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Outcomes of mild cognitive impairment depend on definition: a population study

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Abstract

Objective—To determine the one-year outcomes of individuals classified as having mild cognitive impairment (MCI) by different definitions at the population level.

Design—Inception cohort, one-year followup. Participants classified as MCI using the following definitions operationalized for this study: Amnestic MCI by Mayo criteria, Expanded MCI by International Working Group criteria, Clinical Dementia Rating (CDR)=0.5, and a purely cognitive classification into Amnestic and Non-amnestic MCI.

Setting—General community.

Participants—Stratified random population-based sample of 1982 individuals aged 65+ years.

Main Outcome Measures—For each MCI definition, three outcomes: worsening (progression to dementia (CDR≥1) or severe cognitive impairment); improvement (reversion to CDR=0 or normal cognition); and stability (unchanged CDR or cognitive status).

Results—Regardless of MCI definition, over one year, a small proportion progressed to CDR ≥ 1 (range 0–3%) or severe cognitive impairment (0–20%) at rates higher than their cognitively normal peers. Somewhat larger proportions improved or reverted to normal (6–53%). The majority remained stable (29–88%). Where definitions focused on memory impairment, and on multiple cognitive domains, higher proportions progressed and lower proportions reverted on CDR.

Conclusion—MCI as ascertained by several operational definitions is a heterogeneous entity at the population level but progresses to dementia at rates higher than in normal elderly. Proportions progressing to dementia are lower, and proportions reverting to normal are higher, than in clinical

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populations. Memory impairments and impairments in multiple domains lead to greater progression and lesser improvement. Research criteria may benefit from validation at the community level before incorporation into clinical practice.

Keywords

aging; community; population; epidemiology; MCI; dementia

INTRODUCTION

Mild cognitive impairment (MCI), the cognitive state intermediate between normal cognition and dementia, is interesting because of the potential for MCI to eventually develop into full-blown dementia. The original Mayo Clinic criteria for Amnestic MCI 1 focused on deficits and complaints in memory. The revised International Working Group (IWG) criteria 2 expanded the concept to include objective and subjective impairments in any of several cognitive domains. The Clinical Dementia Rating (CDR)3 approach focuses on decline in cognitively-driven everyday function, rather than objective cognitive deficits. Others have used purely neuropsychological definitions of MCI, based on objective deficits relative to norms.4–7 Regardless of definition, those with MCI progress to dementia in higher proportions than the cognitively normal; however, the actual proportions vary across definitions, 4,5,8–10 and across operational versions of the same definitions.11–13 Rates of progression from MCI to dementia are consistently lower in community settings than in specialty clinical and research programs where individuals with MCI seek services,11,12 despite using the same criteria.14 Notably, all population-based studies find substantial proportions of individuals with variously defined MCI remaining stable or even reverting to normal during follow-up. 4,8,10–12

In a population-based cohort study, we collected data sufficient to apply operational versions of several different MCI definitions simultaneously. Having previously showed that prevalence of MCI varied considerably depending on the definition,15 we now report one-year outcomes of MCI according to these multiple definitions.

METHODS

Study area, sampling, and recruitment

The study cohort named the Monongahela-Youghiogheny Healthy Aging Team (MYHAT) was an age-stratified random sample of the population aged 65+ years, drawn from the publicly available voter registration list for a small-town region of Pennsylvania (USA). Community outreach, recruitment, and assessment protocols were approved by the University of Pittsburgh Institutional Review Board for protection of human subjects.15–17 Recruitment criteria were (a) age 65 years or older, (b) living within the selected towns, (c) not already in long-term care institutions. Individuals were ineligible if they (d) were too ill to participate, (e) had severe vision or hearing impairments, or (f) were decisionally incapacitated. Over a two-year period, 2036 individuals were recruited.

Assessment and classification (overview)

Trained interviewers obtained written informed consent and administered the Mini-Mental State Examination (MMSE)18 and scored it immediately,16 applying a standard correction for age and education.19 We classified 54 (2.7%) individuals scoring <21 /30 (age-education corrected) as moderately / severely impaired and thus unsuited to a study of mild impairment; we did not assess them further. Designating the remaining 1982 participants as normal or only mildly impaired, we immediately performed a detailed assessment15,17 on

them; a year later, we invited them to undergo a repeat assessment.20 At each assessment, we classified participants according to several criteria for mild cognitive impairment: the Clinical Dementia Rating (CDR), a purely cognitive classification,20 and the standard Mayo 1 and IWG criteria.2 All results reported here refer to our operational definitions of these criteria.

Neuropsychological assessment

We assessed cognitive functioning using a comprehensive test battery17,20 on which we have reported population-based norms 17 also available on our study website (http://www.wpic.pitt.edu/research/dementia_epidemiology/MYHAT/MYHATHomePage.htm). We categorized these tests according to the principal cognitive domain that they tap (attention/processing speed, executive function, language, memory, and visuospatial function) and created a composite score for each domain. 17

Clinical Dementia Rating

Appropriately certified 21 interviewers rated participants on the CDR scale3 using an assessment protocol composed of standardized questions and observations regarding everyday functioning in the six areas of memory, orientation, judgment, home and hobbies, community affairs, and personal care. Most of these normal or only mildly impaired older adults provided their own self-report information and did not have surrogate informants; thus our CDR may be considered a field-adaptation for population settings. The CDR for each participant was finalized by consensus among two or more interviewers, ignoring the neuropsychological data but determining that the reported or observed functional impairments were attributable to cognitive rather than, e.g., sensory or motor, difficulties.

Cognitive Classification

To complement the purely functionally based CDR, we developed a solely neuropsychologically based Cognitive Classification.15 Based on normative reference points,17 we classified participants as follow: (a) cognitively normal: composite scores in all domains within 1.0 standard deviation (SD) of the mean for the individual's age-sex-education group; (b) severe cognitive impairment: composite scores in at least two domains 2.0 SD below the mean for the appropriate reference group; (c) MCI single domain: composite score in one domain > 1.0 SD below the mean, with all other domains in the normal range; (d) MCI multi-domain: composite scores in two or more domains 1.0 – 2.0 SD below the appropriate mean, *or* no more than one domain composite > 2.0 SD below the mean with other domains 1.0 – 2.0 SD below the mean. We also explored a "narrow" variation of these definitions, using a more stringent MCI threshold of 1.5 SD rather than 1.0 SD below the mean, eliminating those with scores between 1.0 and 1.5 SD.

Standard MCI Criteria

For the Mayo Criteria for Amnestic MCI 1 and the expanded IWG Criteria, 2 we operationalized the objective cognitive deficit criteria as in the Cognitive Classification described above (memory domain alone for Mayo MCI, and any domain for IWG MCI). For subjective reports /complaints, we operationalized the Mayo criterion as at least 2 items (median score) endorsed from a list of 16 "remembering" questions; for the IWG criteria, we included an additional 5 questions on non-"remembering" functions. We defined absence of dementia as CDR <1, essentially normal daily functioning as no impaired instrumental activities of daily living (IADL) on the OARS scale,22 and essentially normal mental status as MMSE ≥21. Details have been reported previously.15

Since the original Mayo Criteria1 did not specify that domains other than memory could be impaired, we operationalized them as requiring isolated (single-domain) memory deficit. Subsequently we also explored a multi-domain definition, having been advised by co-author Dr. Petersen that the Mayo group did include individuals with impairments in additional domains. We also examined the effects of (i) raising the MMSE threshold from ≥ 21, at the 5^{th} percentile of our original cohort, to >23, at its 10^{th} percentile, thus eliminating those with scores of 21–23; and (ii) lowering the cognitive composite threshold from 1.0 to 1.5 SD below the appropriate mean. As both these changes reduce the number of people classified as MCI, we refer to them as "narrow versions."

Statistical Analysis

For each baseline MCI group, we identified two outcome variables at follow-up: CDR and our cognitive classification. For each outcome, we examined three possibilities.

- **i.** Worsening: progression to (a) CDR≥1 (dementia) among individuals with baseline CDR <1, or (b) severe cognitive impairment (defined above), in persons with baseline cognitive classification of normal or MCI.
- **ii.** Improvement: reversion to (a) CDR=0 (no dementia) among those with baseline CDR >0 or (b) normal cognition (defined above), among those with baseline cognitive classification of MCI.
- **iii.** Stability: no change in (a) CDR or (b) cognitive classification.

We compared proportions of those experiencing these six outcomes using the one-sample proportion Z test at $p<0.05$. This test allows proportions to be compared between non-independent (overlapping) samples by treating one of the samples as though it were the population from which the other sample was drawn.23 Finally, we compared the characteristics of those assessed at followup to those lost to followup.

RESULTS

At baseline, of 1982 cohort members with normal or mildly impaired cognition (MMSE ≥ 21), all participants were rated on the CDR; 1941 participants had sufficient neuropsychological data to be classified by the cognitive definitions; 1950 and 1957 provided sufficient cognitive, functional (IADL), and subjective report data to be classified by the Mayo 1 and IWG criteria.2 Proportions of those meeting these criteria, corresponding to our published prevalence estimates,15 and their demographic characteristics, were identified (Table 1.) Note the MCI definitions overlap: the Mayo Criteria are a subset of the IWG Criteria, and both overlap with the CDR; the four cognitive classification subgroups are mutually exclusive with one another but overlap with the CDR and the Mayo and IWG criteria. Of 697 individuals with MCI by Cognitive Classification, 433 (62.1%) had CDR=0; the majority of these (n=233) had non-amnestic single domain impairment. Of 45 participants meeting Mayo Criteria, 13 (28.9%) had CDR=0; among 350 meeting IWG Criteria, 143 (40.9%) had CDR=0. As expected, the "narrow" versions reduced baseline prevalence for the standard and cognitive criteria. Some individuals were classified as MCI under the original versions and as normal under the narrow versions; others originally classified as multi-domain MCI became reclassified as single-domain MCI.

Participants meeting the operationalized Mayo Criteria were significantly ($p<0.05$) younger than those with CDR=0.5, were more likely to be men and had more education than those classified by the IWG Criteria, by the CDR=0.5, and by the Cognitive Classification. Those fulfilling the IWG Criteria were significantly ($p< 0.05$) younger and better educated than those with CDR=0.5. The narrowed versions of the criteria had minimal effects on the demographics of MCI (Table 1 footnote).

At one-year follow-up, 1697 (85.6%) of the original 1982 cohort members underwent repeat assessment. The total attrition of 14.4% represented 3% from mortality and 11.4% from other causes including relocation, illness, and elective dropout. The 285 attrited individuals were significantly older (78.7 *vs.* 77.5 years, $p < 0.05$) and less likely to be women (55.1% vs. 62.1%, $p < 0.05$) than those who were seen at follow-up, with no significant difference in educational level (16.8% and 13.3% with less than high school education).20 Those lost to followup had slightly but significantly lower mean baseline MMSE (26.4 ± *2.7 vs.* 27.0 ± 2.4, $p<0.001$), had a lower proportion with baseline CDR=0 (60.0 % vs. 73.2% %, $p <0.0001$), and were significantly ($p<0.0001$) more likely to be classified at baseline by CDR and all Cognitive definitions, except multidomain amnestic MCI, than those re-assessed.

One-year CDR Outcomes (Table 2)

Progression to CDR>=1 ranged from 0% for the *purely cognitive* non-amnestic multi-domain MCI to 2.8% for the Mayo Criteria, noting that the latter figure represents only one participant.

Reversion to CDR=0 ranged from 10.8% in those with baseline amnestic multi-domain MCI (and CDR=0.5), to 26.5% in those with non-amnestic single domain MCI (and CDR=0.5).

CDR stability was uniformly high across groups, ranging from 72% for both CDR=0.5 and the Mayo Criteria, and 78% for the purely cognitive amnestic single-domain MCI, to between 80% and 88% for all other definitions.

One-year Cognitive Outcomes

Progression to severe cognitive impairment ranged for 1.1% for *purely cognitive* non-amnestic single-domain MCI to 19.8% for amnestic multi-domain MCI.

Reversion to cognitively normal ranged from 6.3% for purely cognitive amnestic multi-domain MCI to 53.4% for non-amnestic single-domain MCI.

Cognitive classification stability ranged from 28.6% for the non-amnestic single domain category to 54.5% for CDR=0.5.

Varying the definitions

Expanding Mayo MCI, allowing impairment in additional domains besides memory, increased baseline prevalence from 2.27% to 6.21%, i.e., 123 individuals, of whom 96 completed followup; 70 had baseline CDR=0.5, of whom 1 (1.4%) progressed to CDR>=1 at followup, 8 (11.4%) reverted to CDR=0, and 61 (87.1%) remained at CDR=0.5. Of 26 with baseline CDR=0, 7 (26.9%) progressed to CDR=0.5 and none to CDR>=1, while 19 (73.1%) were stable at CDR=0. Overall, progression from a lower to a higher CDR level was seen in 8 (8.3%).

Narrowing the definitions by raising the MMSE threshold to 24 (Mayo and IWG criteria) and by lowering the cognitive threshold to 1.5 SD below the appropriate mean (Mayo, IWG, and Cognitive Classification), in reducing prevalence, also reduced the denominator for calculating proportions with the different outcomes (eTables1 and 2). Although the actual numbers were mostly too small to be compared for statistical significance, the overall pattern was that the narrow definitions very slightly increased the proportions that worsened, reduced the proportions that improved on CDR, reduced sensitivity, and increased specificity.

Attrition effects : sensitivity analyses. The actual outcomes of those lost to followup are not knowable. In the worst case, if all attrited participants with baseline MCI had remained in

the study and worsened at followup, the overall proportions that worsened to CDR >=1 (range 11.5% to 25.8%) or severe cognitive impairment (range 11.8% to 39.9%) would be significantly increased, for all MCI definitions except multidomain non-amnestic MCI. Note these percentages represent small numbers.

DISCUSSION

In a randomly sampled population-based cohort, the baseline prevalence of MCI varied by definition,15 as would be expected with any syndromic entity. Over one-year follow-up, the same MCI definitions led to different proportions of progression (worsening), reversion (improvement), and stability. As the various criterion sets overlap only partially, individuals can be classified as impaired by one definition and as normal by another. For example, with the Mayo Criteria defined as including CDR <1, MCI individuals could be either CDR=0 or CDR=0.5; among these, only those at CDR=0.5 can revert to CDR=0. Similarly, by designating worsening as progression to CDR >=1, we could be underestimating progression by not including worsening from CDR=0 to CDR=0.5.

With the above *caveats*, across MCI definitions, relatively small proportions (0–3%) progressed to dementia defined as CDR >=1 but at significantly higher rates than those with normal cognition. Progression was most likely to be seen among the definitions emphasizing memory. Larger proportions (1–20%) were found to worsen when the outcome was defined as severe cognitive impairment; again, MCI definitions with amnestic components showed had the highest progression. Within the purely cognitive classification, multi-domain amnestic impairment showed more progression than single-domain amnestic impairment, while non-amnestic impairments had the lowest progression.

Greater proportions of individuals with baseline MCI showed improvement, compared to worsening, at one-year followup. With CDR=0 as the outcome, the range of reversion was about a quarter of those with baseline CDR=0.5 alone. When reversion was characterized as normal cognition, the lowest proportion reverted from amnestic multi-domain MCI (which also had the highest proportion progressing to severe cognitive impairment). While reversion in the purely cognitive definition could be attributed to instability of measurement or intra-individual variability, the same phenomenon was also observed for our functional (CDR) and combined cognitive-functional (Mayo and IWG) definitions.

However, the most frequent outcome was stability, i.e. no change in MCI status. These proportions ranged from 72% to 88% for stable CDR, and from 33% to 79% for stable MCI by broad cognitive classification. The single-domain MCIs, whether amnestic or non-amnestic, were the least likely to remain cognitively unchanged while the CDR=0.5 group was the most likely to remain cognitively unchanged.

Our cohort study indicates, as have previous studies,4،8،10–12 that the MCI syndrome is a heterogeneous entity at the population level regardless of definition. A small proportion progresses to dementia or severe cognitive impairment, a somewhat larger proportion reverts to normal, while the majority remain unchanged. Most individuals with mild impairment remain at least mildly impaired. Some individuals who meet MCI criteria may have always functioned at a mildly impaired level, invoking the concept of “accidental MCI.”24 The heterogeneity in outcome observed here is greater than reported from clinical settings, where individuals seek care for cognitive impairment, and where progression occurs at the rate of 12–15% annually.13

Heterogeneity in outcome suggests heterogeneity in the underlying pathology. MCI definitions reflecting impairment in memory predicted more progression, and less reversion, than impairment in other domains, regardless of whether the definition is

neuropsychological, functional, or both. Since memory deficits are the hallmark of dementing disorders such as Alzheimer's disease (AD), MCI definitions centered on memory may be identifying individuals in the early stages of these disorders, which may be in the minority at the population level.

Finally, our data indicate that mild impairment in one domain, memory or otherwise, is more likely to predict reversion to normal than mild impairment in two or more domains, as was also observed in another population study.25 This source of variation could represent heterogeneity in etiology and/or in stage along the course of a given disease. For example, an individual with a non-progressive condition, e.g., depression, medication side-effects, or hypoxia, might suffer transient or reversible cognitive impairment reflecting resolution of the underlying condition. Alternatively, a person at a very early stage of AD might not manifest cognitive deficits unless a second condition is also present; if the second condition resolves, improvement might be noted temporarily. Further, a person with any progressive dementia may experience lability or "wobble" in function and performance early in the disease course, before the deficits become more pervasive and sustained, and this intra-individual variability itself may reflect underlying brain disease.26 Compared to single-domain impairments, impairment in two domains suggests a greater likelihood of underlying disease, which has reached a later stage, closer to the dementia threshold. Even within the normal range of cognition, poorer neuropsychological test scores predict subsequent decline in CDR.20 In our cohort, as in clinical practice, a minority of individuals did not return for followup assessment at one year because of death, relocation, illness, or elective dropout. At study entry, these individuals had been older, less educated, and more cognitively impaired than those who were followed up. Had they remained in the study, and experienced worsening in large enough proportions, they may have increased the progression rates for most but not all MCI definitions.

While one year is a relatively short period in which to observe MCI outcomes, it mirrors clinical practice where the first annual followup is often essential to validate the original diagnosis. While longer prospective studies usually report annual progression rates averaged over multiple years, 5،8،12، 14 the annual rate changes over time.12 Repeated assessments of this cohort over a longer followup period will clarify these patterns and identify the profiles of individuals whose mild impairments are likely to develop into dementia eventually. The incorporation of biomarker and risk factor assessments may further improve the characterization of MCI at the population level.

Population-based cohorts suffer less selection bias and are more representative of the community than specialty clinic samples. Being large, they are powered to detect relatively small effects. However, participants recruited randomly from the community are not necessarily concerned about their cognition; their subjective reports ("complaints") are not spontaneously offered but rather elicited by standardized questions, and may vary in clinical and prognostic significance. Normal or mildly impaired individuals in the community who are not seeking care for cognitive difficulties may not have surrogate informants more knowledgeable than themselves about their own everyday functioning. Dementia ratings based on participants' self-reports plus raters' observations may differ from ratings based on family reports typically obtained in specialty clinics. In most population studies, participants are assessed using standardized protocols implemented by research personnel who, while highly trained, are not expert clinicians exercising judgment regarding help-seeking patients in the clinic. Classification is based on statistical or actuarial criteria, which in clinical settings could be overridden by expert clinical judgment. Thus, both heterogeneity in the participant pool and methodological factors can account for variance in proportions with progression and reversion in MCI between clinical and community studies, with results fairly consistent within these groups of studies. 27 Population-based data illustrate the

importance of validating research criteria at the community level before they are recommended for clinical practice.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Frequencies, proportions and demographic characteristics of cohort subgroups at baseline and first annual followup

MCI definition at baseline	No. *(% of 1982)* at baseline *a,b*	No. *(% of 1982)* at baseline also assessed at one-year followup	Narrow version[c] No. *(% of 1982)* at baseline also assessed at one-year followup	Age[d] Mean*(SD)* at baseline	Gender[d] No. *(%)* women	Educational Level[d]		
						No. *(%)* Less than high school	No. *(%)* High school	No. *(%)* Greater than high school
STANDARD MCI CRITERIA1,2[b]								
Mayo Criteria1	45 *(2.3)*	36 *(1.8)*	15 *(0.8)*	78.6 *(7.1)*	18 *(50.0)*	2 *(5.6)*	20 *(55.6)*	14 *(38.9)*
International WG Criteria2	350 *(17.7)*	290 *(14.6)*	121 *(6.1)*	78.1 *(7.4)*	177 *(61.0)*	33 *(11.4)*	142 *(49.0)*	115 *(39.7)*
MYHAT COGNITIVE CLASSIFICATION15[b]								
Amnestic single-domain MCI	90 *(4.5)*	72 *(3.6)*	34 *(1.7)*	78.1 *(7.2)*	43 *(59.7)*	7 *(9.7)*	33 *(45.8)*	32 *(44.4)*
multidomain MCI	151 *(7.6)*	114 *(5.8)*	36 *(1.8)*	78.9 *(7.0)*	72 *(63.2)*	17 *(14.9)*	52 *(45.6)*	45 *(39.5)*
Any amnestic MCI	241 *(12.2)*	186 *(9.4)*	70 *(3.5)*	78.6 *(7.1)*	115 *(61.8)*	24 *(12.9)*	85 *(45.7)*	77 *(41.4)*
Non-amnestic single-domain MCI	316 *(15.9)*	267 *(13.5)*	175 *(8.8)*	77.7 *(7.5)*	166 *(62.2)*	35 *(13.1)*	119 *(44.6)*	113 *(42.3)*
Non-amnestic multi-domain MCI	140 *(7.1)*	119 *(6.0)*	37 *(1.9)*	77.8 *(8.1)*	72 *(60.5)*	17 *(14.3)*	56 *(47.1)*	46 *(38.7)*
Any non-amnestic MCI	456 (23.0)	386 *(19.5)*	212 *(10.7)*	77.7 *(7.7)*	238 *(61.7)*	52 *(13.5)*	175 *(45.3)*	159 *(41.2)*
Any "purely cognitive" MCI	697 *(35.2)*	572 *(28.9)*	282 *(14.2)*	78.0 *(7.5)*	353 *(61.7)*	76 *(13.3)*	260 *(45.5)*	236 *(41.3)*
Normal cognition	1190 *(60.0)*	1054 *(53.2)*	1345 *(67.9)*	77.2 *(7.2)*	657 *(62.3)*	140 *(13.3)*	474 *(45.0)*	440 *(41.8)*
CLINICAL DEMENTIA RATING3[b]								
CDR=0.5	546 *(27.5)*	440 *(22.2)*	n/a	79.3 *(7.3)*	250 *(56.8)*	83 *(18.9)*	189 *(43.0)*	168 *(38.2)*
CDR=0	1413 *(71.3)*	1242 *(62.7)*	n/a	76.8 *(7.2)*	798 *(64.3)*	137 *(11.0)*	568 *(45.7)*	537 *(43.2)*

[a] Equivalent to "prevalence" at baseline. 15

[b] Among those with sufficient data to be classified by a given MCI definition

[c] Narrow version: MMSE threshold 24 rather than 21; cognitive threshold 1.5 SD rather than 1.0 SD below the appropriate mean

[d] In pairwise comparisons of demographics of "narrow" and original versions of Mayo, IWG, and Cognitive definitions of MCI, all mean differences in age were <=0.6 years; all per cent gender differences were < 5% in size except for the non-amnestic multidomain, where the narrow version identified 48.7% women compared to 60.5% in the original version. For education less than high school, all percent differences were < 3%. For high school education, all per cent differences were < 6% except for the Mayo criteria (narrow version identified 46.7%), and amnestic single domain where the narrow version identified 35.3%.

Table 2

One-year outcome of mild cognitive impairment, defined by Clinical Dementia Rating3

MCI definition at baseline	No. with baseline CDR <1 also assessed at followup	No. *(%)* worsened to CDR >=1	No. *(%)* unchanged CDR	No. with baseline CDR =0.5	No. *(%)* improved from CDR=0.5 to CDR=0
STANDARD MCI CRITERIA (operational definitions)1,2					
Mayo Criteria1	36	1 *(2.8)*	26 *(72.2)*	23	4 *(17.4)*
IWG criteria2	290	2 *(0.7)* [a]	232 *(80.0)* [b]	164	30 *(18.3)*
COGNITIVE CLASSIFICATION15					
Amnestic single-domain MCI	72	1 *(1.4)*	56 *(77.8)*	26	4 *(15.4)*
Amnestic multi-domain MCI	114	2 *(1.8)*	100 *(87.7)* [b,d]	65	7 *(10.8)*
Any amnestic MCI	186	3 *(1.6)*	156 *(83.9)* [b]	91	11 *(12.1)*
Non-amnestic single-domain MCI	267	2 *(0.8)* [a]	230 *(86.1)* [b,d]	68	18 *(26.5)* [b]
Non-amnestic multi-domain MCI	119	0 *(0.0)*	101 *(84.9)* [b]	48	7 *(14.6)*
Any non-amnestic MCI	386	2 *(0.5)* [a]	331 *(85.8)* [b,d]	116	25 *(21.6)*
Any cognitively defined MCI	572	5 *(0.9)* [a]	487 *(85.1)* [b,d]	207	36 *(17.4)*
Normal cognition (for comparison)	1054	1 (0.1) [a,c]	925 *(87.8)* [b,d]	200	75 *(37.5)* [b,d]
CLINICAL DEMENTIA RATING (field adapted version)3					
CDR=0.5	440	8 *(1.8)* [d]	318 *(72.3)* [c]	440	114 *(25.9)* [b,d]
CDR=0 (for comparison)	1242	1 *(0.1)* [a,c]	1137 *(91.5)* [b,d]	n/a	n/a

Proportions compared for significant differences using one–sample Z test ($p<0.05$)

[a] significantly lower than Mayo criteria;

[b] significantly higher than Mayo criteria

[c] significantly lower than IWG criteria;

[d] significantly higher than IWG criteria.

Table 3

One-year outcome of MCI, defined by cognitive classification 15

MCI definition at baseline	No. with baseline normal or mildly impaired cognition also assessed at followup [a]	No. *(%)* worsened to severe cognitive impairment	No. *(%)* with unchanged cognitive classification	No. *(%)* improved to cognitively normal [a]
STANDARD MCI CRITERIA1,2				
Mayo Criteria 1	35	3 *(8.6)*	13 *(37.1)*	6 *(17.1)*
IWG criteria 2	285	20 *(7.0)*	103 *(36.1)*	85 *(29.8)* [c]
COGNITIVE CLASSIFICATION15				
Amnestic single-domain MCI	69	4 *(5.8)*	21 *(30.4)*	17 *(24.6)*
Amnestic multi-domain MCI	111	22 *(19.8)* [c,e]	49 *(44.1)*	7 *(6.3)* [b,d]
Any amnestic MCI	180	26 *(14.4)* [c,e]	70 *(38.9)*	24 *(13.3)* [d]
Non-amnestic single-domain MCI	262	3 *(1.1)*[b,d]	75 *(28.6)* [b,d]	140 *(53.4)* [c,e]
Non-amnestic multi-domain MCI	116	5 *(4.3)*	39 *(33.6)*	19 *(16.4)* [d]
Any non-amnestic MCI	378	8 *(2.1)*[b,d]	114 *(30.2)* [b,d]	159 *(42.1)* [c,e]
Any cognitively defined MCI	558	34 *(6.1)*[b]	184 *(33.0)*[b]	183 *(32.8)* [c]
Normal cognition (for comparison)	1046	3 *(0.3)*[b,d]	846 *(80.9)* [c,e]	(n/a)
CLINICAL DEMENTIA RATING3				
CDR=0.5	400	22 *(5.5)* [b]	218 *(54.5)* [c,e]	39 *(19.2)* [d,f]
CDR=0 (for comparison)	1204	15 *(1.2)* [b,d]	812 *(67.4)* [c,e]	144 *(40.6)* [c,e,g]

[a] Excluding participants with insufficient neuropsychological data to be classified at either baseline or followup.
Based on one-sample Z test (P<0.05)

[b] Significantly lower than Mayo criteria;

[c] significantly higher than Mayo criteria;

[d] significantly lower than IWG criteria;

[e] significantly higher than IWG criteria

[f] denominator is 203 after excluding cognitively normal at baseline

[g] denominator is 355 after excluding cognitively normal at baseline