Baseline Amnestic Severity Predicts Progression From Amnestic Mild Cognitive Impairment to Alzheimer Disease Dementia at 3 Years

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Background: Given the long preclinical disease course of Alzheimer disease (AD) pathology, novel treatments may be more efficacious if administered before the emergence of dementia. Thus, accurate prediction of who will develop AD dementia is of key importance in selecting individuals for trials of treatment and may become crucial for future selection of patients for therapy.

Methods: As part of the Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing, 901 individuals who did not have dementia were recruited. We assigned individuals according to Petersen criteria and Winblad criteria for Mild Cognitive Impairment (MCI) at baseline. We then stratified individuals with amnestic MCI into 2 groups according to the severity of their memory impairment on baseline neuropsychological assessment. Incident diagnosis of AD dementia was established by consensus of an expert panel at 36 months.

Results: At 36 months, 725 (80.5%) participants were followed up, 54 (7.4%) of whom developed AD dementia. Subjects with amnestic MCI according to Petersen criteria were more likely to develop AD dementia [positive predictive value; PPV, 24.1%; 95% confidence interval (CI), 18.4-30.6] than healthy controls (PPV, 1.0%; 95% CI, 0.3-2.3). Winblad criteria were also effective, with multiple domain amnestic MCI being most accurate at predicting AD dementia (PPV, 47.3%; 95% CI, 33.7-61.2). Finally, more severe amnestic impairment below the median was useful for predicting the development of AD dementia in single domain amnestic MCI (PPV, 28.1%; 95% CI, 17.0-41.5) and in multiple domain amnestic MCI (PPV, 65.7%; 95% CI, 47.8-80.9).

Conclusions: Memory impairment *per se*, impairment in multiple cognitive domains and severity of memory impairment were all associated with greater risk of developing AD dementia in this sample. Characterizing the severity of memory impairment may provide prognostic stratification within Petersen or Winblad taxonomies of amnestic MCI.

Key Words: Alzheimer disease, biomarker, cognition, dementia, mild cognitive impairment, memory

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Accurate prediction of who will develop Alzheimer disease (AD) dementia is of key importance to understand the disease's clinical presentation and its natural history. In turn, understanding risk factors should facilitate identification of biological substrates, allow selection enrichment of individuals for trials of treatment and may fulfill the ultimate goal of selection of patients for preventative treatments.

Mild cognitive impairment (MCI) is an intermediate state that exists on the continuum of cognitive health between intact cognition and dementia. It has varying definitions and diagnostic criteria that are applied inconsistently. Dominant taxonomies treat MCI as a categorical diagnosis,[1,2] though it may be equally valid to view it as a continuum. With the advent of disease biomarkers for prodromal and preclinical AD, attempts have been made to incorporate these biological measures as predictors of the course of MCI.[3] In doing so, criteria move beyond MCI as a purely clinical definition incorporating history and examination findings to a preclinical or prodromal state with biological evidence of evolving AD. However, meta-analyses so far have failed to support a clear role for FDG-PET,[4] amyloid PET,[5] or CSF biomarkers[6] in predicting progression from MCI to AD dementia, though this may reflect sample sizes reported to date. Although the clinical utility of these measures should be evaluated further, the clinical characterization of MCI and cognitive factors that predict progression to AD dementia should also be studied further to determine how much they can contribute to predicting progression.

The definition put forward by Petersen et al[2] identifies amnestic MCI (aMCI), which is characterized by subjective

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memory impairment or informant report as well as objective memory impairment. Petersen and colleagues observed that patients recruited from a community-based medical clinic who were themselves concerned about their cognition, or whose carers or physicians were concerned, tended to perform 1.5 SD below (ie, $z \leq -1.5$ SD) the age-adjusted and education-adjusted mean.[7] Although Petersen did not advocate for a strict adherence to this cut-off and subsequently utilized a cut-off of approximately 1.5 to 2 SD below the mean,[8] many subsequent studies did adopt the threshold of $z \leq -1.5$ SD on a neuropsychological test of episodic memory.

The Petersen criteria were later revised and refined to include nonmemory domains following a key symposium of experts.[1] These criteria subdivided MCI into amnestic or nonamnestic based on the presence of memory impairment, as well as single domain or multiple domain (sd-MCI and md-MCI) based on whether one or more cognitive domains were impaired.

Some studies have examined explicitly differences between various subtypes of MCI and progression to AD dementia. The most consistent finding is that aMCI is associated with an increased risk of progression to AD dementia.[9–20] Moreover, 6 of 9 studies show that md-aMCI has the best predictive accuracy for progression to AD dementia.[9–11,15,16,19] However, 2 studies showed that sd-aMCI was associated with the highest risk of progression to AD dementia[12,20] and one study found that sd-aMCI and md-aMCI were equally likely to progress to AD dementia.[13] A challenge to the discriminative validity of the Winblad taxonomy is that md-aMCI was the best predictor of progression to vascular dementia as well as to AD dementia.[15] More recent criteria by the NIA-AA consensus panel[3] have dispensed with the distinction between sd-aMCI and md-aMCI.

A possible reason for the discrepant findings regarding sd-aMCI and md-aMCI in the prediction of AD dementia is because of differing definitions of the subtypes across studies. Although all studies purported to employ the Winblad criteria, these were operationalized in different ways, for example using hierarchical cluster analysis of neuropsychological data rather than clinical judgement[12] or not including information about subjective memory complaint.[9] Moreover, psychometric impairment was defined in one study as at least 1.5 SD below the mean for an age-matched and education-matched sample on a neuropsychological battery[20] or as at least 1.0 SD below the mean for an age-matched and education-matched sample on indices derived from the MoCA.[10]

Many studies show that impairments on neuropsychological tests of memory predict progression from MCI to AD dementia.[21–23] Very few, however, have shown that more severe memory impairment is associated with an increased risk of progression from MCI to AD dementia,[24,25] and none have implemented this into a clinically useful heuristic.

The aim of this study was to identify which subtypes of MCI predict progression to AD dementia. To achieve this, we employed the 2 most commonly used taxonomies of MCI, that is, Petersen and Winblad. We also aimed to challenge the classification of aMCI as a categorical diagnosis. To this end, we stratified aMCI subjects into subgroups based on the severity of their memory impairment. We hypothesized that increased risk of progression to AD dementia would be seen in aMCI, in md-aMCI and with more severe memory impairment in aMCI.

METHODS

Participants

Participants were recruited as part of the Australian Imaging, Biomarkers and Lifestyle (AIBL) Flagship Study of Ageing, which has been described in detail previously.[26] Briefly, the AIBL study is a large multicenter prospective cohort study of aging and AD that employs various biomarkers, cognitive parameters and lifestyle factors to allow prediction of future cognitive decline.

Participants were recruited through 2 mechanisms. Many participants responded to a media campaign and advertising. Some participants were referred by specialist physicians with diagnoses of either AD dementia or MCI and the spouses and carers of some of these subjects also volunteered to join the study as healthy controls (HCs).

Participants were excluded if they had a history of non-AD dementia, schizophrenia, bipolar disorder, significant current depression, Parkinson disease, cancer (other than basal cell skin carcinoma) within the last 2 years, epilepsy, symptomatic stroke, uncontrolled diabetes, reported past head injury with a posttraumatic amnesia period exceeding 1 hour, diagnosed obstructive sleep apnea or current regular alcohol use exceeding NHMRC guidelines of 2 standard drinks per day for women or 4 for men.

All participants completed a neuropsychological test battery, mood questionnaires, health and lifestyle questionnaires, medical history and physical examination. Some participants also had magnetic resonance imaging (MRI), lumbar puncture, and PET amyloid imaging. At baseline this PET amyloid imaging was conducted with Pittsburgh B compound (PiB) but later in the study some participants were imaged with other fluorinated compounds which bind to brain amyloid.

A monthly clinical review panel meeting chaired by DA comprising old age psychiatrists, neurologists, geriatricians, and neuropsychologists (with a minimum of three panelists including at least 1 medical practitioner and at least 1 neuropsychologist forming a quorum) reviewed cases with a diagnosis of AD or MCI or HCs who showed psychometric impairment, relevant medical history, report of cognitive decline or use of medications that could affect cognition. The panel was kept blind to results of amyloid imaging. A consensus diagnosis was established for each participant according to DSM-IV,[27] ICD-10,[28] and NINCDS-ADRDA[29] criteria. In addition, the Clinical Dementia Rating (CDR) scale was applied to each participant and each rating was reviewed by DA to ensure consistency. Individuals were considered eligible for the present study if they had a CDR of 0 or 0.5 at baseline and had not been given a diagnosis of AD dementia.

Individuals were followed up at 18-month intervals. We chose a 3-year follow-up period for the present study as it represented the best balance between participants lost to follow up and a clinically meaningful period of follow up.

All participants provided written informed consent. The AIBL study was approved by the institutional ethics committees of Austin Health, St. Vincent's Health, Hollywood Private Hospital and Edith Cowan University.

Cognitive Examination

All participants completed a battery of psychometric tests that were administered as per standardized protocols (see Table 1), except for Logical Memory from the WMS, for which only Story A was presented to each participant.

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TABLE 1. Neuropsychological Tests and Indices Considered for Diagnosis of Mild Cognitive Impairment

Domain	Test	Indices	Source/Normative Data
Memory	CVLT-II	Total learning trials 1-5, short delay free recall, long delay free recall, d' recognition	CVLT-II manual[30]
	Logical memory	Immediate recall, delayed recall, percentage retention	WMS,[31] novel-generated normative data (see text for description)
	Rey figure	Immediate recall, delayed recall, recognition	Myers[32]
Attention	Digit span	Scaled score	WAIS-III[33]
	Digit symbol coding	Scaled score	WAIS-III[33]
Language	Boston naming	Spontaneous response	30-item version[34]
	Fluency tasks	Animals/boys names	DKEFS[35]
Executive function	Stroop test	Color/dots ratio	Victoria version[36]
	Fluency tasks	FAS total words, Fruit/furniture total	DKEFS[35]
Visuospatial	Rey figure	Copy	Mitrushina, Boone, Razani et al[37]

CVLT-II indicates California Verbal Learning Test-second edition; DKEFS, Delis-Kaplan Executive Function System; WAIS-III, Wechsler Adult Intelligence Scale third edition; WMS, Wechsler Memory Scale.

Novel normative data for Logical Memory were generated for individuals identified as HCs according to the original AIBL criteria[26] and who remained classified as HCs at 3-year follow up. These individuals were then stratified into 5-year age bands and means and SDs were used to generate z scores for each participant for immediate recall, delayed recall, and percentage retention. The neuropsychological tests and the cognitive domains in which they were classified are shown in Table 1.

Subjective memory complaint was determined by positive endorsement of the question "Do you have difficulties with your memory?"

MCI and HC Classification

The classification of participants is summarized in Table 2. For the current analyses participants were classified as cognitively normal HCs if they had either no subjective memory complaint or they had no neuropsychological performance ≥ 1.5 SD below the mean (ie, no $z \leq -1.5$ SD).

Previous studies with the AIBL cohort have employed a different classification of MCI on account of the 2 different routes of entry into the study.[26] People who were referred by a clinician with a diagnosis of MCI were required to have subjective memory complaint and 1 neuropsychological test $z \leq -1.5$ SD, whereas those who were recruited from the community were required to have subjective memory complaint and 2 neuropsychological tests $z \leq -1.5$ SD to be classified as MCI by the AIBL study.[26] Given the present study aimed to examine systematically the difference between Petersen (1999) and Winblad (2004) criteria, we adopted de novo definitions based on operationalization of the Petersen and Winblad criteria.

Participants were initially classified as aMCI if they had subjective memory complaint and objective performance on at least one memory test of $z \leq -1.5$ SD. Alternatively, participants were classified as nonamnestic MCI (naMCI) if they had a subjective memory complaint, no impairment on a memory test, and impairment on at least one nonmemory test. In accordance with the Winblad criteria, the aMCI subgroup was then subdivided into sd-aMCI and md-aMCI subgroups based on additional impairment of a nonmemory domain. Similarly, the naMCI group was subdivided based on impairment of one or more nonmemory domains.

Severity of Amnestic Impairment

Within the Petersen-defined aMCI group, we extracted each aMCI participant's lowest memory performance from the 10 memory indices as shown in Table 1. The median lowest memory performance in the Petersen-defined aMCI group was $z = -2.29$. This score was used to stratify aMCI participants arbitrarily into grade 1 or grade 2 severity

TABLE 2. Criteria for Classification of Each MCI Group

	Group	Subjective Memory Complaint	Lowest Memory Performance	Lowest Nonmemory Performance
All analyses	Healthy controls	Either no subjective memory complaint or No neuropsychological performance $z \leq -1.5$ SD		
Petersen criteria	aMCI	Yes	Lowest measure $z \leq -1.5$ SD	Any score possible
Winblad criteria	aMCI single domain	Yes	Lowest measure $z \leq -1.5$ SD	All measures $z > -1.5$ SD
	aMCI multiple domain	Yes	Lowest measure $z \leq -1.5$ SD	Lowest measure $z \leq -1.5$ SD
	naMCI single domain	Yes	All measures $z > -1.5$ SD	Lowest measure $z \leq -1.5$ SD in one domain, but all other domains $z > -1.5$ SD
	naMCI multiple domain	Yes	All measures $z > -1.5$ SD	At least two domains $z \leq -1.5$ SD
Amnestic severity	Grade 1	Yes	Lowest measure $z \leq -1.5$ SD, but $z \geq -2.29$ SD	
	Grade 2	Yes	Lowest measure $z < -2.29$ SD	

aMCI indicates amnestic mild cognitive impairment; MCI, mild cognitive impairment.

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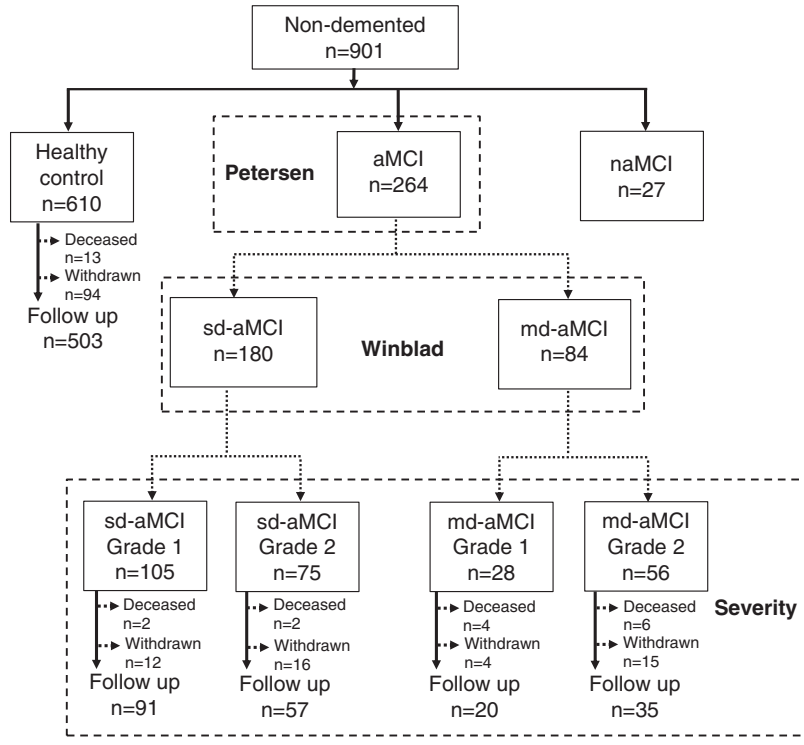

FIGURE 1. Stratification of subjects in subgroups for 3 levels of analysis with numbers at baseline, deceased or withdrawn at 3-year follow up and those successfully followed up at 3 years. md-aMCI indicates multiple domain amnestic mild cognitive impairment; sd-aMCI, single domain amnestic mild cognitive impairment.

according to whether their lowest memory performance was above or below this cut-off, respectively. Finally, the same cut-off (ie, $z = -2.29$) was used to stratify participants from the sd-aMCI or md-aMCI groups into grade 1 or grade 2 severity (see Fig. 1).

Analysis

Positive predictive values (PPV) were calculated for each group for comparison with each other for their predictive ability for AD dementia. Sensitivity was also calculated for each group. False negative cases were difficult to calculate because the Winblad taxonomy of MCI is not binary. For example, for analysis using the Winblad taxonomy, a participant classified as md-aMCI who developed AD dementia by 3 years would be considered as a false negative in the sd-aMCI group. Thus specificities, negative predictive values, odds ratios, likelihood ratios, and relative risks were not calculated. This method of analysis is ecologically valid because it is not clinically appropriate to apply a binary diagnosis to a patient presenting with undifferentiated cognitive impairment that is not dementia, that is, an individual with cognitive impairment that does not cause significant functional impairment. This method of analysis has previously been employed in a similar context.[17] Our data were analyzed using Stata (StataCorp; Stata/IC 14.2 for Mac). The usefulness and limitations of this analysis are considered in greater detail in the Discussion.

RESULTS

Totally 1166 participants were recruited. Fifty-four people were excluded because of comorbid illness and 211 were diagnosed with AD dementia, leaving 901 individuals who were not demented at baseline. Mean (SD) age was 70.9 (7.3) years (range, 59 to 96). At baseline, 530 of 901 (58.8%) participants expressed subjective memory complaint. It was a well-educated sample (12.3 ± 3.0 y) with intact general cognition on a global screening measure [mean Mini-Mental State Examination (MMSE), 28.3 ± 3.0]. A total of 725 (80.5%) participants was followed up by 36 months. Twenty-seven (3.0%) individuals were deceased at 3-year follow up. A total of 149 (16.5%) participants was lost to follow-up at 3 years; these participants were mean (SD)

TABLE 3. Baseline Characteristics of the Sample Grouped by Petersen Criteria

	Mean (SD)		
	Healthy Control	**aMCI**	***P***
n	621	245	NA
Age	70.1 (7.1)	72.7 (7.6)	<0.001*
Sex (male) [n (%)]	269 (43.3%)	99 (40.4%)	0.43†
Years of education, mean (SD)	12.6 (3.0)	11.5 (2.8)	0.002*
WTAR IQ, mean (SD)	109.0 (6.7)	106.2 (8.9)	<0.001*
MMSE, mean (SD)	28.8 (2.4)	27.4 (2.4)	<0.001*
HADS-D, mean (SD)	2.4 (2.2)	3.1 (2.4)	<0.001*
HADS-A, mean (SD)	4.3 (2.9)	4.7 (3.2)	0.11*
CDR SOB, mean (SD)	0.0 (0.2)	0.7 (0.9)	<0.001*

*Independent samples *t* test.
†χ^2.
aMCI indicates amnestic mild cognitive impairment; CDR SOB, clinical dementia rating scale sum of boxes; HADS-A and HADS-D, Hospital Anxiety and Depression Scale-anxiety and Hospital Anxiety and Depression Scale-depression subscale; MMSE, Mini-Mental State Examination; WTAR, Wechsler Test of Adult Reading.

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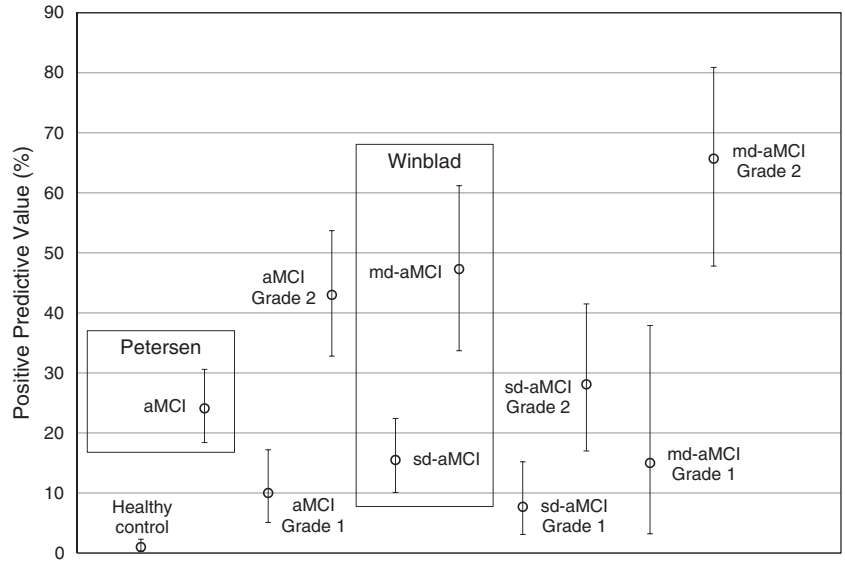

FIGURE 2. Positive predictive value (PPV; with 95% CI) of various definitions of MCI grouped according to Petersen (1999) criteria, Winblad (2004) criteria and severity of amnestic impairment. aMCI indicates amnestic mild cognitive impairment; CI, confidence interval; MCI, mild cognitive impairment; md-aMCI, multiple domain aMCI; sd-aMCI, single domain aMCI.

73.3 (8.1) years old and had a mean (SD) MMSE 27.6 (3.2) (Table 3).

Incident Dementia Because of AD

Fifty-four (7.4%) individuals were diagnosed with AD dementia by 3-year follow up. All aMCI groups were more likely than HCs to develop AD dementia during the study (see Fig. 2). There were only 27 participants classified as naMCI, none of whom was diagnosed with AD dementia at 36 months. Given the low number of participants in this group, they were not analyzed further. HCs were unlikely to develop AD dementia [PPV, 1.0; 95% confidence interval (CI), 0.3-2.3]. Subjects with aMCI were more likely to progress to AD dementia (PPV, 24.1; 95% CI, 18.4-30.6). When stratifying for severity of memory impairment within Petersen aMCI, individuals with grade 2 impairment had a higher rate of progression (PPV, 43.0; 95% CI, 32.8-53.7) than did individuals with grade 1 impairment (PPV, 10.0; 95% CI, 5.1-17.2).

When considering the Winblad taxonomy, subjects with md-aMCI were more likely (PPV, 47.3; 95% CI, 33.7-61.2) than sd-aMCI (PPV, 15.5; 95% CI, 10.1-22.4) to develop AD dementia. When stratifying for severity of memory impairment within sd-aMCI, individuals with grade 2 impairment had a higher rate of progression (PPV, 28.1; 95% CI, 17.0-41.5) than did individuals with grade 1 impairment (PPV, 7.7; 95% CI, 3.1-15.2). Similarly, within the md-aMCI group, individuals with grade 2 impairment also had a higher rate of progression (PPV, 65.7; 95% CI, 47.8-80.9) than did individuals with grade 1 impairment (PPV, 15.0; 95% CI, 3.2-37.9) (Table 4).

DISCUSSION

We have demonstrated that aMCI is associated with an increased risk of incident AD dementia during a 36-month follow up. Furthermore, impairment that extends to a nonmemory domain confers an increased risk of developing AD dementia. Finally, in aMCI increased severity of memory impairment is also associated with a greater risk of progressing to AD dementia.

In the present study, the progression rate for aMCI was 24.1% (95% CI, 18.4-30.6) over a period of 36 months. This corresponds approximately to an annual progression rate of 8.0% (95% CI, 6.1-10.2). This annual progression rate is slightly lower than previous reports of 10% to 15% for aMCI.[38] This may be because of the strict exclusion criteria of the present study based on previously described medical conditions including symptomatic cerebrovascular disease, uncontrolled diabetes, psychiatric illness, Parkinson disease, head injury, obstructive sleep apnea, or excessive alcohol use. Another possible reason for the slightly lower progression rate is the younger age of our cohort compared to other studies.[7,39] Despite our stringent exclusion criteria and younger cohort, participants with md-aMCI grade 2 had the highest rate of progression to AD dementia at 36 months (PPV, 65.7%; 95% CI, 47.8-80.9), which approximates to an annual progression rate of 21.9% (95% CI, 15.9-27.0).

Amnestic MCI participants with impairment of a second cognitive domain were more likely to progress to AD dementia than participants with impairment restricted to memory alone. This finding is consistent with some literature,[9–11,15,16,19] but is not universally demonstrated.[12,13,20] A possible reason for this discrepancy is that the latter studies employed nontraditional methods, using hierarchical cluster analyses to identify clusters of MCI participants with distinct cognitive profiles.[12]

Finally, participants with more severe memory impairment were more likely to develop AD dementia regardless of whether they had impairment of memory alone or impairment of an additional cognitive domain. This has important clinical implications for an individual presenting with MCI. If this finding is supported by further research, it could be incorporated into the diagnostic workup and counseling of MCI patients regarding their prognosis.

Taken together the current results indicate that MCI criteria could be expanded to include severity of amnestic impairment because this has important implications for prognosis and rate of progression to AD dementia.

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TABLE 4. Thirty-six–month Follow-up Characteristics of the Sample According to Subgroups of MCI

	Healthy Control	aMCI	aMCI Grade 1	aMCI Grade 2	sd-aMCI	md-aMCI	sd-aMCI Grade 1	sd-aMCI Grade 2	md-aMCI Grade 1	md-aMCI Grade 2
n at baseline	610	264	132	133	180	84	105	75	28	56
Deceased [n (%)]	13 (2.1)	14 (5.3)	6 (4.5)	8 (6.0)	4 (2.2)	10 (11.9)	2 (1.9)	2 (2.7)	4 (14.3)	6 (10.7)
Followed up [n (%)]	503 (82.5)	203 (76.9)	110 (83.3)	93 (69.9)	148 (82.2)	55 (65.5)	91 (86.7)	57 (76.0)	20 (71.4)	35 (62.5)
Incident AD dementia	5	49	11	40	23	26	7	16	3	23
False positive	498	154	99	53	125	29	84	41	17	12
True negative	85	693	591	637	565	661	606	649	673	678
False negative	49	5	43	14	31	28	47	38	51	31
Sensitivity [% (95% CI)]	9.3 (3.1-20.3)	90.7 (79.7 96.9)	20.4 (10.6-33.5)	74.1 (60.3-85.0)	42.6 (29.2-56.8)	48.1 (34.4-62.2)	13.0 (5.4-24.9)	29.6 (18.0-43.6)	5.6 (1.2-15.4)	42.6 (29.2-56.8)
PPV [% (95% CI)]	1.0 (0.3-2.3)	24.1 (18.4 30.6)	10.0 (5.1-17.2)	43.0 (32.8-53.7)	15.5 (10.1-22.4)	47.3 (33.7-61.2)	7.7 (3.1-15.2)	28.1 (17.0-41.5)	15.0 (3.2-37.9)	65.7 (47.8-80.9)
Annual progression rate [% (95% CI)]	0.3 (0.1-0.8)	8.0 (6.1-10.2)	3.3 (1.7-5.7)	14.3 (10.9-17.9	5.2 (3.4-7.5)	15.8 (11.2-20.4)	2.6 (1.0-5.1)	9.4 (5.7-13.8)	5.0 (1.1-12.6)	21.9 (15.9-27.0)

AD indicates Alzheimer's disease; aMCI, amnestic mild cognitive impairment; CI, confidence interval; MCI, mild cognitive impairment; md-aMCI, multiple domain aMCI; PPV, positive predictive value; sd-aMCI, single domain aMCI.

An individual with md-aMCI grade 2 impairment has an annual progression rate of 21.9% (95% CI, 15.9-27.0), whereas an individual with sd-aMCI grade 1 has a much lower annual progression rate 2.6% (95% CI, 1.0-5.1). A limitation to the present study is that it was a retrospective analysis of a prospective cohort study. As such, it may be subject to data-mining bias. To remedy this, an additional data set from an expansion cohort from the AIBL study will be examined to test the conclusions of this study when sufficient individuals have been followed for at least 3 years. Another potential limitation was the unstandardized administration of Logical Memory and the novel normative data that were generated for this study. The main results and conclusions were essentially unchanged when analyses were repeated using doubled raw scores for immediate and delayed recall of story 1 and compared with the Mayo's Older Americans Normative Studies (MOANS) normative data.[40] Finally, the use of PPV in the present study was used as a measure of rate of diagnostic progression. Given PPV is dependent on underlying prevalence in the sample, the rates of progression *per se* should be extrapolated with caution to samples with different prevalence of AD dementia, which was 7.4% in the present study.

CONCLUSIONS

MCI criteria could be expanded to include severity of amnestic impairment because this has important implications for prognosis and rate of progression to AD dementia. This is the first study to implement into a clinically useful heuristic the observation that severity of amnestic impairment in MCI may be used to stratify risk of progression to AD dementia.

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