Detection of memory impairment in the general population: screening by questionnaire and telephone compared to subsequent face-to-face assessment

Detection of memory impairment in the general population: screening by questionnaire and telephone compared to subsequent face-to-face assessment.

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Keypoints

- The definition and accompanying operationalisation of MCI differs considerably between (epidemiological) studies and has to be taken into account when interpreting results of studies in subjects with MCI.
- For recruitment of large numbers of subjects with MCI for (epidemiological) trials, comprehensive clinical examinations may be less suitable because of ethical, logistic and financial reasons.
- Telephone screening is a suitable method to identify large numbers of subjects with a below normal cognitive performance. Moreover, it is easy applicable, relatively fast and inexpensive.

Abstract

Background: Development of efficient methods for identifying subjects with Mild Cognitive Impairment (MCI) from the general population is warranted, because these subjects represent an important group for (epidemiological) research purposes.

Objectives: 1) To describe a two-step population screening for identifying adults with MCI from the general population for research purposes, by questionnaire and telephone; 2) To compare screening by telephone (method one) to a subsequent face-to-face assessment (method two).

Methods: In method one, subjects with memory complaints were identified from the general population (n=5491) by a postal questionnaire. Subsequently, cognitive status and memory were assessed in a telephone interview using the Telephone Interview for Cognitive Status and the 10 Word Learning Test. Next, subjects with MCI according to method one were subjected to a face-to-face assessment for method two, in which cognitive status and memory were assessed using the Mini Mental State Examination (MMSE) and the Auditory Verbal Learning Test (AVLT).

Results: 227 subjects completed both the telephone interview and the face-to-face assessment. 93 subjects (41%) had MCI according to both methods. Seven subjects (3%) failed to meet MCI criteria according to method two because of an MMSE score < 24; 127 subjects (56%) failed because of normal AVLT scores.

Conclusion: 1) The two-step population screening was able to detect a considerable number of MCI-subjects in the general population; 2) agreement between both methods was moderate. Therefore, the method of recruiting subjects for (epidemiological) studies has to be taken into consideration when interpreting results of these studies.

Introduction

Society of the future will be a double aging one because of increasing numbers of elderly people, who will also grow older than before. This phenomenon will be associated with all concomitant burdens of degenerative chronic diseases (Davis and Rockwood, 2004;Gao *et al.,* 1998), such as dementia. According to the WHO, by the year 2020 there will be almost 29 million demented adults worldwide (Haan and Wallace, 2004). These adults will put both a substantial financial burden on healthcare systems, as well as a personal burden on their significant others. Therefore, selecting possible target groups for the prevention of cognitive decline has consequently become an important issue in the field of cognitive aging research (Burns and Zaudig, 2002). In this respect, increasing attention has been paid in particular to the concept of amnestic Mild Cognitive Impairment (MCI). MCI refers to a potential transitional stage in which persons experience memory loss to a greater extent than one would expect for age, but do not meet clinical Alzheimer's Disease (AD) criteria (Petersen *et al.,* 2001). Although several MCI criteria have been suggested (Davis and Rockwood, 2004;Palmer *et al*., 2003), the Petersen criteria (Petersen *et al.,* 1999) are the most widely used: 1) memory complaints; 2) impaired memory; 3) normal mental status; 4) normal daily function; 5) not demented. Since MCI criteria have been operationalised using different neuropsychological outcome measures and/ or cut-off points, prevalence reports of MCI in the general population differ and range from three to 19 percent (Bischkopf *et al.*, 2002; Ganguli *et al.,* 2004; Low *et al.*, 2004). Although it is possible for individuals with MCI to remain stable or recover, it is generally agreed upon that compared to cognitively healthy adults they have an increased risk to convert to AD. Reported conversion rates to AD vary from approximately eight to 41 percent per year (Tierney *et al.,* 1996; Petersen *et al.*, 1999; Larrieu *et al.,* 2002; Amieva *et al., 2004;* Ganguli *et al.*, 2004; Geslani *et al*., 2005). As the stage of MCI is the optimum stage to intervene with potentially preventive therapies to prevent conversion to dementia (Chertkow, 2002), for research purposes, the development of efficient methods suitable for identifying subjects with MCI from the general population is warranted. While face-to-face neuropsychological assessment is commonly used, it's main limitation is that it is time consuming. In this respect, telephonic cognitive screening instruments that are able to discriminate between normal and dementing

elderly are readily available (Plassman *et al.*, 1994; Welsh *et al.*, 1993). Because screening over the telephone enables researchers to reach large groups of elderly in a relatively short time period, this seems an attractive alternative.

The aim of this study is twofold: 1) To describe a two-step population screening for identifying MCI-subjects by questionnaire and telephone from the general population for participation in a randomised controlled trial; 2) To compare screening by telephone to a subsequent face-to-face assessment with respect to the number of identified MCI-subjects.

Methods

Study design

The two-step population screening was developed to identify MCI-subjects from the general population for participation in a Randomised Controlled Trial (RCT) (van Uffelen et al. 2005). In the present study, the two-step population screening (method one) is described and compared to a subsequent face-to-face assessment (method two). Operational criteria for MCI according to both methods, are described in table 1. First, subjects with memory complaints were identified by a postal questionnaire. Subsequently, cognitive status and memory were assessed in a telephone interview. Next, only MCI-subjects according to method one, were subjected to the subsequent face-to-face assessment.

Subjects

All community-dwelling adults in a medium-sized Dutch town aged 70 to 80 years (n=5491) received study information and a postal questionnaire by mail. Their addresses were obtained from the register of the municipality. The study protocol, including the recruitment of participants, was approved by the VU University Medical Center ethics committee. Informed consent was obtained prior to the start of the study.

Method one: two-step population screening

Postal questionnaire

The aim of the questionnaire was to select subjects with memory complaints and unaffected Activities of Daily Living (ADL) for the subsequent telephone interview and to check eligibility for an RCT (van Uffelen *et al.*, 2005) by addressing other inclusion criteria (table 2). Memory complaints were assessed in two ways. First, subjects were asked if they had memory problems (yes/no). Additionally, the cognitive domain of the Strawbridge scale was administered (Strawbridge *et al.,* 1998). This scale consists of four questions concerning self-perceived cognitive function (difficulty paying attention, trouble finding the right word, difficulty remembering things, forgetting where something was put). Answer categories were: never, sometimes, often, and very often. ADL function was assessed using the Groningen Activity Restriction Scale (GARS) (Kempen *et al.*, 1996). This scale consists of eleven questions concerning ADL and seven questions concerning instrumental ADL. Subjects were asked if they were able to perform these activities easily, with difficulty or not at all. They were considered as having intact ADL functioning if they reported no disabilities on the ADL items.

Telephone interview

The aim of the telephone interview was to assess mental status and memory performance. Mental status was assessed using the Telephone Interview for Cognitive Status (TICS) (Brandt *et al.*, 1988), which examines the most important aspects of cognitive function (orientation, concentration, memory, naming, comprehension, calculation, reasoning, judgement and praxis). The score ranges from 0 to 41, with a higher score indicating better cognitive function. Memory performance was assessed using a Dutch version of the 10 Word Learning Test (10 WLT) (Morris *et al.,* 1989). The 10 WLT measures immediate and delayed memory. The examiner reads aloud a list of ten words (trial 1) and after hearing the list, the participant is asked to repeat the words he or she remembers. This procedure is repeated two more times (trial 2 and 3). Five minutes later, delayed recall is assessed by asking the participant to recall the words, leading to a maximum recall score of ten words. Percentage savings is defined as the number of recalled words as a percentage of the score in the third trial. The telephone interview was performed by trained interviewers and took at most 15 minutes.

Those with MCI as determined by method one:

- Answered “yes” to the broad memory complaint question, OR
- Answered at least “sometimes” on two or more of the four Strawbridge questions, AND
- Reported no disabilities in activities of daily living on the GARS-scale, AND
- Met eligibility criteria for the RCT as mentioned in table two, AND
- Scored ≥ 19 on the TICS, AND
- Had a delayed recall score ≤ 5/10 on the third trial of the 10 WLT (this applied cut-off point for memory impairment corresponds with one standard deviation below normal performance (Welsh *et al.*, 1994) and is in accordance with other population studies (Busse *et al.,* 2003;Ganguli *et al.,* 2004) AND
- Had an absolute percentage savings ≤ 100 percent.

Method two: face-to-face assessment for those meeting MCI criteria according to method one

During this face-to-face assessment, mental status and memory functioning were assessed using respectively the Mini Mental State Examination (MMSE) (Folstein et al. 1975) and the Auditory Verbal Learning Test (AVLT) (Rey 1964). The Dutch modification of the AVLT was used to assess memory. The principle of the AVLT is similar to the 10 WLT administered during the telephone interview, but the AVLT consists of 15 words and 5 trials for direct recall. Delayed recall is measured after 20 minutes of non-memory related questions. The face-to-face assessments were administered by trained interviewers who were blind to the participant’s performance during the telephone screening. During the face-to-face assessment, performance on other neuropsychological measures was assessed to provide a further description of the population. The Digit Symbol Substitution Test measures attention, perceptual speed, motor speed, visual scanning and memory (Uiterwijk, 2001). The Letter Fluency Test measures expressive language (Lezak, 2004). The Abridged Stroop Colour Word Test is a measure of complex processing (Klein et al. 1997). These measures have been described in detail somewhere else (van Uffelen et al. 2005).

Those with MCI as determined by method two:

- Had an MMSE score ≥ 24 (Folstein et al. 1975), AND

- Had an AVLT delayed recall score of 1 SD or more below the mean of healthy controls.

Agreement between both methods

Finally, the percentage of agreement between both methods was examined. The subjects therefore fell into three groups:

- Those meeting MCI criteria according to both methods,
- Those who failed to meet MCI criteria of method two because of an MMSE score < 24,
- Those who failed to meet MCI criteria of method two because of an AVLT performance better than 1 SD below the mean of healthy controls.

Data analysis

All analyses were carried out using SPSS, version 12.0.1. P-values < 0.05 were considered statistically significant. First, subjects fulfilling MCI criteria according to method one and subjects not fulfilling these criteria were compared regarding sociodemographic characteristics and TICS and 10 WLT performance. Differences were tested using independent student's T-tests, Mann Whitney U tests and Chi-square tests.

To detect the number of MCI-subjects according to method two, the number of subjects performing worse than 1 SD below the mean of the AVLT was determined. This was done by translating AVLT recall scores into Z-values adjusted for age, gender and education using regression analyses as derived from the normative sample (Van der Elst *et al.*, 2005). Subsequently, the percentage of agreement between both methods was examined.

Results

In September 2003, questionnaires were sent to 5491 community-dwelling adults aged 70 to 80 years. The response rate was 36 percent (n=1953), of which 1487 subjects wanted to participate. After applying inclusion criteria for the RCT (table 2), 569 adults were eligible for the telephone interview. The telephone interview was administered to 495 subjects. Due to various reasons no telephone interview was available from 74 subjects. Of the 495 subjects who completed the telephone interview, 249 had MCI according to method one (see figure 1) and

246 had not. In addition to the expected significant differences between subjects with and without MCI according to method one in TICS and WLT 10 performance, MCI-subjects were significantly more often men, had a lower educational level and were more often living together (table 3).

The face-to-face assessment was completed by 227 of the 249 MCI-subjects according to method one. Twenty subjects withdrew after receiving the invitation for the face-to-face assessment due to various reasons, e.g.: too busy, only wanted to participate with a not for the study selected partner. Two subjects withdrew during the face-to-face assessment. Of these 227 subjects, 93 (41%) met the criteria for MCI according to both methods. Consequently, the other 134 subjects only met MCI criteria according to method one; seven of them (5%) did not meet MCI criteria according to method two because of an MMSE score < 24. One of these subjects had a normal AVLT score and was counted in the MMSE < 24-group only. Of the remaining 127 subjects (95%), the AVLT performance was too good to be classified as having MCI according to method two. These 127 subjects performed significantly better on the AVLT delayed recall than subjects in the other two groups (table 4).

Discussion

In order to identify large numbers of subjects with MCI for research purposes, efficient and inexpensive methods for population screening need to be developed. In the present study, a two-step population screening for identifying older adults with MCI from the general population by postal questionnaire and a telephone interview is described. Moreover, screening by telephone (method one), was compared to a subsequent face-to-face assessment (method two).

The percentage of agreement between both methods was 41 percent. This is in concordance with the study of Lines et al. (Lines *et al*., 2003), in which an agreement of 43 percent was found. In that study, also more men than women met MCI criteria. In contrast to their findings, in our study subjects with MCI were lower educated than subjects without MCI. However, in

general, higher educated individuals perform better on cognitive tests (Lezak, 2004). The observed moderate agreement may have been caused by various reasons. Even though our cut-off point for the TICS was lower than advised (Brandt *et al.,* 1988), only seven subjects out of 227 had an abnormal MMSE score in combination with a normal TICS score. Thus, the moderate agreement between the methods can be attributed mainly to differences in performance on the 10 WLT and the AVLT. All selected subjects had a 10 WLT delayed recall score of one standard deviation below the mean in the telephone interview, but 56 percent of them had a normal performance on the AVLT during the face-to-face assessment. First, this may have been caused by the experience of the subjects with the conceptual basis of the test. Due to their experience with the 10 WLT during the telephone interview, subjects may have expected to recall the AVLT word list during the face-to-face assessment. Second, differences between the telephone and the face-to-face assessment may have existed regarding feelings of being at ease and audibility. However, in another study comparing telephone and in person assessment of verbal memory, no difference in performance was found (Carpenter *et al.,* 1995). Finally it can be questioned whether the 10 WLT and the AVLT measure aspects of memory to the same extend, because both word learning tasks differ with respect to the number of words, the number of trials for direct recall and the retention time.

Limitations of the study

In the present study, only MCI-subjects according to method one were subjected to the subsequent face-to-face assessment. As a consequence, no data are available on sensitivity and specificity of the telephone screening compared to the face-to-face assessment. Since there is no gold standard for diagnosing MCI, the estimation of sensitivity and specificity would have been difficult in any case. Moreover, methods for population screening for identifying subjects for trials do not need to be highly sensitive by clinical standards as their purpose is to provide a group of individuals with an increased risk for cognitive decline.

Also, no comprehensive clinical examinations of subjects identified as having MCI according to both methods are available, because this could not be realised for financial and time reasons.

Certainly, the two-step population screening alone will not suffice to provide clinical individual diagnoses. Clinical screening includes elaborate measures such as neuro-imaging, and judgement of a clinician, while for epidemiological research often solely neuropsychological examination is feasible. However, even though we did not primarily intend to develop a diagnostic tool applicable in clinical practice, one could use the described screening to select a population with a preponderance of individuals with MCI for further detailed screening. Our two-step population screening was successful in doing so, because by applying it, the percentage of subjects with MCI increased from three to four percent in the general population (Ganguli *et al.*, 2004) to 41 percent in subjects selected by the two-step population screening. Therefore, the results of the present study may also be of interest with regard to the development of urgently needed cost-effective instruments for clinical purposes. Obviously, for clinical purposes, sensitivity and specificity are very important issues, which have to be further addressed in future research. Meanwhile, the identification of older adults with MCI from the general population for clinical (research) purposes can be done e.g. by general practitioners using observation instruments, such as the Observation List for Early signs of Dementia (Hopman-Rock *et al.* 2001).

In sum, the described two-step-population screening can be used for identifying a population with a large preponderance of individuals with MCI. For research purposes, such a population could be useful e.g. for randomized controlled trials where the diagnostic error of the tests would presumably be balanced across various groups assigned to different kinds of interventions, or where a lower “yield” of true prodromal Alzheimer’s Disease would simply mean that larger numbers must be enrolled. For clinical purposes, one could use the method described here to provide a population for further detailed screening for a “purer” group of individuals with MCI according to clinical criteria.

Conclusion

Since the concept of MCI is operationalised in many different ways, the cognitive qualities of subjects defined as MCI-patients can differ considerably between studies. For this reason, the

method of identification of MCI has to be taken into consideration when interpreting results of studies targeting subjects with MCI. Our two-step population screening was able to detect a considerable number of MCI-subjects in the general population. Moreover, because telephone screening is fast, easy to apply and inexpensive, it should be considered as a valuable tool to be used in future cognitive aging studies in which large groups of subjects at risk for cognitive decline have to be detected at an early stage.

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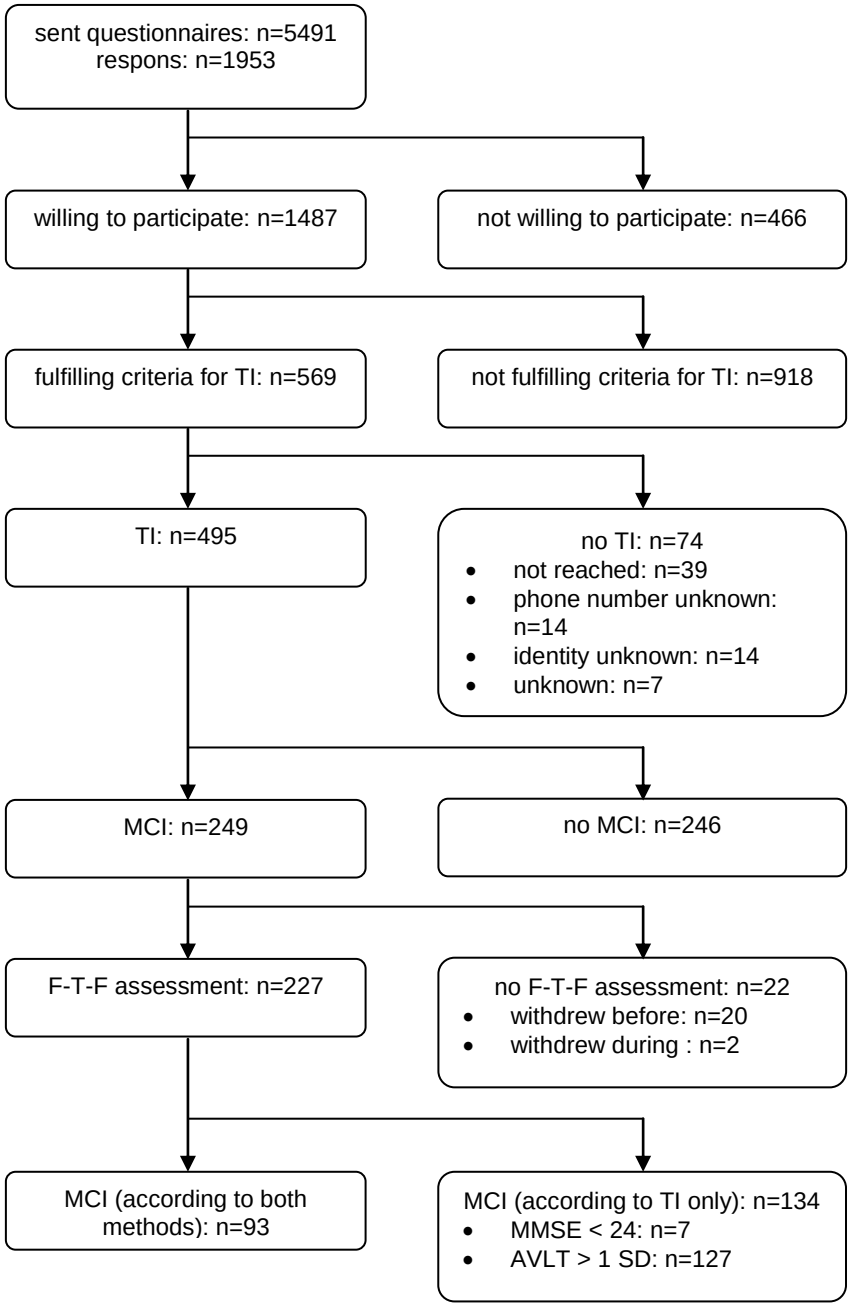

Figure 1: Flow chart

TI= Telephone Interview, MCI= Mild Cognitive Impairment, F-T-F assessment= Face-To-Face assessment

Table 2: Selection criteria for telephone screening

Criteria for MCI (1-2) and other inclusion criteria for the RCT (3-9)
1. Self reported memory complaints (answer yes to question 'do you have memory complaints', or at least twice 'sometimes' on the cognition scale of Strawbridge);
2. No report of disability in activities of daily living on GARS-scale, except on the item 'taking care of feet and toe nails';
3. Being able to perform physical activities of moderate intensity, without making use of walking devices, e.g. a rollator or a walking frame;
4. Not using vitamin supplements/ vitamin injections/ drinks with dose of vitamin B6, B11 or B12 comparable to the vitamin supplement given in intervention;
5. Not suffering from epilepsy, multiple sclerosis, Parkinson's disease, kidney disorder requiring haemodialysis, psychiatric impairment;
6. Not suffering from depression as measured by the GDS (cut off ≤ 5);
7. Not using medication for rheumatoid arthritis or psoriasis interfering with vitamin supplement;
8. No alcohol abuse (men < 21 consumptions a week, women < 15 consumptions a week);
9. Not currently living in a nursing home or on a waiting list for a nursing home.

GARS= Groningen Activity Restriction Scale, GDS= Geriatric Depression Scale, MCI= Mild Cognitive Impairment, RCT= Randomised Controlled Trial

Table 3: Characteristics of subjects with and without MCI according to method one (mean values (SD), unless indicated otherwise)

	MCI N= 249	No MCI N = 246	Total group N= 495
Age (years)	75.0 (3.0)	74.6 (2.8)	74.8 (2.9)
Gender (% male) *	56.6	38.8	47.8
Education (% low/intermediate/high) †*	57/ 27/ 17	42/ 36/ 22	49/ 31/ 19
Marital status (% married or living together)*	69.1	54.7	61.9
TICS **	31.8 (3.4)	34.2 (2.9)	33.0 (3.3)
Direct recall 10 WLT **	15.3 (3.3)	20.7 (3.9)	18.0 (4.5)
Delayed recall 10 WLT**	3.7 (1.3)	7.1 (1.3)	5.4 (2.2)
Percentage savings**	60.1 (22.1)	89.3 (22.0)	74.6 (26.4)

MCI= Mild Cognitive Impairment, method1= two-step population screening, SD= Standard Deviation, TICS= Telephone Interview for Cognitive Status, 10 WLT= 10 Word Learning Test

† Education: low= no education, primary education, lower vocational training; intermediate= intermediate level secondary education, intermediate vocational training; high= higher level secondary education, higher vocational training, university training.

* $p< 0.01$, X^2 test; ** $p= 0.00$, t-test difference between MCI and no MCI

Table 1: Petersen criteria for MCI and operationalisation in both methods

Petersen MCI criteria	Method 1	Method 2
1) Memory complaints	answer yes to question ‘do you have memory complaints’, or at least twice ‘sometimes’ at cognition scale of Strawbridge	-
2) Objective memory impairment	10 WLT delayed recall ≤ 5 + percentage savings ≤ 100	AVLT delayed recall ≤1SD
3) Normal mental status	TICS ≥ 19	MMSE ≥ 24
4) Intact daily function	no report of disability in activities of daily living on GARS-scale, except on the item ‘taking care of feet and toe nails’.	-
5) Absence of dementia	TICS ≥ 19	MMSE ≥ 24

MCI= Mild Cognitive Impairment, method1= two-step population screening, Method 2= face-to-face assessment, 10WLT= ten Word Learning Test, AVLT= Auditory Verbal learning Test, TICS= Telephone Interview for Cognitive Status, MMSE= Mini Mental State Examination, GARS= Groningen Activity Restriction Scale

Table 4: Characteristics and cognitive test performance of subjects classified with MCI according to both methods and of subjects classified with MCI according to method 1 only (mean values (SD) unless indicated otherwise)

	MCI (both methods) N = 93	MCI (method 1 only, MMSE < 24) N = 7	MCI (method 1 only, AVLT > 1 SD) N = 127
Age	75.3 (3.0)	76.3 (3.0)	75.2 (2.8)
Gender (% male)	61	100	56
Education (% low/middle/high)†	57/28/15	86/0/14	53/26/21
Marital status (% living together)	72	100	68
MMSE (Median (10^{th}-90^{th} ‰))*	28 (24-30)	21 (17-23)	29 (27-30)
AVLT direct recall**	26.0 (6.6)	18.9 (5.0)	36.3 (6.3)
AVLT delayed recall**	3.3 (1.6)	2.0 (1.6)	7.3 (1.8)
Other neuropsychological measures			
Stroop Word‡**	21.2 (6.0)	28.0 (9.4)	19.7 (4.3)
Stroop Colour‡**	28.4 (8.6)	41.3 (20.9)	25.9 (4.9)
Stroop Colour/Word‡**	69.3 (23.4)	97.9 (30.4)	60.0 (19.9)
DSST**	35.1 (11.2)	22.9 (8.6)	36.2 (9.7)
VFT***	28.0 (10.2)	20.3 (14.5)	30.8 (10.0)

MCI= Mild Cognitive Impairment, method 1= two-step population screening, Method 2= face-to-face assessment, MMSE= Mini Mental State Examination, AVLT= Auditory Verbal Learning Test, DSST= Digit Symbol Substitution Test, VFT= Verbal Fluency Test

† Education: low= no education, primary education, lower vocational training; intermediate= intermediate level secondary education, intermediate vocational training; high= higher level secondary education, higher vocational training, university training.

‡ lower score indicates better performance. *p= 0.00, Kruskal Wallis Test; **p= 0.00, one-way ANOVA, ***p< 0.05, one-way ANOVA