Validation of the Greek translation of the Cognitive Disorders Examination (Codex) for the detection of dementia in primary care

**OBJECTIVE** To validate the Greek translation of the Cognitive Disorders Examination (Codex) and to investigate its potential for implementation for the detection of dementia in the Greek population.

**METHOD** Subjects aged ≥60 years with and without dementia, based on the diagnostic criteria DSM-IV-TR, were included in the study. Translation of the test Codex from French to Greek and back-translation from Greek to French were conducted to verify the validity of the translation. The Greek version of the Codex and the Mini Mental State Examination (MMSE) were administered to 17 patients with dementia and 27 patients without dementia.

**RESULTS** The median age of the participants was 82 years (range 61–93 years) for patients with dementia and 73 years (range 61–84 years) for patients without dementia. The average level of education was 9.0 years (range 2–20 years) for patients with dementia and 10.5 years (range 3–16 years) for those without. The average score on the MMSE was 15.7 (range 7–27) for patients with dementia and 28.3 (range 25–30) for those without dementia. The sensitivity of Codex for the detection of dementia was 94.1% and its specificity was 88.9%.

**CONCLUSIONS** The Greek version of Codex can detect dementia reliably. Its validation as a diagnostic tool for use in the Greek population will require testing on a larger sample of individuals.

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**Key words**
Cognitive Disorders Examination (Codex)
Cognitive impairment
Dementia
Primary care

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Dementia is a major problem in later life and has a significant social impact both in Greece and worldwide. The prevalence of dementia is constantly increasing, given that life expectancy is raising and the prevalence of dementia increases with age. It has been estimated that the number of people who suffer from dementia doubles every 20 years and will reach 81 million in 2040.1

According to data available from Alzheimer Europe, the mean prevalence of dementia in the European Union (EU-28) in 2012 was estimated to be 1.55%, which is equivalent to 8,702,033 cases. This estimation was based on the number of diagnosed cases of dementia, but as many patients with dementia have not received a formal diagnosis the real prevalence may be much higher. In Greece, it is estimated that 1.77% of the general population suffers from dementia, equivalent to 201,766 people. According to Alzheimer Hellas, it is believed that around 50,000 people in Greece are living with dementia that has not been diagnosed.2

Subjective memory complaints are very common in older people, but this does not necessarily mean that there is a cognitive decline, as shown by objective neuropsychological tests. In some cases, there may be an underlying cognitive dysfunction in the form of mild cognitive impairment (MCI), which is often a prodrome of dementia. In other cases, the person may suffer from depression or anxiety disorder with cognitive symptoms. Evidence of memory loss is one of the conditions for diagnosing dementia, but this alone is not enough. In addition to memory decline there

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Eπικύρωση της ελληνικής μετάφρασης του Codex (Cognitive Disorders Examination) για την ανίχνευση της άνοιας στην πρωτοβάθμια φροντίδα υγείας

Abstract at the end of the article

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needs to be at least one of the following four characteristics: Language disturbance, impaired ability to carry out motor activities, failure to identify objects, disturbance in executive functioning. Reversible physical causes or other mental illnesses need to be excluded. The criteria for the diagnosis of dementia are presented in Table 1. The most common cause of dementia is Alzheimer’s disease (AD), followed in decreasing frequency by vascular dementia, dementia with Lewy bodies, frontotemporal dementia and other rarer forms of dementia.

Among the tools used for diagnosing dementia, the most popular is the Mini Mental State Examination (MMSE), which has been validated in Greek. The MMSE consists of 30 questions covering orientation, learning, attention and calculation, recall of three words, language, triple command and copying. A score of below 24 indicates the presence of cognitive disorder. The main disadvantage of MMSE is that the outcome is dependent on the educational level of the individual, and in addition it is subject to cultural differences. As an example of its limitations, individuals of a higher educational level may need more detailed neuropsychological assessment to reveal mild cognitive decline. Conversely, individuals of a lower educational level may have difficulty in completing some of its components, without this meaning that they have a cognitive deficit. Moreover, its duration (approximately 10–15 minutes) is often a barrier to its implementation in the primary care setting.

Another popular tool for the assessment of cognitive functions is the Montreal Cognitive Assessment (MoCA), which has also been translated into Greek. The basic advantages of MoCA over MMSE are that it can be used with people of a lower educational level and it is very sensitive in detecting MCI and AD at an early stage.

Other tests that are used for the detection of dementia in primary care are the Clock Drawing Test (CDT), for which there is a variety of scoring systems, Mini Cog, General Practitioner Assessment of Cognition (GPCOG), which has been translated into Greek, Test Your Memory (TYM), that has been validated in Greek, and Addenbrooke's Cognitive Examination, and there are many other tools.

In 2007 Belmin and colleagues developed an ultra-rapid test for the detection of dementia, which they named Cognitive Disorders Examination (Codex). Codex consists of 3-word recall and a simplified Clock Drawing Test (sCDT) as the first step. If the individual does not perform correctly in one of the two components of the first step, then we proceed to the second step, which includes 5 questions of orientation in space. Codex consists of a decision tree which stratifies patients in four diagnostic categories based on the probability of dementia. The validation of Codex in France was conducted in a population of patients attending a memory clinic for consultation because of a subjective memory complaint. Its initial development was based on data from 242 individuals (derivation study) and it was subsequently validated in 323 individuals (validation study). The sensitivity of the test was 93% and its specificity 85%.

The objective of the present study was to validate the translation of Codex into the Greek language and to explore its potential for implementation in the Greek population.

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Table 1. Diagnostic criteria for dementia of the Alzheimer type (DSM-IV-TR).

<table>
<thead>
<tr>
<th>A. The development of multiple cognitive deficits manifested by both:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Memory impairment (impaired ability to learn new information or to recall previously learned information)</td>
</tr>
<tr>
<td>2. One (or more) of the following cognitive disturbances:</td>
</tr>
<tr>
<td>a. Aphasia (language disturbance)</td>
</tr>
<tr>
<td>b. Apraxia (impaired ability to carry out motor activities despite intact motor function)</td>
</tr>
<tr>
<td>c. Agnosia (failure to recognize or identify objects despite intact sensory function)</td>
</tr>
<tr>
<td>d. Disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)</td>
</tr>
</tbody>
</table>

| B. The cognitive deficits in criteria A1 and A2 each cause significant impairment in social or occupational functioning, and represent a significant decline from a previous level of functioning |

| C. The course is characterized by gradual onset and continuing cognitive decline |

<table>
<thead>
<tr>
<th>D. The cognitive deficits in criteria A1 and A2 are not due to any of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Other central nervous system conditions that cause progressive deficits in memory and cognition (e.g., cerebrovascular disease, Parkinson disease, Huntington disease, subdural hematoma, normal-pressure hydrocephalus, brain tumor)</td>
</tr>
<tr>
<td>2. Systemic conditions that are known to cause dementia (e.g., hypothyroidism, vitamin B12 or folic acid deficiency, niacin deficiency, hypercalcemia, neurosyphilis, HIV infection)</td>
</tr>
<tr>
<td>3. Substance-induced conditions</td>
</tr>
</tbody>
</table>

| E. The deficits do not occur exclusively during the course of a delirium |

| F. The disturbance is not better accounted for by another axis I disorder (e.g., major depressive disorder, schizophrenia) |
MATERIAL AND METHOD

Translation of Codex

Codex was first translated from French to Greek by C.A. after which a back-translation of the test from Greek to French was made by E.S.K. The back-translation was then checked by J.B., who is the creator of the original test in French. The Greek version of Codex and the decision tree are presented in Appendix 1 and Appendix 2.

Description of Codex

Codex consists of two steps, the second being conditional on the outcome of the first step. The first step includes two tests, a 3-word recall and a sCDT. First we ask the individual to repeat and keep in mind three simple words pronounced by the examiner, without scoring at this point. We then give the person a piece of paper on which is printed a circle 10 cm in diameter and ask the individual to draw the numbers of a clock face. We ask the individual to draw the clock hands to represent exactly the specific time requested (noted for later assessment). For the performance on the test to be considered normal at this step, the following conditions need to be fulfilled: The numbers are all present, their positions is correct, the direction of the hands shows approximately the time requested and we can distinguish the shorter from the longer hand. If one or more of these conditions are not met, then we consider the clock drawing test to be abnormal.

We subsequently ask the individual to recall the three words that were said to them earlier. This item is scored as normal if the patient remembers all three words. If both the 3-word recall and the sCDT are correct, the test Codex is ended and the person is classified in category Codex A, which is associated with a very low probability of dementia (92%). If both items of the first step are abnormal, the test Codex is also ended, but the patient is classified in category Codex D, which is related to a very high probability of dementia (92%).

If the result of one of the items of the first step is normal and the other is abnormal, we proceed to the second step. The second step includes 5 questions of orientation in space (see Appendix 1). Each correct answer is given 1 point, so that the overall score in this step may range from 0 to 5. If the score of the second step is 4 or 5, the person is classified in category Codex B, which is associated with low to moderate probability of dementia (23%). If the score is 0–3, the person is classified in category Codex C, which is related to a high probability of dementia (71%).

In general, categories A and B are considered to represent a negative result for dementia, indicating the need for investigation of alternative diagnoses. Categories C and D represent a positive result for dementia, and the patient should be referred to a specialist in dementia.

Study population

The study population included patients from the following settings:

(a) Patients attending the Neochori general practice, belonging to the Health Center of Argalasti in Magnesia, for chronic disease management or routine medical prescription.

(b) Patients attending the Unit for the Management of Alzheimer's Disease and Associated Disorders in Volos for examination by a psychologist due to of reported memory loss. These patients underwent complete neuropsychological assessment.

(c) Patients with a diagnosis of dementia who attended the Day Center of the Unit for the Management of Alzheimer's Disease and Associated Disorders in Volos to participate in various group activities.

All the participants were aged ≥60 years and all could see, hear and read (patients who could not read and those with severe visual or hearing impairment were excluded from the study). All patients gave their consent for inclusion in the study.

Methodology

All the participants were administered first Codex and then MMSE. The examination with these two tools was performed in such a way that the administration of Codex did not interfere with the administration of MMSE. Specifically, during the administration of Codex, for the 3-word recall we used the same three words which are used in MMSE, and during the subsequent administration of MMSE we used the score obtained earlier without repeating the 3-word recall test.

Basic demographic data (age, sex, and years of education) were recorded for all participants, who were divided into two groups: These who had dementia based on the diagnostic criteria DSM-IV-TR and those who did not have dementia (referred to as the control group or patients without dementia). The findings from the examination with Codex and MMSE were correlated with the clinical diagnosis (dementia or not) and the sensitivity, specificity, positive predictive value and negative predictive value of the Greek version of Codex were estimated.

Statistical analysis

Statistical analysis of the results was performed with the software Statistical Package for Social Sciences (IBM SPSS Statistics), version 22.0. Comparison among percentages was made with Pearson's chi square ($\chi^2$) test, and among continuous variables with the independent samples t-test. The results on Codex and MMSE were compared and the sensitivity, specificity, positive predictive value and negative predictive value of the Greek version of Codex were calculated.

RESULTS

In total, 44 patients participated in the study, among whom 17 had dementia based on DSM-IV-TR diagnostic...
criteria, and 27 did not have dementia. The median age of the patients with dementia was 82 years (range 61–93 years). In this group there were 13 women (76.5%) and 4 men (23.5%) and the mean level of education was 9 years (range 2–20 years). The mean MMSE score of the group with dementia was 15.7 (range 7–27).

In the group of patients without dementia, the median age was 73 years (range 61–84 years). There were 16 women (59.3%) and 11 men (40.7%) with a mean level of education of 10.5 (range 3–16 years). Their mean MMSE score was 28.3 (range 25–30). Among the patients without dementia, 17 (63%) reported a subjective memory decline when they were asked specifically, while the remaining 10 (37%) did not have any subjective memory complaint.

In both groups of patients there were more women than men, but the sex distribution did not differ significantly between patients with and without dementia (p=0.241). The level of education did not differ significantly between the two groups (p=0.314). As expected, the mean MMSE score was significantly higher in the group of individuals without dementia (p<0.0001).

In the group of individuals with dementia 16/17 were classified as Codex category D, and only one as Codex category B (this represents a negative result when the disease is present, i.e., a false negative result). In the group of individuals without dementia 11/27 were classified in Codex category A, 13/27 in Codex category B and 3/27 in Codex category D (the latter is a positive result when the disease is not present, i.e., a false positive result) (tab. 2).

The sensitivity of a test shows its ability to detect a disease when it is present and for the Greek version of Codex it was calculated as the percentage of true positive results out of the total number of patients with dementia (16/17), i.e., 94.1%.

The specificity of a test shows its ability to exclude a disease when it is not present. In this case it was calculated as the percentage of true negative results out of the total number of patients without dementia (24/27), i.e., 88.9%.

The positive predictive value of the Greek version of Codex was calculated as the percentage of true positive results out of the total number of positive results (16/19), i.e., 84.2%.

The negative predictive value of the test was calculated as the percentage of true negative out of the total number of negative results (24/25), i.e., 96%.

A comparison between the results of Codex and MMSE in the study patients is depicted in table 3. The score on MMSE was available in 41 patients (missing in 3). From these data, it appears that there is equivalence between the results of Codex and MMSE. Even though the numbers are small, these findings imply that Codex may have higher sensitivity and lower specificity than MMSE. In 5 individuals for whom the test Codex was positive, but who did not fulfill the criteria for dementia, the MMSE score was ≥24 (negative). Specifically, the MMSE scores of these 5 patients ranged between 25 and 27.

**DISCUSSION**

The general practitioner (GP) plays an important role in the investigation and management of people with cognitive disorders. The diagnosis of dementia is often made a considerable time after the onset of symptoms. GPs often have difficulty in recognizing dementia in the early stages

<table>
<thead>
<tr>
<th>Codex category</th>
<th>n</th>
<th>MMSE &lt;24 (positive for dementia) (n)</th>
<th>MMSE ≥24 (negative for dementia) (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients without dementia</td>
<td>0</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>Patients with dementia</td>
<td>14</td>
<td>25</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2. Cognitive Disorders Examination (Codex) diagnostic categories in patients with and without dementia.

<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Codex category</th>
<th>n</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with dementia</td>
<td>A</td>
<td>0</td>
<td>FN</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>FN</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>TP</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>16</td>
<td>TP</td>
<td></td>
</tr>
<tr>
<td>Subtotal</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients without dementia</td>
<td>A</td>
<td>11</td>
<td>TN</td>
</tr>
<tr>
<td>B</td>
<td>13</td>
<td>TN</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>FP</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>3</td>
<td>FP</td>
<td></td>
</tr>
<tr>
<td>Subtotal</td>
<td>27</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Comparison between the results of the Mini Mental State Examination (MMSE) and Cognitive Disorders Examination (Codex) in 44 older people with and without dementia.
and they do not always comply with the guidelines for the management of dementia. The main reasons for this are the limited time available for consultation in the primary care setting, a lack of relevant knowledge and appropriate education, the attitude of doctors towards the diagnosis of dementia, and the interaction between the complexity of the case and time pressures. A systematic review showed that there are significant differences among GPs regarding practices in diagnosing and managing dementia. The percentage of doctors who examined cognitive functions based on a validated diagnostic tool varied from 4% to 96%, depending on the study. More recently published studies indicate a shift in care practices, with an increase in intervention and specialist referral for dementia. A recent clinical trial in Australia aims to improve the education of GPs in the diagnosis and management of dementia in primary care.

The question of whether older people should be screened for dementia is a topic of debate. On the one hand, diagnosing dementia in its early stages has certain advantages: It enables the recognition of reversible causes of dementia and the timely onset of treatment aimed at delaying the progress of the disease, either with medication or with non-pharmacological methods, and provides the opportunity for planning the legal regulations that will be needed when the person no longer has the mental capacity to make decisions. On the other hand, the recognized criteria for mass screening are not fulfilled, as there is insufficient evidence that the implementation of screening has improved the outcome of the disease, and cost-effectiveness has not been proven. The gravity of the psychological cost and iatrogenic complications of an erroneous diagnosis in case of a false positive result should not be overlooked. For the above reasons, guidelines do not recommend screening of the general population for dementia. The identification of individuals with dementia (case finding) appears to be a more suitable approach.

The patient who presents at the GP surgery with reported memory loss should be examined in order to exclude or confirm an objective decline of memory or other cognitive functions. In many cases the individual is not aware of or does not complain about memory loss, but behavior changes are noticed by relatives. Such changes may be related to memory (e.g., the individual forgets to take medication, forgets to attend an important meeting, does not remember which day of the week it is, etc.) or other cognitive functions (e.g., neglect of personal hygiene, avoidance of complex cooking recipes, etc.). In such cases the GP is expected to recognize and investigate the symptoms.

Codex has been validated in French as a useful tool for the rapid detection of dementia. It has also been shown that an abnormal Codex result in patients without known dementia before surgical repair of hip fracture is associated with postoperative delirium.

This study was conducted as a first attempt to implement Codex in the Greek language and in the Greek population, in the context of primary care. The advantages of the test are its short duration (3 minutes) and ease of administration. According to these preliminary findings, the sensitivity of Codex in the detection of dementia is high (94.1%) and its specificity is also good (88.9%). It has also satisfactory positive predictive value (84.2%) and a high negative predictive value (96%). These findings are encouraging and show that the Greek translation of Codex may be used effectively in the Greek population.

In addition, comparison between the results of the Greek versions of Codex and MMSE showed that there is equivalence between the two tests. Despite the small size of the sample, the findings indicate that Codex may have higher sensitivity and lower specificity than MMSE. The individuals for whom the Codex result was positive, but who did not fulfill the diagnostic criteria for dementia had MMSE scores between 25 and 27. It is of note that the median level of education in this group of patients was 10 years; hence, these were people with a moderate to high level of education. This finding is consistent with the recommendation that the diagnostic threshold of MMSE should be adjusted to 27 (instead of 24) for people of a high educational level.

The main limitation of the present study is the small sample of patients. In order to validate Codex as a diagnostic tool in the Greek population, the study of a larger number of individuals is required, using rigorous methodology, including re-testing, inter-rater variability, and the definition of thresholds for positive and negative results.

This study, however, accomplished its main objective, which was the validation of the translation of Codex into the Greek language. Under the current extremely adverse financial circumstances in Greece, the familiarization of GPs with simple diagnostic tools for dementia can significantly help the elderly, a vulnerable group of people who are particularly affected by the financial crisis.

In conclusion, Codex is an easy, reliable and rapid test for the detection of dementia in the primary care setting. Use of the Greek version of Codex has provided the first encouraging results that can lead to its implementation in the Greek population after a larger validation study.
ACKNOWLEDGEMENTS – AUTHORS’ CONTRIBUTIONS

We warmly thank the patients who gave their consent to participate in the study. The study took place in the context of the dissertation of C.A. for the Diploma of Gerontology (Capacité de Gérontologie) at the University Pierre et Marie Curie (Université Paris 6) with supervisor the Professor Joël Belmin.

J.B. put forward the initial concept of the study, participated in the validation of the translation and supervised the study. C.A. and K.K. recruited the patients and administered the tests. E.S.K. participated in the validation of the translation. C.A. translated the test into Greek, did the statistical analysis and wrote the first draft of the manuscript. All the authors have read and approved the final version of the manuscript.

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Δοκιμασία CODEX – Φύλλο 1
Cognitive Disorders Examination

Όνομα ασθενούς: ................................................... ................................................... ................................................... ...
Ημερομηνία: .............. /.............. /..............
Πρώτο στάδιο:
Θα σας πω τρεις λέξεις. Σας παρακαλώ να τις επαναλάβετε μετά από μένα. Οι λέξεις είναι:
- Λεμόνι
- Κλειδί
- Μολύβι

«Σας ζητώ να τις κρατήσετε στη μνήμη σας, γιατί θα σας τις ζητήσω αμέσως μετά».

Δώστε στο άτομο ένα μολύβι και ένα φύλλο χαρτί στο οποίο είναι τυπωμένος ένας κύκλος διαμέτρου περίπου 10 cm (φύλλο 2).

«Αυτός ο κύκλος αντιπροσωπεύει το καντράν ενός ρολογιού χειρός ή ενός ρολογιού τοίχου. Σας παρακαλώ να γράψετε τους αριθμούς που βλέπουμε πάνω στο καντράν». Να προσέξετε το άτομο να μη χρησιμοποιήσει πρότυπο (ρολόι χειρός, ρολόι τοίχου).

Όταν το άτομο έχει τελειώσει: «Τώρα σας παρακαλώ να σχεδιάσετε τους δείκτες, με τρόπο που να αντιπροσωπεύουν την ακόλουθη ώρα: .............. » (ο εξεταστής υποδεικνύει την ώρα της επιλογής του. Σημειώνει την ώρα που ζητήθηκε: [ ___ ] / [ ___ ]).

Όταν το άτομο έχει τελειώσει: «Σας παρακαλώ να μου πείτε τις 3 λέξεις που σας ζήτησα να συγκρατήσετε». (αξιολόγηση)

### Αξιολόγηση του πρώτου στάδιου (κυκλώστε τις απαντήσεις):

- Θεσπισμένες λέξεις:
  - ΝΑΙ = φυσιολογικό
  - ΟΧΙ = μη φυσιολογικό
- Ρολόι:
  - ΝΑΙ = οι αριθμοί είναι όλοι παρόντες και σωστά σε προσέγγιση
  - ΟΧΙ = οι αριθμοί είναι όλοι παρόντες και δεν είναι σωστά σε προσέγγιση

Μπορούμε να διακρίνουμε τον μικρό και τον μεγάλο δείκτη = ΝΑΙ – ΟΧΙ
4 ΝΑΙ = φυσιολογικό
Σε κάθε άλλη περίπτωση = μη φυσιολογικό

### Οδηγίες διεξαγωγής του δεύτερου σταδίου:

Θέστε τις ακόλουθες ερωτήσεις, μία προς μία. Περιμένετε την απάντηση πριν να περάσετε στην επόμενη ερώτηση.

«Ποιο είναι το όνομα του νοσοκομείου όπου βρισκόμαστε*?»
«Ποιο είναι το όνομα του δρόμου του ιατρείου;»
«Σε όποιον όροφο είμαστε;»
«Σε ποιον όροφο είμαστε;»
*Στην πόλη: Ποιο είναι το όνομα του δρόμου του ιατρείου;

### Αξιολόγηση του δεύτερου στάδιου:

1 βαθμός για κάθε σωστή απάντηση = 

### Ερμηνεία

**CODEX μη φυσιολογικό:** Υψηλή πιθανότητα άνοιας. Θεωρήστε πιθανή τη διάγνωση της άνοιας. Παραπέμπετε τον ασθενή σε έναν ειδικό για την άνοια.

**CODEX φυσιολογικό:** Χαμηλή πιθανότητα άνοιας. Θεωρήστε πιθανές άλλες διαγνώσεις. Παρακολουθήστε τον ασθενή.
Δοκιμασία CODEX – Φύλλο 2
COgnitive Disorders EXamination

Όνομα ασθενούς: …………………………………………………
Ημερομηνία: ……../…../……

APPENDIX 2. Decision tree for the administration and interpretation of the Greek version of the Cognitive Disorders Examination (Codex).