

# Implementing Diagnostic Criteria and Estimating Frequency of Mild Cognitive Impairment in an Urban Community

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**Background:** Reported rates of mild cognitive impairment (MCI) range widely depending on methodologic differences, including specific sample characteristics, cognitive measures used, normative samples used for neuropsychological tests, and diagnostic criteria.

**Objectives:** To operationalize diagnostic criteria for MCI and examine the frequency of MCI in ethnically and linguistically diverse elders (individuals older than 65 years).

**Design:** Prospective, community-based longitudinal cohort study.

**Setting:** Northern Manhattan, New York, NY.

**Participants:** A cohort of 1315 nondemented elderly participants.

**Main Outcome Measure:** A diagnosis of MCI was assigned retrospectively on the basis of comprehensive neuropsychological, functional, and neurologic assessments. Amnesic MCI, as well as forms of mild impairment with other cognitive characteristics, were classified.

**Results:** The frequency of amnesic MCI was 5.0% (95% confidence interval, 3.8-6.2). Other subtypes of MCI ranged in frequency from 2.1% to 6.2%. Mild cognitive impairment was more common among those older than 75 years compared with those aged 65 to 75 years. Individuals with fewer than 9 years of schooling were more likely to meet MCI criteria. Apolipoprotein (APOE) E4 allele was more frequent among those with amnesic MCI.

**Conclusions:** When proper normative values are used, only age and education, and not race or ethnicity, are associated with higher frequency of MCI. The proportion of nondemented elders with isolated memory deficits is smaller than the proportion with deficits in multiple cognitive domains. The strong association of the APOE E4 allele with only amnesic MCI suggests that there are likely to be multiple causes of cognitive impairment and differential rates of conversion to Alzheimer disease within the cognitive subtypes of MCI.

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**M**ILD COGNITIVE IMPAIRMENT (MCI) is used in clinical research to describe the transitional state between normal aging and Alzheimer disease (AD)<sup>1-3</sup> or dementia.<sup>4</sup> The criteria proposed by Petersen and colleagues<sup>2</sup> for amnesic MCI are as follows: (1) not demented, (2) memory complaint, (3) preserved general cognitive function, (4) intact activities of daily living, and (5) impaired memory for age and education. The criteria for diagnosis of patients with MCI have come under increased scrutiny because of the importance of accurate identification of people with the earliest signs of dementia. Patients with MCI have been included in randomized clinical trials

to slow progression of cognitive decline, and for research on risk factors for AD and other dementias.<sup>5</sup>

Petersen and colleagues<sup>2</sup> did not specify which instruments should be used to operationalize MCI criteria, allowing considerable flexibility for clinical or research teams that use different cognitive and functional assessment batteries. In fact, operationalization of the criteria for diagnosis differs widely among published studies.<sup>5</sup> This variability, in combination with differences in mean age of samples and methods of recruitment, has resulted in prevalence estimates of amnesic MCI that range from 1.03% to 26.4%<sup>6</sup> among community-based elderly participants in epidemiologic studies.

Perhaps the most significant confusion and controversy related to MCI criteria are associated with the neuropsychological criteria for mild impairment, on which the diagnosis heavily relies. For amnesic MCI, there is no consensus regarding the specific memory domain (eg, verbal or visuospatial), the number of tests to be considered within the memory domain, the minimum required psychometric properties of the instruments (eg, sensitivity, specificity, and positive predictive value), and the specific indexes within each instrument to be considered (eg, immediate vs delayed memory). The number of tests, definition of a cognitive domain, and quality of normative studies become increasingly important if investigators expand their criteria to include multiple subtypes of MCI such as a single nonmemory domain (eg, language, visuospatial) or multiple cognitive domains with or without memory impairment, defined according to performance on a large battery of neuropsychological measures. In addition, individuals with preclinical dementia are in normative samples because most neuropsychological normative data are collected on individuals screened for dementia at one time point only. This significantly reduces the sensitivity of normed cognitive measures for detecting MCI. The robust norms approach<sup>7</sup> eliminates from the normative sample elders who develop functional and cognitive impairment sufficient for a diagnosis of dementia at a follow-up evaluation, and should be used in studies of MCI where accurate detection of subtle impairment is crucial.

Finally, the Petersen et al criteria<sup>2</sup> state that age and education should be used in setting a normative value by which neuropsychological test scores should be compared. Despite the well-documented effect of cultural factors on neuropsychological test performance,<sup>8,9</sup> race, ethnicity, and language were not mentioned. This is most likely because, with a few notable exceptions,<sup>10</sup> most studies of MCI have included white, well-educated participants, and the original criteria were developed in a sample with almost no racial-ethnic or linguistic diversity.<sup>6</sup>

The purpose of the current study was to report the prevalence of MCI among participants in a large, community-based study of elders (individuals older than 65 years) residing in an ethnically and linguistically diverse urban area of northern Manhattan, New York, NY. To determine cutoffs for cognitive impairment, we gathered information from a normative sample that was appropriate for our population and was screened for individuals with preclinical dementia. We used diagnostic criteria that would allow us to estimate the frequency of the more traditionally studied amnesic form of MCI, as well as forms of mild impairment with other cognitive characteristics.

## METHODS

The Columbia University Institutional Review Board reviewed and approved this project. All individuals discussed the study with a trained research assistant and provided written informed consent before their baseline visit.

### SAMPLING PLAN AND PARTICIPANTS

A random sample of elderly Medicare recipients residing in 3 contiguous census tracts of Washington–Hamilton Heights and

Inwood in Manhattan was asked to participate in a longitudinal study of aging, cognitive function, and dementia. The population from which participants were drawn is composed of individuals from several different countries of origin and representing 3 broadly defined racial-ethnic categories (Caribbean Hispanic, African American, and non-Hispanic white). Potential participants were excluded if they did not speak English or Spanish. A total of 4865 individuals were sent letters in the recruitment of this cohort in 1992. Of these, attempts at follow-up by telephone or in-person visit indicated that 470 (9.7%) had died, 896 (18.4%) no longer lived in the region, 50 (1.0%) were ineligible, and 1324 (27.2%) did not wish to participate. The total number recruited in 1992 was 2125. A randomly selected portion of the cohort underwent a standardized medical, neurologic, and neuropsychological examination.

Data were used only from participants who had completed measures assessing the key components of the Petersen et al MCI criteria.<sup>2</sup> Therefore, participants were considered for a diagnosis of MCI only if they had sufficient neuropsychological, functional, and medical and neurologic data at baseline. Of the 1722 participants on whom a full neuropsychological examination was attempted, 0.4% did not complete the cognitive battery because of hearing impairment ( $n=2$  [0.1%]) or refusal ( $n=5$  [0.3%]). Approximately 0.3% ( $n=5$ ) of those with complete neuropsychological examinations did not complete the questions regarding daily functioning and memory complaints. Twelve elders were omitted from the current analyses because they identified their race/ethnicity as other than non-Hispanic white, black, or Hispanic, and thus our demographically corrected norms could not be applied to their cognitive test scores. The remaining 1698 individuals were included in the current sample. Their mean  $\pm$  SD age was  $77.8 \pm 6.8$  years, and they had  $8.2 \pm 4.9$  years of education. The cohort was 19.4% non-Hispanic white, 33.9% non-Hispanic black, and 46.7% Hispanic, and 69.7% were women. Approximately 93% of the Hispanics were interviewed and tested in Spanish; the remaining 7% requested to be tested in English. Subjects included in the current prevalence sample ( $n=1698$ ) did not differ from those who were excluded because of missing data ( $n=427$ ) with respect to age, years of schooling, sex distribution, or dementia status; however, significantly more elders in the prevalence sample (46.7%) than among those who were excluded (37.6%) identified themselves as Hispanic ( $\chi^2=14.0$ ,  $P=.001$ ).

A new cohort of participants was recruited from the same community in 1999. The goal was to recruit a cohort of ethnically and educationally diverse, nondemented elders. The sampling and recruitment strategies differed from the initial cohort: (1) the final sample would be equally divided among the 3 primary racial-ethnic groups in the area (Hispanic, African American, and non-Hispanic white); (2) the cohort would represent equal proportions of 2 broad age groups, 65 to 74 years and 75 years and older; and (3) potential participants were excluded if, during the initial telephone screen, they or their caregivers reported that they had significant cognitive problems or had been diagnosed as having dementia. Recruitment letters were sent to a total of 7120 persons. Of these, attempts at follow-up by telephone or in-person visit indicated that 265 (3.7%) had died, 1541 (21.6%) no longer lived in the region, 662 (9.3%) were ineligible, and 2810 (27%) did not wish to participate. The total number recruited in 1999 was therefore 1842.

## ASSESSMENT PROCEDURES

### Racial-Ethnic Group

At baseline, racial-ethnic group was documented by self-report using the format of the 2000 US census. All individuals

were first asked to report their racial group (ie, American Indian–Alaska Native, Asian, Native Hawaiian or other Pacific Islander, black or African American, or white) and then, in a second question, were asked whether they were of Hispanic origin.

### Medical and Neurologic Evaluation

A physician recorded medical history and medications in a semistructured format. Neurologic and brief physical examinations were performed, including assessment of extrapyramidal signs and functional status. From this information, the physician independently determined whether the participant met criteria for delirium or dementia by means of *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition*<sup>11</sup> criteria. In 88% of the current sample, the physician examined the participant on the same day as the neuropsychological evaluation; the mean time between the 2 examinations was 0.60±8.23 days.

### Psychiatric Status

The research physician asked a series of questions, based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*,<sup>12</sup> to determine whether each participant met criteria for a major depressive episode within the past week. History of other major psychiatric disorders, such as schizophrenia, anxiety disorders, or alcohol or other drug dependence, was determined by a semistructured interview conducted by a physician.

### Assessment of Activities of Daily Living

Items from the Disability and Functional Limitations Scale<sup>13–15</sup> were used to elicit self- and observer ratings of instrumental activities of daily living, such as using the telephone, preparing meals, handling money, and completing chores. A summary measure was created, compiling complaints from 6 domains. On the basis of a cutoff capturing 95% of the normative sample, participants were considered to be functionally intact if they or their caregivers reported difficulty on 2 or fewer of these items.

### Memory Complaints

Perceived difficulty with memory was assessed with 11 items from the Disability and Functional Limitations Scale, described previously, and the Blessed Functional Activities Scale.<sup>16</sup> Participants were asked whether they had memory difficulties in general, as well as difficulties in specific areas such as memory for names. Participants were considered to have memory complaints if they indicated that they had problems on 1 or more of the items.

### Neuropsychological Battery

The neuropsychological measures used in the current study were selected to assess cognitive functions that are typically affected in dementia and have been shown to effectively distinguish between normal aging and dementia in this community.<sup>17,18</sup> The evaluation included measures of learning and memory, orientation, abstract reasoning, language, and visuospatial ability. Specific ability areas and tests administered included verbal list learning and memory (Selective Reminding Test<sup>19</sup>), nonverbal memory (multiple-choice version of the Benton Visual Retention Test [BVRT]<sup>20</sup>), orientation (items from the Mini-Mental State Examination<sup>21</sup>), verbal reasoning (Similarities subtest of the Wechsler Adult Intelligence Scale–Revised<sup>22</sup>) nonverbal reasoning (Identities and Oddities sub-

test of the Mattis Dementia Rating Scale<sup>23</sup>), naming (15-item version of the Boston Naming Test<sup>24</sup>), letter fluency (Controlled Word Association<sup>25</sup>), category fluency (animals, food, and clothing, using procedures from the Boston Diagnostic Aphasia Examination [BDAE]<sup>26</sup>), repetition (high-frequency phrases of the BDAE<sup>26</sup>), auditory comprehension (first 6 items of the Complex Ideational Material subtest of the BDAE<sup>26</sup>), visuoconstruction (Rosen Drawing Test<sup>27</sup>), and visuooperceptual skills (multiple-choice matching of figures from the BVRT<sup>20</sup>).

### Consensus Diagnosis

After each clinical assessment, a group of physicians and neuropsychologists reviewed the functional, medical, neurologic, psychiatric, and neuropsychological data and reached a consensus regarding the presence or absence of dementia by *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition* criteria.<sup>11</sup> If dementia was diagnosed, the cause was determined by means of published research criteria for probable and possible AD,<sup>28</sup> vascular dementia,<sup>29</sup> Lewy body dementia,<sup>30</sup> and other dementias. Severity of dementia was rated with the Clinical Dementia Rating Scale.<sup>31</sup> Only those who were not diagnosed as having dementia were considered for a diagnosis of MCI.

### MCI Diagnostic Criteria

Criteria for MCI were retrospectively applied among nondemented individuals after the consensus conference. Consistent with standard criteria,<sup>2</sup> for all subtypes of MCI, those considered for MCI were required to have (1) a memory complaint (defined previously); (2) objective impairment in at least 1 cognitive domain based on the average of the scores on the neuropsychological measures within that domain and a 1.5-SD cutoff using normative corrections for age, years of education, race/ethnicity, and sex; (3) essentially preserved activities of daily living (defined previously); and (4) no diagnosis of dementia at the consensus conference.

To cast the widest net to determine prevalence of MCI and to determine which individuals were more likely to progress to dementia, the original Petersen et al criteria,<sup>2</sup> which focus on memory impairment, were expanded to include mutually exclusive subtypes based on cognitive features. Our first subtype, MCI-amnesic, corresponds most closely to the original definition used by Petersen and colleagues. Memory impairment was defined as a score less than 1.5 SDs below the demographically corrected mean on an average composite measure comprising the following learning and memory measures: (1) total recall from the Selective Reminding Test, (2) delayed free recall from the Selective Reminding Test, and (3) recognition from the BVRT. Performance on composite scores from all other cognitive domains (ie, executive, language, and visuospatial) was required to be within normal limits (score must be  $\geq 1.5$  SDs below the demographically corrected mean). Other MCI subtypes were classified that allowed for impairment in a single nonmemory domain if performance on composite scores from all other cognitive domains was within normal limits. The subtype MCI–executive function was assigned if impairment was demonstrated on an average composite measure comprising the following measures: (1) letter fluency, (2) category fluency, and (3) the Wechsler Adult Intelligence Scale–Revised Similarities subtest. The subtype MCI–language was defined as isolated impairment on an average composite measure comprising the (1) Boston Naming Test, (2) BDAE Repetition test, and (3) BDAE Comprehension test. The subtype MCI–visuospatial was assigned if impairment was demonstrated on an average composite score comprising (1) Rosen Drawing and (2) BVRT Matching.

Finally, we allowed for impairment in multiple cognitive domains in the absence of dementia. A diagnosis of MCI—multiple cognitive domains with memory impairment was made if there was objective impairment on the memory domain composite score and if there was impairment on at least 1 other cognitive domain. The diagnosis of MCI—multiple cognitive domains without memory impairment was assigned if there was impairment in 2 or more of the 3 nonmemory domains, and if the memory domain composite score was within normal limits. Again, classification into the 6 subtypes was mutually exclusive.

### Sample and Procedure for Regression-Based Neuropsychological Test Norms

The normative sample used to define cognitive impairment was selected from participants recruited in 1992 and 1999 by means of the robust norms approach.<sup>7</sup> Participants were included in the normative sample if they were judged to be nondemented and had a Clinical Dementia Rating Scale score of 0 at the consensus conference at their first visit with complete neuropsychological, neurologic, medical, and functional data and at a follow-up visit that occurred 1 to 4 years (average, 24 months) after the initial visit. Potential participants were excluded from the normative sample if they had a history of Parkinson disease, stroke, head injury with loss of consciousness longer than 30 minutes, or other neurologic illness. Elders were also excluded from the normative sample if they had a history of psychosis, current mental illness such as major depression or anxiety disorder, or current alcohol or other drug dependence. A total of 1063 elders were included in this sample. Their mean  $\pm$  SD age was 75.2  $\pm$  5.7 (range, 66–102 years), with 11.6  $\pm$  4.3 years of education (range, 0–20 years); 37.1% were white, 28.7% were Hispanic, 34.2% were African American, 25.5% were Spanish-speaking, and 69.4% were female.

Demographically corrected T scores were developed on the basis of the Heaton et al<sup>32</sup> regression method. Influences of age, years of education, race/ethnicity, and sex on each cognitive test score were assessed by performing multiple linear regression analyses. Racial-ethnic group and language (ie, Spanish vs English) were highly related, since most of the Hispanics were tested in Spanish and all of the whites and African Americans were tested in English; therefore, we did not add language into the model. Each of the 4 cognitive domain scores used in the MCI diagnostic criteria were included as dependent variables: memory (average composite of total raw scores for immediate recall and delayed recall from the Selective Reminding Test and BVRT recognition); language (average composite of total correct on the 15-item Boston Naming Test, number of phrases correctly produced on BDAE repetition, and number correct on BDAE comprehension); executive function (average composite of total correct on the Mattis Identities and Oddities, raw score on Wechsler Adult Intelligence Scale—Revised Similarities subtest, and mean number of words generated during three 60-second trials for category and letter fluency); and visuospatial skill (average composite of number correct on the Rosen Drawing Test and BVRT matching). Continuous predictors were age and years of education. Sex was a categorical predictor, as was racial-ethnic classification (ie, non-Hispanic black, non-Hispanic white, and Hispanic). For each of the 4 regression analyses, we first included all 4 predictors in the model, retaining only the variables that significantly contributed to prediction of cognitive test score. The  $\beta$  weights of each of these predictors in the final model, as well as the standard error of each regression model, were used to calculate predicted scores on each test. These predicted scores were subtracted from each participant's actual composite score to calculate residual scores.

Residual scores were converted to T scores according to the following formula:

$$T \text{ score} = [(\text{Residual Score}/\text{SE of Estimate for the Regression Equation}) \times 10] + 50.$$

T scores have a mean of 50 and an SD of 10, allowing a T score of 35 to be the  $-1.5$ -SD mark for each of the 4 composite scores.

## DATA ANALYSES

### Evaluation of Criteria for MCI

The frequency of each of the criteria for MCI (ie, memory complaint, functional status, and neuropsychological impairment meeting cutoffs for each of the MCI subtypes) were calculated among the nondemented participants in the 1992 cohort within age groups split at the median of 75 years (65–75 years, >75 years), and 95% confidence intervals about these frequencies (assuming a Poisson distribution) were determined. The relationship of the criteria to age, years of schooling, and distribution of sex and race/ethnicity was examined by Pearson correlation coefficients, 2-tailed *t* tests, and analyses of variance where appropriate.

### Prevalence

Age-specific prevalence for each of the MCI subtypes was calculated within age groups split at the median of 75 years (65–75 years, >75 years), and 95% confidence intervals about these rates (assuming a Poisson distribution) were calculated separately for the entire population, for men and women, by racial-ethnic group, and by years of education (0–7 years vs  $\geq 8$  years).

## RESULTS

Of the 1698 elders who had complete data at baseline, 22.6% ( $n = 383$ ) were diagnosed as demented at the consensus conference. This estimate of dementia prevalence over the entire sample is consistent with that reported for the full 1992 cohort of 2125.<sup>33</sup>

### EVALUATION OF MCI CRITERIA

**Table 1** shows the number of subjects and frequency of each of the criteria for the diagnosis of MCI for the remaining sample of 1315 nondemented elders, including memory complaint, functional status, and neuropsychological impairment for each of the 6 MCI subtypes. When age was dichotomized as up to and above the median of 75,  $\chi^2$  analyses showed that frequency of functional impairment ( $\chi^2_{1,1313} = 9.5, P = .002$ ), isolated memory deficits ( $\chi^2_{1,1313} = 5.4, P = .02$ ), and isolated visuospatial deficits ( $\chi^2_{1,1313} = 5.1, P = .02$ ) differed significantly by age group. There were no age group differences in frequency of memory complaints or isolated neuropsychological deficits in executive or language domains, as well as impairment in multiple cognitive domains with or without memory impairment.

When education was split at the median, there were no differences in proportions of participants meeting criteria for memory complaints or functional normality. However, participants with fewer than 9 years of school-

**Table 1. Prevalence of Functional, Memory Complaint, and Neuropsychological Criteria for MCI Subtypes Among 1315 Elders Without Dementia**

Criteria	No. of Participants	Prevalence, %	95% CI, %
Memory complaints	974	74.1	71.8-76.5
Age 65-75 y	476	71.9	68.5-75.3
Age >75 y	498	76.3	73.0-79.5
Normal daily function	1205	91.6	90.2-93.3
Age 65-75 y	622	94.0	92.1-95.8
Age >75 y	583	89.3	86.9-91.7
Isolated memory impairment	84	6.4	5.1-7.7
Age 65-75 y	32	4.8	3.2-6.5
Age >75 y	52	8.0	5.9-10.0
Isolated executive function impairment	39	3.0	2.0-3.9
Age 65-75 y	19	2.9	1.6-4.1
Age >75 y	20	3.1	1.7-4.4
Isolated language impairment	75	5.7	4.5-7.0
Age 65-75 y	35	5.3	3.6-7.0
Age >75 y	40	6.1	4.3-8.0
Isolated visuospatial impairment	110	8.4	6.9-9.9
Age 65-75 y	44	6.6	4.8-8.5
Age >75 y	66	10.1	7.8-12.4
Multiple cognitive domains with memory impairment	130	9.9	8.3-11.5
Age 65-75 y	58	8.8	6.6-10.9
Age >75 y	72	11.0	8.6-13.4
Multiple cognitive domains without memory impairment	140	10.6	9.0-12.3
Age 65-75 y	61	9.2	7.0-11.4
Age >75 y	79	12.1	9.6-14.6

Abbreviations: CI, confidence interval; MCI, mild cognitive impairment.

ing were more likely than those with 9 or more years of schooling to meet criteria for language deficit (7.9% vs 3.9%;  $\chi^2_{1,1302}=11.2, P=.001$ ), visuospatial deficit (12.5% vs 4.2%;  $\chi^2_{1,1302}=30.5, P<.001$ ), and impairment in multiple cognitive domains without memory impairment (13.4% vs 8.0%;  $\chi^2_{1,1302}=10.3, P=.001$ ). Elders with 9 or more years of schooling were more likely than those with fewer than 9 years of schooling to have isolated impairment in memory (8.0% vs 4.8%;  $\chi^2_{1,1314}=5.6, P=.02$ ) and executive function (4.5% vs 1.5%;  $\chi^2_{1,1302}=10.6, P=.001$ ). Women were more likely than men to have significant functional complaints (9.7% vs 5.4%;  $\chi^2_{1,1315}=7.5, P=.006$ ) and have isolated impairment in memory (7.5% vs 3.9%;  $\chi^2_{1,1314}=6.7, P=.01$ ). Men were more likely than women to have isolated impairment in language (7.9% vs 4.8%;  $\chi^2_{1,1302}=4.6, P=.03$ ). Finally,  $\chi^2$  analyses showed that there were no racial or ethnic differences in frequency of meeting functional or memory complaint criteria among those who exhibited isolated memory impairment, or those who had impairment in multiple cognitive domains with or without memory impairment. However, the frequency of isolated deficits on language tests was somewhat higher among whites (5.7%) than among African Americans (3.2%) and Hispanics (1.5%;  $\chi^2_{1,1302}=10.8, P=.005$ ). Hispanics were more likely to meet criteria for isolated language deficits (7.9%) than were African Americans (3.7%)

**Table 2. Number of Participants and Prevalence of All Subtypes of MCI Among 1315 Nondemented Elders**

	Total	MCI, No. (%)	
		No MCI, No.	With Memory Impairment
No. of participants	1315	943	148 (11.3)
Age, y			
65-75	662	503	61 (9.2)
>75	653	440	87 (13.3)
Sex			
Female	905	651	108 (11.9)
Male	410	292	40 (9.8)
Education, y			
0-8	665	456	62 (9.3)
≥9	650	487	86 (13.2)
Race/ethnicity			
Non-Hispanic white	287	208	40 (13.9)
Non-Hispanic black	438	317	54 (12.3)
Hispanic	590	418	54 (9.2)

Abbreviations: CI, confidence interval; MCI, mild cognitive impairment.

and whites (4.6%) ( $\chi^2_{1,1302}=9.0, P=.01$ ). Hispanics (11.1%) and African Americans (8.0%) were more likely to meet criteria for isolated visuospatial deficits than were whites (3.5%;  $\chi^2_{1,1302}=16.0, P<.001$ ).

#### FREQUENCY OF MCI

The frequency of MCI classification with and without memory impairment is presented in **Table 2**. The presence of MCI with memory impairment ( $\chi^2_{1,1091}=7.6, P=.006$ ) and without memory impairment ( $\chi^2_{1,1167}=6.7, P=.01$ ) was more frequent among those older than 75 years than those 75 years and younger. The presence of MCI without memory impairment was more frequent among elders with fewer than 9 years of schooling ( $\chi^2_{1,1167}=22.0, P<.001$ ). There were no differences in rates of MCI with or without memory impairment by sex or racial-ethnic group.

The frequency of MCI overall and of each of the MCI subtypes is presented in **Table 3**. The frequency of all subtypes of MCI was higher among those older than 75 years ( $\chi^2_{1,1315}=12.0, P=.001$ ); when frequency of the individual subtypes were compared, the rates of MCI characterized by isolated deficits in memory ( $\chi^2_{1,1314}=4.3, P=.04$ ) and language ( $\chi^2_{1,1302}=6.6, P=.01$ ) were significantly higher among those older than 75 years.

**Table 4** summarizes the apolipoprotein (APOE) E4 allele status and presence of medical comorbidities for elders with no MCI, MCI with memory impairment, MCI without memory impairment, and amnesic MCI. A subset of the prevalence sample (n=1048; 79.7%) had APOE allele data. The frequency of APOE E4 was higher among elders with MCI with memory impairment and amnesic MCI than among those without MCI; only the difference between amnesic MCI and those without MCI met statistical significance ( $\chi^2_{1,811}=7.8, P=.005$ ). This discrepancy remained significant even after the sample was segregated into those aged 65 to 75 years ( $\chi^2_{1,450}=5.2, P=.02$ )

and 76 years and older ( $\chi^2_{1,409}=10.2, P=.001$ ). In terms of medical comorbidities, elders with MCI without memory impairment had higher rates of hypertension ( $\chi^2_{1,103}=6.0, P=.02$ ), but the rates of stroke, diabetes mellitus, and heart disease were similar in the normal and MCI groups.

**COMMENT**

This is, to our knowledge, the first study to identify, characterize, and compare the frequency of MCI in a population cohort of white, African American, and Caribbean Hispanic elders. Each participant had detailed neuropsychological testing, which allowed us to identify mutually exclusive subtypes of MCI based on cognitive characteristics. The advantage of dividing the sample into these subtypes is to allow for comparison with other studies that used different definitions of MCI and, in the

future, to evaluate any differences by subtype in transition to dementia.

Because the original criteria for MCI were developed through the use of primarily white, well-educated patients presenting to a clinic for an evaluation, we carefully examined the frequency and associations of each aspect of the criteria in our ethnically and educationally diverse community-based cohort. These analyses showed that frequency of reported functional impairment was low in this nondemented group (8.5%), but that participants older than 75 years were more likely to have significant functional complaints, and thus would not be appropriate for the diagnosis of MCI. We found that memory complaints, as assessed by a semistructured interview, were quite frequent in the nondemented cohort (74%), but this unexpectedly did not differ by age.

By definition, in our normative sample, rates of impairment in each of the cognitive domains across age, sex, education, and racial-ethnic groups were equal. Our normative sample was screened for preclinical dementia, in that individuals who demonstrated significant functional decline at a follow-up visit were excluded. Using these robust norms, and criteria for functional normality and memory complaints, we found that MCI isolated deficits in memory and visuospatial domains were more frequent in the oldest old, while other specific cognitive criteria did not differ by age. Participants with fewer than 9 years of schooling were more likely to be classified as having isolated deficits in language and visuospatial domains, as well as deficits in multiple cognitive domains with memory impairment. However, elders with more years of schooling were more likely to have isolated impairment in memory and executive domains. Therefore, it appears that both age and education have an impact on rates of impairment on cognitive measures when the normative sample is screened for preclinical dementia. Future study will demonstrate the diagnostic utility of the criteria involving functional status, memory complaints, and cognitive test performance in predicting cognitive decline and conversion to dementia and AD.

Comparison of the prevalence of MCI across studies is difficult because of variability in criteria used and differences in the populations under study. However, as a result of the emphasis on the amnesic subtype of MCI, most population studies have published prevalence of isolated memory deficits, in the context of memory com-

**Table 3. Prevalence of MCI Subtypes Among 1313 Elders Without Dementia**

MCI Subtype	No. of Participants	Prevalence, %	95% CI
All subtypes	372	28.3	25.9-30.8
Age 65-75 y	159	24.0	20.8-27.3
Age >75 y	213	32.6	29.0-36.2
Amnesic	66	5.0	3.8-6.2
Age 65-75 y	25	3.8	2.3-5.2
Age >75 y	41	6.3	4.4-8.1
Executive function	27	2.1	1.3-2.8
Age 65-75 y	14	2.1	1.0-3.2
Age >75 y	13	2.0	0.9-3.1
Language impairment	52	4.0	2.9-5.0
Age 65-75 y	23	3.5	2.1-4.9
Age >75 y	29	4.4	2.9-6.0
Visuospatial impairment	68	5.2	4.0-6.4
Age 65-75 y	24	3.6	2.2-5.1
Age >75 y	44	6.7	4.8-8.7
MCDM	82	6.2	4.9-7.6
Age 65-75 y	36	5.4	3.7-7.2
Age >75 y	46	7.0	5.1-9.0
MCDN	77	5.9	4.6-7.1
Age 65-75 y	37	5.6	3.8-7.3
Age >75 y	40	6.1	4.3-8.0

Abbreviations: CI, confidence interval; MCDM, multiple cognitive domains with memory impairment; MCDN, multiple cognitive domains without memory impairment; MCI, mild cognitive impairment.

**Table 4. Demographic Variables and Frequency of Medical Diagnoses by MCI Subtype**

Characteristic*	No MCI, No. (%)	MCI, No. (%)		
		With Memory Impairment	Without Memory Impairment	Amnesic
<i>APOE</i> E4 allele present (1047)†	215 (28.2)	35 (34.3)	49 (26.8)	23 (47.9)
Medical or psychiatric status				
Stroke (1244)	80 (9.0)	14 (9.9)	14 (6.5)	5 (8.1)
Hypertension (1244)	416 (46.8)	69 (49.3)	120 (56.1)	29 (46.8)
Diabetes (1244)	160 (18.0)	26 (18.6)	38 (17.8)	11 (17.7)
Heart disease (1244)	147 (16.5)	22 (15.6)	37 (17.3)	7 (11.3)
Major depression (1311)	30 (3.2)	9 (6.1)	9 (4.0)	3 (4.5)

Abbreviations: *APOE*, apolipoprotein; MCI, mild cognitive impairment.

\*Numbers in parentheses indicate the total number of subjects for whom data were available for that characteristic.

†*APOE* E4 status was available in a subset of 1048 participants (79.7% of the total sample).

plaints and intact daily functioning among nondemented elders. We found that the proportions of participants with amnesic MCI (5.0%) and isolated memory impairment (6.4%) are small, but similar to those reported in the Cardiovascular Health Study Cognition Study (5%),<sup>6</sup> the Canadian Study of Health and Aging (5%),<sup>34</sup> and the Monongahela Valley Independent Elders Survey (2.9 to 4.0%).<sup>35</sup> In one population-based study of people 60 years or older, retrospective application of neuropsychological criteria for memory impairment of 1 SD below the average of their cohort<sup>36</sup> resulted in a prevalence of slightly more than 3%. In the Indianapolis Study of Health and Aging,<sup>10</sup> a mainly African American cohort, approximately 12.5% of subjects were classified as having "medically unexplained memory loss," comparable to amnesic MCI. In the programme de recherche paquid sur l'epidemiologie (PAQUID) study,<sup>37</sup> the prevalence of MCI was 2.8%, as defined by self-reported memory complaints, impairment in visual memory, and normal-range score on the Mini-Mental State Examination, a measure of general cognitive functioning.

As expected, we found that participants older than 75 years were more likely to be diagnosed as having MCI with or without memory impairment, and that less well-educated elders were more likely to have MCI without memory impairment. Nearly 50% of the participants classified as having amnesic MCI had an APOE E4 allele, as compared with about 28% of the normal participants. Reported rates of diabetes mellitus (18%), hypertension (49%), and heart disease (16.6%) were high in this cohort, but were consistent with other recent large epidemiologic studies of ethnically diverse elders such as the National Health and Nutrition Examination Survey,<sup>38</sup> Atherosclerosis Risk in Communities Study,<sup>39</sup> and the National Health Information Survey.<sup>40</sup> Although diabetes and hypertension have been found to increase risk of cognitive decline, we found that elders meeting MCI criteria were not more likely to be hypertensive or diabetic or to have heart disease, stroke, or major depression. Perhaps nondemented elders with these chronic medical conditions were also more likely to report functional impairment that subsequently excluded them from a diagnosis of MCI.

A limitation of this study is the absence of brain imaging, which would allow for characterization of cerebrovascular disease. We cannot confirm that the elders in the normative cohort, who were excluded if they had signs or symptoms of clinical stroke, did not have silent strokes. In addition, it is possible that cerebrovascular disease was underdetected in the prevalence cohort, since neuroimaging was not available to detect infarcts and white-matter disease among those who did not report a clinical stroke. However, the prevalence of asymptomatic severe cerebrovascular disease is low and is more often associated with a higher risk of clinical stroke than with dementia. Therefore, while it is possible that there were persons included with severe cerebrovascular disease who did not have clinical stroke, it is unlikely that they represented a large proportion of the participants in this study. In addition, we collected a detailed history of signs and symptoms of stroke, and the frequency of a history of stroke was equal in the groups of elders with and without MCI.

The results of this study underline the importance of considering types of MCI other than that classified by isolated memory impairment. Nearly 17% of this nondemented cohort was classified as having MCI in single or multiple domains other than memory. Longitudinal study of these individuals will be necessary to compare cognitive decline and rate of conversion to AD and other dementias within subtypes of MCI with and without memory impairment.

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