ISSN 0755-4982

ELSEVIER MASSON

la Presse Médicale

Volume 36 - N°9
Septembre 2007
cahier 1

©2923 - Publication périodique mensuelle

www.masson.fr/revues/pm

Indexé dans / Indexed in :
MEDLINE/PubMed, Current Contents/Clinical Medicine, Current Contents/Life sciences, EMBASE/Excerpta Medica, Science Citation Index/SCI, PASCAL (INIST-CNRS)

Presse Med. 2007; 36: 1183–90

en ligne sur / *on line on*
www.masson.fr/revues/pm

The cognitive disorders examination (Codex) is a reliable 3-minute test for detection of dementia in the elderly (validation study on 323 subjects)

Joël Belmin[1], Sylvie Pariel-Madjlessi[1], Philomène Surun[1], Caroline Bentot[2], Dorin Feteanu[3], Véronique Lefebvre des Noettes[4], Fannie Onen[5], Olivier Drunat[6], Christophe Trivalle[3], Philippe Chassagne[2], Jean-Louis Golmard[7]

1. Consultation mémoire, Hôpital Charles Foix et Université Paris 6, Ivry-sur-Seine (94)
2. Consultation mémoire, Hôpital Bois Guillaume et Université de Rouen, Rouen (76)
3. Consultation mémoire, Hôpital Paul Brousse, Villejuif (94)
4. Consultation mémoire, Hôpital Émile Roux, Limeil-Brévannes (94)
5. Consultation mémoire, Hôpital Bichat et Université Paris 7, Paris (75)
6. Consultation mémoire, Centre hospitalier, Plaisir (78)
7. Service de Biostatistiques, Hôpital Pitié-Salpétrière et EA 3974, Université Paris 6, Paris (75)

Correspondence:
Joël Belmin, Service de gériatrie, Hôpital Charles Foix et Université Paris 6,
7 avenue de la République, 94 200 Ivry-sur-Seine, France.
Tel.: +33 1 49 59 45 65
Fax: + 33 1 49 59 43 79
joel.belmin@cfx.aphp.fr

Received May 2, 2006
Accepted December 7, 2006

Available online:
12 April 2007

Résumé

Codex, un test fiable en 3 minutes pour la détection de la démence chez le sujet âgés (étude de validation sur 323 sujets)

Contexte > *La démence est souvent diagnostiquée au stade modéré ou sévère, ce qui constitue une perte de chance pour les patients. Une détection plus précoce de la démence pourrait être améliorée par des outils faciles à employer en soin primaire.*
But > *Élaborer et valider un test très bref pour la détection de la démence.*
Méthodes > *Étude d'élaboration : chez les patients consécutifs d'une consultation mémoire vus pendant 2 ans, le niveau de l'éducation, les scores et sous-scores du* Mini Mental Status Examination *(MMSE) et un test d'horloge simplifié (THs) ont été recueillis. Le diagnostic de*

Summary

Background > Dementia often remains undiagnosed until it has reached moderate or severe stages, thereby preventing patients and their families from obtaining optimal care. Tools that are easy to use in primary care might facilitate earlier detection of dementia.
Aim > Develop and validate a very brief test for the detection of dementia.
Methods > In the derivation study, we recorded educational level, Mini Mental State Examination (MMSE) scores and subscores and results of a simplified clock-drawing test (sCDT) for consecutive patients attending a single memory clinic over a two-year period,. Dementia was diagnosed according to DSM-IV criteria. The independent variables related to dementia were determined by a multivariable logistic model (MLM) and used to develop a decision tree to predict this diagnosis. In the validation study, the decision tree was

doi: 10.1016/j.lpm.2007.03.016

démence (présence/absence) a été porté en utilisant les critères DSM-IV. Les variables indépendantes liées à la démence ont été déterminées par modèle logistique multivarié (MLM), et employées pour élaborer un arbre de décision pour prédire ce diagnostic. Étude de validation : l'arbre de décision obtenu a été appliqué aux patients consécutifs de 6 consultations mémoire pour qui le diagnostic de démence a été précédemment posé ou infirmé en utilisant les critères DSM-IV. L'arbre de décision, les MLM et les MMSE ont été appliqués pour détecter la démence dans ces patients. La sensibilité et la spécificité de chaque outil de diagnostic ont été estimées et comparées.

Résultats > Étude d'élaboration : chez les 242 patients inclus, les variables indépendantes corrélées à la démence étaient le sexe, le THs, et 2 items du MMSE, le rappel de 3 mots et l'orientation spatiale. En utilisant des statistiques bayésiennes, un arbre d'analyse de décision bref 2 (2 ou 3 mn) a été obtenu et a été appelé "Codex" (examen à 2 étapes des désordres cognitifs). Étude de validation : codex a été appliqué à 323 patients. Les sensibilité et spécificité étaient 92 % et 85 % respectivement. Les valeurs correspondantes étaient 88 % et 87 % pour le MLM, 94 % et 67 % ou 91 % et 70 % pour le MMSE (selon le seuil employé pour la décision). La sensibilité du Codex s'est avérée significativement plus grande que celle du MLM, et de sa spécificité significativement plus grande que celle du MMSE.

Conclusion > Codex est un test simple, bref et fiable pour détecter la démence et pourrait être approprié pour une utilisation en soin primaire parce que simple et très bref, accompli en 3 minutes ou moins.

applied to consecutive patients of six memory clinics for whom status about dementia was previously determined with DSM-IV criteria. The decision tree, MLM, and MMSE were applied to detect dementia in these patients. The sensitivity and specificity of each diagnostic tool were estimated and compared.

Result > Of 242 patients in the derivation study, the following independent variables were correlated with dementia: sex, sCDT, and two MMSE subscores — the 3-word recall test and spatial orientation. We used Bayesian statistics to develop a brief 2-step decision analysis tree (2-3 min.), which we named Codex (cognitive disorders examination). The validation study applied Codex to 323 patients. Sensitivity was 93% and specificity 85%. The corresponding values were 88% and 87% for the MLM, 94% and 67% or 91% and 70% for the MMSE, depending on the MMSE cutoff score. The sensitivity of Codex was significantly higher than that of MLM, and its specificity was significantly greater than that of MMSE.

Conclusion > Codex is a simple, brief, and reliable test for detecting dementia and requires three minutes or less to administer. Its simplicity and brevity make it appropriate for and easy to use in primary care.

Dementia is a major health problem among the elderly because of its high prevalence rate [1, 2], dramatic effects on patients' quality of life, burden on caregivers, and considerable economic costs [3-5]. Despite major advances in agreement on diagnostic criteria [6], dementia is underdiagnosed and underdetected, even at severe stages [1, 3, 7]. In roughly one third of patients, dementia has not been diagnosed, and in another third, the diagnosis is not made until the disease has reached a severe stage [8]. This delay prevents patients and their families from obtaining optimal care, health benefits, and social assistance as early as possible [9]. In Alzheimer disease [10], for example, controlled trials show that drug treatment can postpone or slow both cognitive [11] and other [12] impairment. Because the patients' quality of life, mobility, and independence become much worse as the disease progresses [13, 14], attempts to treat patients earlier are essential to reduce disease burden [10, 15].

Simple cognitive instruments for assessing cognitive function in the elderly have advanced considerably. The Mini Mental State Examination (MMSE), developed in 1975 by Folstein *et al.* [16], is commonly used in hospital settings and specialized centers for both in- and out-patients. Despite its popularity, the MMSE is used infrequently in primary care, mainly because it is considered to be too long for this setting: it takes 10-15 min to administer [17].

What was already known

- **Dementia** is a frequent but underdiagnosed problem in the elderly.
- **Cognitive testing with standard tests** is long and therefore performed infrequently by general practitioners.

What this study adds

- **A simple and rapid (3-min) test (Codex)** was developed from the informative items of classic tests, as identified by a multivariate statistical analysis in a sample of patients with memory complaints.
- **This test was effective in** detecting dementia in another sample of elderly patients with memory complaints.
- **Codex helps to detect dementia** and may be very useful for this purpose in primary care.

Moreover, cutoff points to diagnose cognitive impairment depend on the subject's educational level. These points limit use of the MMSE as a screening tool for dementia in primary care. Less time-consuming instruments have been proposed [18-20], but since they still take 5 to 10 min to administer, none has replaced the MMSE for detecting dementia.

We have developed a brief and simple decision tree to detect dementia and conducted this study to assess it, validate it, and compare its performance to that of MMSE.

Methods

Patients

Derivation study

To build the decision tree, we studied 249 consecutive new subjects attending the memory clinic of a geriatric hospital ward over a 2-year period. All were referred for the assessment of cognitive symptoms, and subjects with a previous diagnosis of dementia were excluded from the study. We recorded each patient's age, sex, and educational level (low, intermediate, and high).

Validation study

This study included 323 subjects who had not participated in the derivation study. They were consecutive subjects attending six different memory clinics (including the one whose patients contributed to development of the decision tree) for the assessment of cognitive symptoms. Subjects with a previous diagnosis of dementia were excluded from the validation study. We again recorded age, sex, and educational level (low, intermediate, high) for each subject.

Diagnostic instruments

At the first examination, all patients completed the MMSE (total and subscores) and a simplified clock drawing test (sCDT) on a sheet of paper with a plain circle printed on it (10 cm in diameter). They were asked first to put in all the numbers on the clock and then to draw the hands setting the clock to a time specified by the investigator. The sCDT was scored as normal (1 point) if all three of the following criteria were met: all the numbers were written down and correctly placed; small and large hands were recognizable; and their direction correctly indicated the time given. If one or more of these criteria was not met, the sCDT was considered abnormal (no point). Because this simplified scoring method was new, we investigated the inter-judge concordance. Two investigators (JB and PS), blinded to final diagnosis (presence or absence of dementia), independently scored 100 sCDTs randomly selected from the derivation study.

At the same visit, the memory clinic's expert physicians used DSM-IV criteria to diagnose dementia [6]. To ascertain cognitive performance and determine whether these criteria were met, a psychologist performed additional tests when necessary, mainly the Grober and Buschke test [21], trail-making tests A and B [22], Stroop test [23], and other standard neuropsychological tests. This process was not standardized for the study but was performed according to each center's usual practices. All participating physicians were unaware of the results obtained by the experimental decision tree indeed, they were not informed about its scoring and interpretation at the time of the validation study.

Statistical analysis

Development of the decision tree

We first assessed the relations between several variables: age, sex, educational level (low, intermediate or high, coded as 0, 1, and 2 respectively), MMSE total score, MMSE subscores, sCDT score (0/1), and dementia status for patients in the derivation study. This study used Student's t test or a chi-square test. In a second step, the independent variables related to dementia were determined by a stepwise multiple logistic regression analysis that used dementia (coded as 0 no dementia and 1 dementia) as a dependent variable, and the variables significantly associated with dementia in the univariate analysis (at $p < 0.05$) as the initial variables. To make the test simple for clinicians to use without any calculator or computer, we constructed a decision tree based on the independent variables selected by stepwise multiple regression analysis. Bayesian statistics made it possible to examine the discriminant ability of several decision trees and led us to select a simplified 2-step decision tree able to distribute patients into one of four diagnostic categories. The cutoff point for dementia was determined by ROC curve analysis. We named our decision tree Codex, for cognitive disorders examination.

Subsequent validation of the decision tree and comparison with MMSE

The application of Codex to patients in the validation study enabled us to determine its sensitivity and specificity for the detection of dementia. We also calculated the sensitivity and specificity of the MMSE for the same purpose, by two separate analyses. First, we used 27 as the MMSE cutoff score for all subjects. We next used the MMSE with the cutoff values adjusted for education level: 27 for subjects with a high or intermediate educational level, and 24 for poorly educated subjects (MMSE-adj).

Finally, the sensitivity and specificity of the diagnostic tests were compared with those of Codex with the McNemar test.

Results

Development of the decision tree

Of the 249 subjects selected, seven were excluded from the study due to missing data (MMSE or sCDT in four cases), inability to perform assessment because of aphasia (one case), poor

TABLE I

Characteristics of the subjects of the derivation study designed to construct the decision tree

	No dementia (n=99)	Dementia (n=143)	p
Age (years)	71.7 (10.1)	79.1 (7.1)	<0.0001
Females	64 (65%)	113 (79%)	0.0131
Educational level			
Low	21 (21%)	61 (43%)	
Intermediate	41 (41%)	53 (38%)	
High	37(37%)	27 (19%)	0.0004
MMSE total score (0-30)	27.1 (3.4)	17.9 (5.9)	<0.0001
MMSE subscores			
Temporal orientation (0-5)	4.6 (0.8)	2.6 (1.6)	<0.0001
Spatial orientation (0-5)	4.4 (0.9)	2.2 (1.5)	<0.0001
3-word learning (0-3)	2.9 (.4)	2.8 (0.7)	0.0080
Attention (0-5)	4.2 (1.2)	2.3 (2.0)	<0.0001
3-word recall (0-3)	2.4 (0.9)	0.8 (1.0)	<0.0001
Language (0-8)	7.7 (0.6)	6.5 (1.8)	<0.0001
Praxis (0-1)	0.9 (0.3)	0.6 (0.5)	<0.0001
Clock drawing test			
Abnormal	26 (26%)	127 (89%)	<0.0001

MMSE: Mini Mental Status Examination.
Results are expressed as numbers and percentage in brackets or as mean et SD in brackets.

French language skills (one case), and psychiatric problems (one case). *Table I* summarizes the characteristics of the 242 subjects. Concordance between the two sCDT raters was excellent, with a kappa value of 0.90. Ratings were discordant for only two drawings.

Subjects with dementia were significantly older than the other subjects. This group also included a significantly higher percentage of women and of subjects with a low educational level than the nondemented group (*table I*). Dementia was related to possible or probable Alzheimer disease in 81 cases (56%), vascular or mixed dementia in 50 (35%), Lewy body dementia in 7 (5%), and frontotemporal dementia in 5 (4%). Subjects with dementia had significantly lower MMSE total scores and subscores than did nondemented subjects, as well as significantly more frequent abnormal sCDTs (*table I*). The variables independently related to dementia were sCDT, two MMSE subscores of the MMSE (3-word recall and spatial orientation) and sex (*table II*).

We searched for a simple decision tree providing a decision in no more than two steps. In the first step we included the two variables with the highest standardized coefficients in the multivariate analysis: sCDT and 3-word recall. After trying several models, we selected for the first step a criterion that combined the sCDT and the 3-word recall test as shown in *figure 1*. This step yielded three branches. Two of them allowed decisions: in box A, the probability of dementia was very low and in box D very high. For the middle branch, we looked for another step based on the other variables selected in the model. We found that the spatial orientation score (5 or 4 compared with less than 4) discriminated between high and low probabilities of dementia (boxes C and D). Because sex added only slightly more information, it was not included in the decision tree. Finally, we obtained a very simple tool leading to 4 categories (A through D) characterized by different probabilities for dementia: 6% among the patients in category A, 23% among those in B, 72% among those in C, and 91% among those in D. *Figure 1* presents Codex, the final decision tree. *Figure 2* shows the ROC curve for Codex, drawn from the derivation study sample. Sensitivity for a diagnosis of dementia was 90% and specificity 84% when categories C and D as taken as indicators of dementia. The positive predictive value was 89% and the negative predictive value 86%.

Validation study from the decision tree

Table III summarizes the characteristics of the 323 subjects participating in the validation study. The probability of dementia among patients in each Codex category in the validation study was similar to that in the derivation study (*figure 3*). The specificity of the decision tree was 92% and the sensitivity 85%, for a positive predictive value of 90% and a negative predictive value of 88%.

The specificity of Codex was significantly better than that of the logistic model, and its sensitivity was significantly better than that of the MMSE, regardless of the cutoff points used (*table IV*).

TABLE II

Independent variables significantly related to the presence/absence of dementia by multivariable stepwise logistic model in the derivation study

	Odd-ratio	95% confidence interval	p
Sex (0 for females, 1 for males)	2.950	1.046 - 8.319	0.0418
Abnormal simplified clock drawing test	11.628	4.630 - 29.412	<0.0001
3-word recall (0-3)	0.372	0.246 - 0.561	<0.0001
Spatial orientation (0-5)	0.475	0.329 - 0.686	<0.0001

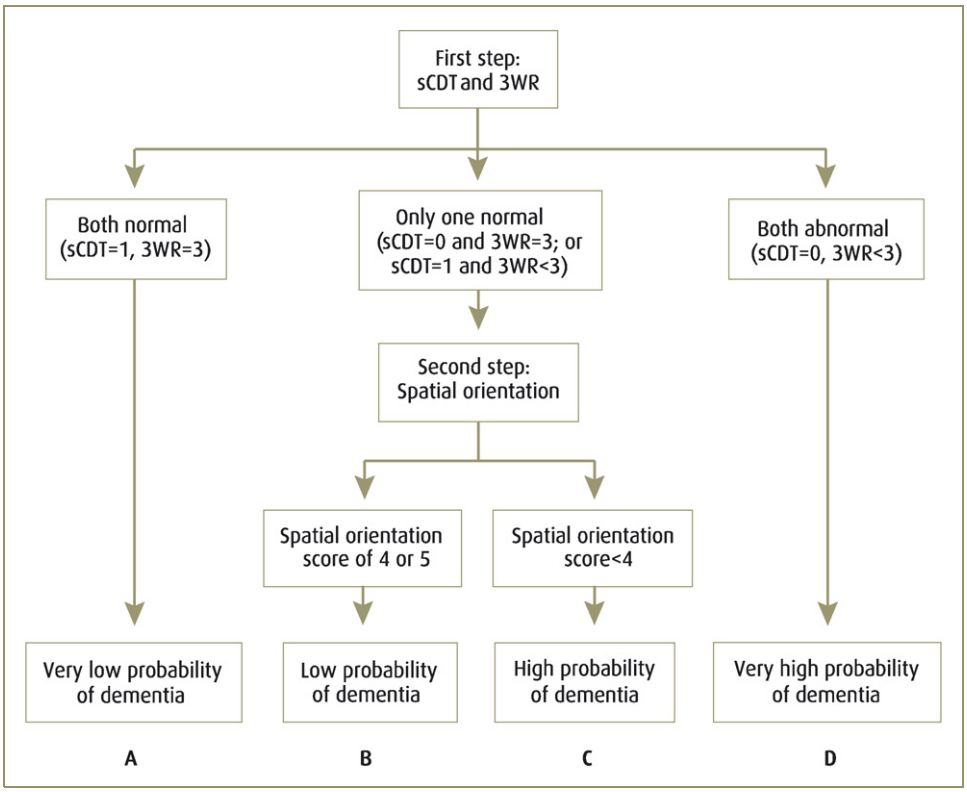

FIGURE 1
Codex: the decision tree designed from the variables selected in the multiple regression analysis

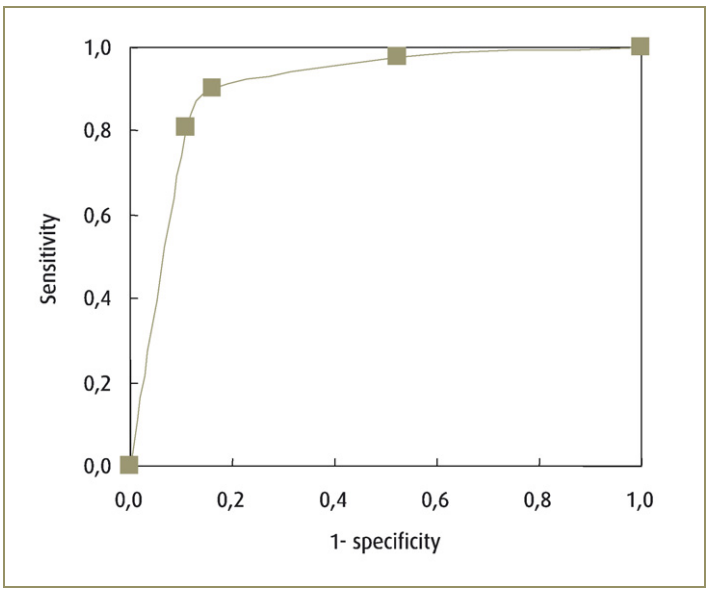

FIGURE 2
Receiver operating curve of Codex for the diagnosis of dementia

Because of the relatively low mean MMSE score in our study, we also examined the performances of Codex after removing from the analysis the 10% of subjects with the lowest MMSE scores. Patients with dementia in the new analysis had a mean MMSE score of 20.3 + 4.0. Codex sensitivity and specificity were then 90 and 85% respectively.

Comments

After analyzing data from elderly patients attending a memory clinic and assessed for cognitive symptoms, we constructed a simple and brief decision tree, called Codex, designed as an easy-to-use test to detect dementia in primary care. Post-hoc validation of this decision tree conducted among patients from several memory clinics showed a sensitivity of 92% and a specificity of 85%. Moreover, the test is very brief: it takes about 2 minutes for most subjects, and another minute more for those who require the spatial orientation test. These characteristics make Codex a promising tool for the detection of dementia in primary care.

To construct the decision tree, we conducted a statistical analysis to select the variables independently related to dementia in a large sample of elderly subjects referred for diagnosis of cognitive symptoms. It is interesting to note that of the three variables retained in our decision tree, one assesses short-term episodic memory (3-word recall), and another assesses executive and visuospatial functions (CDT). These cognitive functions are impaired at early stages of Alzheimer disease [3, 10] and Lewy body disease [24], the two main causes of degenerative

TABLE III
Characteristics of the subjects of the validation study

	No dementia (n=135)	Dementia (n=188)	p
Age (years)	71.1 (9.4)	80.4 (7.1)	<0.0001
Females	103 (76%)	147 (78%)	0.6880
Education level			
Low	10 (8%)	40 (22%)	
Intermediate	47 (36%)	80 (44%)	
High	75 (57%)	63 (34%)	<0.0001
MMSE total score (0-30)	27.1 (2.6)	18.3 (5.7)	<0.0001
MMSE subscores			
Temporal orientation (0-5)	4.6 (0.7)	2.8 (1.6)	<0.0001
Spatial orientation (0-5)	4.5 (0.8)	2.9 (1.7)	<0.0001
3-word learning (0-3)	3.0 (0.0)	2.9 (0.4)	0.0028
Attention (0-5)	4.2 (1.2)	2.3 (1.9)	<0.0001
3-word recall (0-3)	2.4 (0.9)	0.8 (0.9)	<0.0001
Language (0-8)	7.5 (0.6)	6.5 (1.2)	<0.0001
Praxis (0-1)	0.9 (0.3)	0.6 (0.5)	<0.0001
Simplified clock drawing test			
Abnormal	30 (22%)	167 (89%)	<.0001

MMSE: Mini Mental Status Examination.
Results are expressed as numbers and percentage in brackets or as mean and SD in brackets.

dementia in the elderly. Impaired short-term memory is the hallmark of early Alzheimer disease [10], while in early Lewy body disease, executive and visuospatial functions are often impaired, but short-term memory remains intact [24]. Thus the first step of the decision tree determined by this statistical approach fit the clinical features of these two diseases very well. We note that the MiniCog instrument [18], another short instrument designed to detect dementia, also uses the 3-word recall test and the CDT. Codex scores these variables differently than the MiniCog and interprets the results differently.

Codex performed significantly better than MMSE for detecting dementia, regardless of the MMSE cutoff point used. Codex is faster (2-3 min. *versus* 10-15 min.) than the MMSE, and its interpretation is simpler. MMSE cutoff values depend on educational level, which is not considered in the Codex decision. Other quick tests have been proposed for use in primary care settings, but they are designed to detect Alzheimer disease specifically and not dementia. For instance, Solomon *et al.* constructed a 7-minute screening test in a study of 60 subjects with Alzheimer disease and 60 age-matched volunteers [25]. In France, Dubois *et al.* also proposed a very short test, "the 5-word test" to detect Alzheimer disease [26]. The "5-word test" was found to be useful for detecting Alzheimer disease among patients with cognitive symptoms, but its performance was less effective for detecting Alzheimer disease in a general population [27] and for detecting dementia in subjects with cognitive symptoms [28]. Our results indicate that Codex is a suitable tool for detecting dementia in elderly subjects with memory complaints in primary care settings. It may also be an interesting tool for screening for dementia, but this would need to be demonstrated by appropriate studies, given that the prevalence of dementia is much lower in primary care patients than in memory clinic clients.

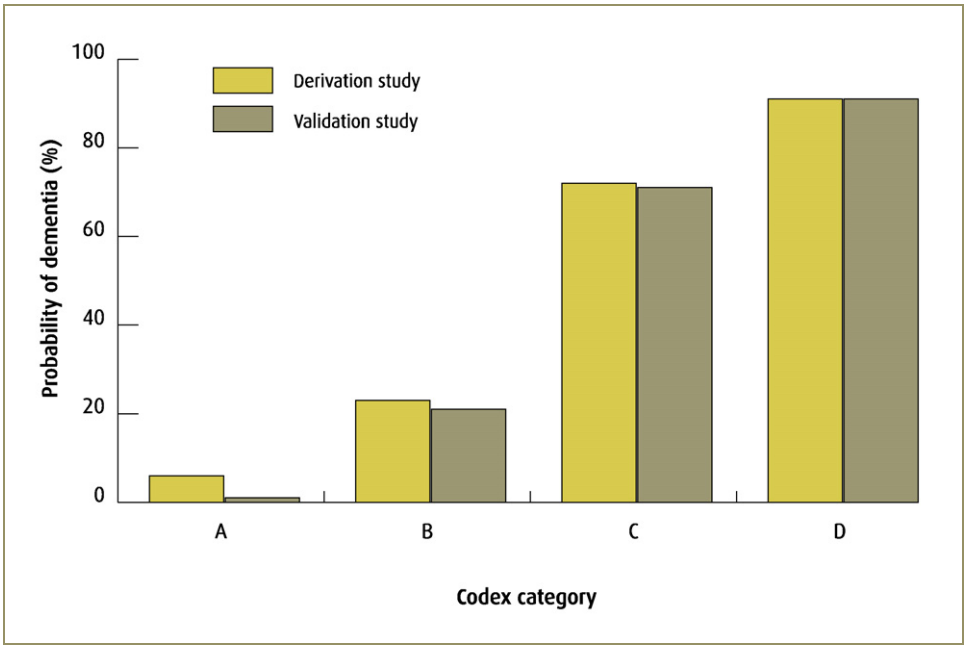

FIGURE 3
Probability of dementia according to Codex category in the derivation and validation studies

TABLE IV

Sensitivity and specificity of Codex, logistic model and MMSE for the detection of dementia in the 323 patients of the validation study

Test	Sensitivity, % [95% CI]	Comparison with Codex (p-value of McNemar's test)	Specificity, % [95% CI]	Comparison with Codex (p-value of McNemar's test)
Codex	92 [87-95]	-	85 [79-91]	-
Logistic model	88 [82-92]	0.0196	87 [79-92]	0.1025
MMSE*	94 [90-97]	0.3173	67 [59-75]	0.0001
MMSE**	91 [86-95]	0.6547	70 [61-77]	0.0001

* using 27 as cut-off; ** using 27 as cut-off in patients with high or medium level of education and 24 in those with low level of education.
MMSE: Mini Mental Status Examination.

Codex does not simply produce a binary conclusion (presence or absence of dementia), but also offers four diagnostic categories corresponding to different probabilities of the disease (*figure 3*). This may also help medical decision-making and make it possible to offer advice differentiated according to probability of dementia. For example, in a screening situation, those classified in Codex category B should be considered to have a low probability of dementia but be asked to return in 6-12 months for another screening. Those classified in Codex C or D should be considered to have a high or very high probability for dementia and be referred to specialized centers. In our experience, most subjects in category D do not required extensive neuropsychological testing, in contrast to those classified in category C. Thus Codex testing before referral may also help specialized centers plan their work-ups.

Now that appropriate tools capable of detecting dementia in primary care are available [18-20, 27], we think that their use by primary care physicians should be promoted. It might help enable early detection of dementia among elderly subjects with symptoms consistent with cognitive disorders and thus early referral to a specialized setting. Several guidelines favor early detection of dementia in primary care, especially in patients with symptoms suggestive of cognitive impairment [29-33]. Screening for dementia in uncomplaining subjects is still a topic of debate and systematic screening is not currently recommended [34]. When treatments capable of stopping the course of Alzheimer disease become available, screening for dementia will become a step towards reducing disease burden. Development and validation of reliable and simple tests for the detection of dementia will probably help to clarify these points and public health authorities to organize dementia screening in the elderly.

Conflict of interest: none

Authors' contributions: Prof Joël Belmin developed the hypothesis and the project, supervised the study, participated in the analysis, and wrote the main portion of the manuscript. Dr Sylvie Pariel-Madjlessi participated in the design of the study, conducted the derivation study, and participated in the discussion of the results and revision of the manuscript. Ms Philomène Surun played a key role in collecting the clinical and neuropsychological data for the validation study; she also participated in the interrater validation of the simplified clock drawing test and was responsible for data management and input. Dr Jean-Louis Golmard conducted the statistical analysis and wrote parts of the manuscript. The other authors (Dr Dorin Feteanu, Dr Fannie Onen, Dr Caroline Bentot, Dr Olivier Drunat, Dr Véronique Lefebvre des Noettes, Dr Christophe Trivalle and Prof Philippe Chassagne) made major contributions to the validation study and also revised the manuscript. All the authors have approved the manuscript submitted.

References

1 Fitzpatrick AL, Kuller LH, Ives DG, Lopez OL, Jagust W, Breitner JC *et al*. Incidence and prevalence of dementia in the Cardiovascular Health Study. J Am Geriatr Soc. 2004; 52: 195-204.

2 Fratiglioni L, Launer LJ, Andersen K, Breteler MM, Copeland JR, Dartigues JF *et al*. Prevalence of dementia and major subtypes in Europe: a collaborative study of population-based cohorts. Neurology. 2000; 54(suppl 5): S4-9.

3 Cummings JL. Alzheimer's disease. N Engl J Med. 2004; 351: 56-67.

4 Ritchie K, Lovestone S. The dementias. Lancet. 2002; 360: 1759-66.

5 Cummings JL, Cole G. Alzheimer disease. JAMA. 2002; 287: 2335-8.

6 American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-IV). Washington: American Psychiatric Association; 1994.

7 Ramaroson H, Helmer C, Barberger-Gateau P, Letenneur L, Dartigues JF. PAQUID. Prévalence de la démence et de la maladie d'Alzheimer chez les personnes de 75 ans et plus : données réactualisées de la cohorte PAQUID. Rev Neurol. 2003; 159: 405-11.

8 Knopman DS, DeKosky ST, Cummings JL, Chui H, Corey-Bloom J, Relkin N *et al*. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001; 56: 1143-53.

9 Rimmer E, Wojciechowska M, Stave C, Sganga A, O'Connel B. Implications of the Facing Dementia Survey for the general population, patients and

caregivers across Europe. J Clin Practice. 2005; 59 (Suppl 146): 17-24.
10 Kawas CH. Clinical practice. Early Alzheimer's disease. N Engl J Med. 2003; 349: 1056-63.
11 Kaduszkiewicz H, Zimmermann T, Beck-Bornholdt HP, van den Bussche H. Cholinesterase inhibitors for patients with Alzheimer's disease: systematic review of randomised clinical trials. BMJ. 2005; 331: 321-7.
12 Trinh NH, Hoblyn J, Mohanty S, Yaffe K. Efficacy of cholinesterase inhibitors in the treatment of neuropsychiatric symptoms and functional impairment in Alzheimer disease: a meta-analysis. JAMA. 2003; 289: 210-6.
13 Tariot PN. Medical management of advanced dementia. J Am Geriatr Soc. 2003; 51(Suppl): S305-13.
14 Vellas B, Gauthier S, Allain H, Andrieu S, Aquino JP, Berrut G *et al.* Consensus statement on dementia of Alzheimer type in the severe stage. J Nutr Health Aging. 2005; 9: 330-8.
15 Leifer BP. Early diagnosis of Alzheimer's disease: clinical and economic benefits. J Am Geriatr Soc. 2003; 51(Suppl): S281-8.
16 Folstein M, Folstein S, McHugh P. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12: 189-98.
17 Lorentz WJ, Scanlan JM, Borson S. Brief screening tests for dementia. Can J Psychiatr. 2002; 47: 723-33.
18 Borson S, Scanlan JM, Watanabe J, Tu SP, Lessig M. Simplifying detection of cognitive impairment: comparison of the Mini-Cog and Mini-Mental State Examination in a multiethnic sample. J Am Geriatr Soc. 2005; 53: 871-4.
19 Brodaty H, Pond D, Kemp NM, Luscombe G, Harding L, Berman K *et al.* The GPCOG: a new screening test for dementia designed for general practice. J Am Geriatr Soc. 2002; 50: 530-4.
20 Buschke H, Kuslansky G, Katz M, Stewart WF, Sliwinski MJ, Eckholdt HM *et al.* Screening for dementia with the memory impairment screen. Neurology. 1999; 52: 231-8.
21 Grober E, Buschke H, Crystal H, Bang S, Dresner R. Screening for dementia by memory testing. Neurology. 1988; 38: 900-3.
22 Tombaugh TN. Trail Making Test A and B: normative data stratified by age and education. Arch Clin Neuropsychol. 2004; 19: 203-14.
23 MacLeod CM. Half a century of research on the Stroop effect: an integrative review. Psychol Bull. 1991; 109: 163-203.
24 MacKeith IG. Spectrum of Parkinson's disease, Parkinson's dementia, and Lewy body dementia. Neurol Clin. 2000; 18: 865-902.
25 Solomon P, Hirschoff A, Kelly B, Relin M, Brush M, DeVeaux RD *et al.* A 7 minute neurocognitive screening battery highly sensitive to Alzheimer's Disease. Arch Neurol. 1998; 55: 349-55.
26 Dubois B, Touchon J, Portet F, Ousset PJ, Vellas B, Michel B. Les "5 mots": épreuve simple et sensible pour le diagnostic de la maladie d'Alzheimer. Presse Med. 2002; 31: 1696-9.
27 Cowppli-Bony P, Fabrigoule C, Letenneur L, Richie K, Alpérovitch A, Dartigues JF *et al.* Le test des 5 mots : validité dans la détection de la maladie d'Alzheimer dans la population générale. Rev Neurol. 2005; 161: 1205-12.
28 Jacus JP, Hamon-Vilcot B, Basset-Berges MF, Campistron E, Malick C, Baud M. Test des 5 mots: insuffisamment sensible, mais très spécifique des troubles mnésiques organiques. Presse Med. 2006; 35: 948-54.
29 Patterson CJ, Gauthier S, Bergman H, Cohen CA, Feightner JW, Feldman H *et al.* The recognition, assessment and management of dementing disorders: conclusions from the Canadian Consensus Conference on Dementia. CMAJ. 1999; 160(Suppl): S1-S15.
30 Dementia Study Group of the Italian Neurological Society. Guidelines for the diagnosis of dementia and Alzheimer's disease. The Dementia Study Group of the Italian Neurological Society. Neurol Sci. 2000; 21: 187-94.
31 American Geriatric Society Clinical Practice Committee. Guidelines abstracted from the American Academy of Neurology's Dementia Guidelines for Early Detection, Diagnosis, and Management of Dementia. J Am Geriatr Soc. 2003; 51: 869-73.
32 Anaes (Agence nationale d'accréditation et d'évaluation en santé). Recommandations pratiques pour le diagnostic de la maladie d'Alzheimer. Presse Med. 2001; 30: 537-9.
33 Petit H, Bakchine S, Dubois B, Laurent B, Montagne B, Touchon J *et al.* Convergences d'un groupe pluridisciplinaire d'experts français sur les modalités du diagnostic et du traitement médicamenteux de la maladie d'Alzheimer au stade démentiel. Rev Neurol. 1998; 154: 432-8.
34 Boustani M, Peterson B, Hanson L, Harris R, Lohr KN. US Preventive Services Task Force. Screening for dementia in primary care: a summary of the evidence for the US Preventive Services Task Force. Ann Intern Med. 2003; 138: 927-37.