be categorized according to the Codex decision tree (A = 25, B = 44, C = 1, D = 35). The probability of dementia in each Codex category with meaningful numbers of patients was A = 0.08, B = 0.07, and D = 0.60; the probability of cognitive impairment in each Codex category was A = 0.12, B = 0.25, and D = 0.86.

Taking Codex categories C and D as indicators of dementia [3], Codex was found to have good sensitivity and specificity for the diagnosis of dementia (0.81 and 0.81 respectively) (Table I, left hand column).

Taking Codex categories C and D as indicators of cognitive impairment (cases of dementia and of MCI combined), Codex sensitivity declined (0.68; more false negatives) whilst specificity improved (0.90; fewer false positives) (Table I, right hand column).

#### Comments

In this study, the Codex decision tree proved easy to use; no patient failed to be categorized according to Codex. The prevalence of dementia and of cognitive impairment was similar to that recorded in a previous recent non-overlapping patient cohort from this clinic (24% dementia and 43% cognitive impairment, respectively [9]).

The results confirmed the good sensitivity and specificity of Codex for the diagnosis of dementia, although the figures (0.81 and 0.81 respectively) were less good than in the validation study of Belmin et al. [3] (values reported in this paper were...
inconsistent, with sensitivity being given as 93% [p. 1184], 85% [p. 1186], and 92% [p. 1187 and p. 1189 Table IV]; and specificity as 85% [p. 1184, 1187 and 1189 Table IV] and 92% [p. 1186]). Positive predictive value was poorer (0.58 vs 90%, p.1186) but negative predictive values were similar (0.93 vs 88%, p. 1186).

These differences with the original study might relate, at least in part, to differences between the case-mix in the two cohorts, in terms of patient numbers (this study \( n = 105 \); Belmin et al. validation study \( n = 323 \)), sex ratio (this study 56% male, Belmin et al. validation study 77% female), dementia prevalence (this study = 24.8%; Belmin et al. validation study = 58.2%) and patient age (this study mean age = 61.9 ± 13.3 years; Belmin et al. validation study mean age dementia patients = 80.4 ± 7.1 years, mean age no dementia patients = 71.1 ± 9.4 years).

The paucity of cases falling into Codex category C in this study (\( n = 1 \)) was of note (absolute numbers per category not given in Belmin et al.), suggesting that it might be possible to simplify the decision tree even further into just three categories (i.e. very low, low, and high probability of dementia).

There were very few false negative diagnoses (5), but of note these included both FTD cases. However, 15 out of 18 AD/CVD cases and all DLB and PSP cases fell into category D. The false positive cases included patients with depression, chronic fatigue syndrome, and previous mild traumatic brain injury.

Extending the scope of Codex to examine not only dementia diagnoses but also MCI diagnoses showed poor sensitivity (0.68) although specificity remained high (0.90). Of note, 9/18 MCI patients were in categories A and B. It appears from this study that Codex may not be equivalent to other instruments designed specifically to identify MCI, such as the Montreal Cognitive Assessment [9,10]. Nevertheless, Codex is confirmed to be a good test for the diagnosis of dementia, the purpose for which it was designed [3]. In the absence of interventions proved to prevent progression of MCI to dementia, and the relatively low frequency of such progression, Codex retains a place in the assessment of cognitive complaints to both rule in and rule out dementia.

**Disclosure of interest:** the author declares that he has no conflicts of interest concerning this article.

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<thead>
<tr>
<th>Table I</th>
<th>Codex diagnostic utility (with 95% confidence intervals)</th>
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<tr>
<td></td>
<td>Diagnosis of dementia</td>
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<tr>
<td>Accuracy</td>
<td>0.81 (0.73–0.88)</td>
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<tr>
<td>Sensitivity</td>
<td>0.81 (0.66–0.96)</td>
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<tr>
<td>Specificity</td>
<td>0.81 (0.72–0.90)</td>
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<tr>
<td>Youden Index (Y)</td>
<td>0.62</td>
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<tr>
<td>Positive predictive value (PPV)</td>
<td>0.58 (0.42–0.74)</td>
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<tr>
<td>Negative predictive value (NPV)</td>
<td>0.93 (0.87–0.99)</td>
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<tr>
<td>Predictive summary index</td>
<td>0.51</td>
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<tr>
<td>Diagnostic odds ratio</td>
<td>17.9 (10.9–29.3)</td>
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<tr>
<td>Positive likelihood ratio (LR+)</td>
<td>4.25 (2.60–6.96) small</td>
</tr>
<tr>
<td>Negative likelihood ratio (LR−)</td>
<td>0.24 (0.15–0.39) small</td>
</tr>
<tr>
<td>Positive utility index (UI+)</td>
<td>0.47 poor</td>
</tr>
<tr>
<td>Negative utility index (UI−)</td>
<td>0.75 good</td>
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<tr>
<td>Area under the ROC curve</td>
<td>0.81 (0.71–0.91)</td>
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References


