Acta Psychiatrica Scandinavica

Acta Psychiatr Scand 2016: 133: 378–385

DOI: 10.1111/acps.12543

Conversion to dementia in mild cognitive impairment diagnosed with DSM-5 criteria and with Petersen's criteria

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Objective: In a background of revision of criteria for states of increased risk for progression to dementia, we compare the conversion rate to dementia and Alzheimer's disease (AD) of mild cognitive impairment (MCI) as diagnosed using DSM-5 (DSM-5-MCI) and Petersen's (P-MCI) criteria.
Method: A population representative cohort of 4057 dementia-free individuals 55+ years of age was followed up at 2.5 and 4.5 years in Zaragoza, Spain (ZARADEMP). Using the Geriatric Mental State-AGECAT for assessment, research psychiatrists diagnosed DSM-5-MCI and P-MCI following operationalized criteria. 'Conversion rate' (CR), 'annual conversion rate' (ACR), and incidence rate (IR) were calculated along with incidence rate ratio (IRR) to compare the performance of the intermediate cognitive definitions.
Results: At 4.5-year follow-up, in individuals aged 65+ years, ACRs for non-cases, P-MCI, and DSM-5-MCI were 0.8, 1.9 and 3.4, respectively, for global dementia. The IRRs were 2.9 and 5.3 for P-MCI and DSM5-MCI, respectively, being the non-cases the reference category. The corresponding values were slightly lower for AD.
Conclusion: Conversion rate to dementia and AD was higher using DSM-5-MCI criteria than using Petersen's criteria. However, prediction of the construct still has some way to go, as most MCI individuals did not convert at 4.5-year follow-up.

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Key words: mild cognitive impairment; Alzheimer's disease; conversion rate; community study; DSM-5

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Accepted for publication November 23, 2015

Significant outcomes

- 'Conversion rate' to dementia and Alzheimer's disease (AD), 'annual conversion rate' and incidence rate were all higher using DSM-5-MCI criteria than using Petersen's criteria.
- Compared with non-cases, the incidence rate ratio of dementia among individuals aged 65+ years was three times higher in the P-MCI cases, but more than five times higher in the DSM-5-MCI cases.
- At 4.5-year follow-up, ~15% DSM-5-MCI individuals and ~10% P-MCI individuals, developed dementia, the corresponding proportions for AD being ~10% and ~5% respectively.

Limitations

- Loss to follow-up in this study limits the generalizability of results.
- Only a limited proportion of cases of dementia and Alzheimer's disease (AD) identified in the community could complete a hospital diagnostic protocol.
- The lack, to date, of harmonization of the operational criteria used for mild cognitive impairment and different metrics used to document conversion to dementia and AD limit the comparability of results.

Introduction

Given current projected increases in the global incidence of dementia and Alzheimer's disease (AD) in the decades ahead, there is interest in identifying individuals with these conditions at the prodromal or preclinical stage to test whether a variety of potential interventions including novel pharmaceutical agents might alter natural history and also to understand how definitions of such 'pre' conditions perform in the variety of settings in which they might be used (1). Among the many different attempts to characterize syndromes of memory and cognitive deficits over the last 30 years leading to dementia, mild cognitive impairment (MCI) (2) has emerged as the most popular with researchers and has been widely adopted in clinical practice. However, the characterizations of states of mild cognitive disorders have been heterogeneous, and there has been a lack of specific, reliable, and validated operationalized criteria that have known and sufficiently good predictive performance (3). Moreover, the performance of any specific set of criteria will depend on subjects such as the diagnostic methods used, the structure of the population or whether it is a selective setting such as secondary or tertiary care settings, primary care, or community study. Wide differences in prevalence have, not surprisingly, been reported (1). In support of this, we have recently shown (4) that the prevalence of MCI in the general population according to the new DSM-5 criteria (DSM5-MCI) (5) is approximately half the number compared to the prevalence reported using the classical Petersen's criteria (P-MCI) of amnestic MCI (2).

Mild cognitive impairment is often considered to be a transitional state from cognitive changes associated with normal ageing to those typically found in dementia, particularly AD (6). However, due to factors such as the instability of the concept, length of follow-up, or loss to follow-up, wide variation in the so-called conversion rate (CR) to dementia has been reported (7, 8). Performance is better, as expected, from high prevalence settings with a range of 21% (9) to 60.9% (10) reported from clinical settings compared with community-based samples [range 5.2% (11) to 51.5% (12)].

Moreover, while most researchers report the CR to dementia over the period covered by their studies (13–15), others calculate an 'annual conversion rate' (ACR) (15–17). Incidence rate (IR) comparisons can be useful as this takes into consideration the amount of time each individual has been in the measured state (in this case, not an 'exposure') (18). This metric has only been reported in a few studies (7, 19, 20).

In view of the low rates of conversion to dementia observed in population-based studies (7), if MCI cases are to be sought as examples of prodromal dementia, then the MCI construct must perform much better than it does at present, with less variability in its predictive power as at present those people given such diagnoses are also burdened with uncertainty about its value (4). Over the last 5 years MCI criteria have undergone piecemeal and also extensive revision (21). For example, in the latest revision of the DSM (DSM-5) (5), MCI has been captured under the new term mild neurocognitive disorder (DSM5-MCI). Compared to classical definitions, such as P-MCI, this new definition is broad, implying a more severe symptom profile that allows for greater compromise in functional independence (4). These revisions bear striking resemblance to 'minimal dementia' used in much older instruments, such as the CAMDEX (22), and might bring some promise to better predicting onset of dementia. In this context, we need population studies to apply the new criteria and test their performance.

Aims of the study

The aim of this study was to compare conversion to dementia (and Alzheimer's disease) in cases of mild cognitive impairment defined using the new DSM-5 criteria and the classical Pestersen definition, using different statistical metrics, in a large

population-based study undertaken in Spain. Superiority of new over classical criteria in predicting conversion to dementia will have important implications for how we think about defining mild cognitive impairment in population-based settings.

Material and methods

Study design and sample

The ZARADEMP project (ZARAgoza DEMentia DEPression project) is a large longitudinal, community-based study designed to examine the incidence and risk factors of dementia (and depression). It was carried out in Zaragoza, a typical, large city in Spain incorporating both urban and rural areas, and the methods have been described in detail (23). In summary, a stratified random sample of individuals aged 55 years and older, with proportional allocation by age and sex, drawn from the eligible individuals from the Spanish official census lists were invited to participate in the baseline examination (Wave 1, starting in 1994). In total, 4803 people were interviewed in the baseline study. Individuals have completed two follow-up visits, the first starting in 1997 (Wave II, 2.5-year follow-up) and the second in 1999 (Wave III, 4.5-year follow-up). For the follow-up, because we were interested in dementia-free individuals, subjects considered to be cases or subcases of dementia at baseline were excluded (see definitions below; $n = 746$), for a starting sample of 4057 participants.

The Ethics Committee of the Instituto Aragonés de Ciencias de la Salud (IACS) and the Fondo de Investigación Sanitaria (FIS) approved this study, according to Spanish Law, and all individuals provided written informed consent.

Instruments

The ZARADEMP interview incorporates several international instruments, previously standardized in Spain by our research group. They include the Geriatric Mental State (GMS) (24)and its computerized diagnostic program, AGECAT (25, 26); the History and Aetiology Schedule (HAS) (27); the Mini-Mental Status Examination (MMSE) (28, 29); Lawton & Brody scale (30) and Katz' index (31) to assess instrumental and basic activities of daily living (ADL's) respectively.

Dementia assessment and diagnosis

Dementia was diagnosed using a two-phase screening design in the baseline study (Wave I) and follow-up waves (Waves II and III). In phase I of each wave, well-trained and regularly supervised lay interviewers (senior medical students) conducted the ZARADEMP interview at the participants' place of residence. Participants were classified as 'probable cases' of dementia based on the GMS threshold 'global' score (1/2) and/or MMSE standard cutoff points (23/24). In phase II, all probable cases of dementia were reassessed in their place of residence by a research psychiatrist using the same methods as well as Hachinski's scale (32) and a brief, previously standardized neurological examination. At the end of the baseline study, identified cases of dementia and subcases of dementia (GMS criteria) were excluded from the follow-up waves (II and III).

In the follow-up waves, incident dementia (including subtype) was initially diagnosed by the research psychiatrist doing the assessment, but the final DSM-IV diagnosis was made by consensus that required at least three psychiatrists in a four-member panel to be in agreement. Our previous studies have supported the validity of this diagnostic process (26). Moreover, to document the accuracy of the panel, a proportion of cases were invited for a hospital diagnostic work-up, and NINCDS-ADRDA criteria (33) were applied to diagnose AD. Agreement on the diagnosis of dementia and type of dementia was reached in 95.8% and 87.5% of the cases respectively.

MCI assessment and diagnosis

The process for the MCI assessment and diagnosis was as follows: First, blind to the results of the field work, a panel of research psychiatrists (and a psychologist) operationalized the relevant items in the ZARADEMP interview to comply with both Petersen et al. (2) and DSM-5 criteria (5) (see Table 1). Second, the research psychiatrists reviewed all the information from the ZARADEMP interview in Wave I and classified the individuals in the appropriate, operationalized categories of MCI 'cases' or 'non-cases'. Based on the DSM-5 criteria (5), individuals with psychosis and severe depression (defined as an AGECAT case symptom level of 3 or above, Stage II) were excluded from the DSM5-MCI construct. No exclusions were applied to Petersen et al. criteria (2).

Data analysis

Statistical analysis was performed using SPSS STATISTICS v.19 (IBM Corp. 2010, New York, NY, USA) for Windows. Statistical significance was set at

Table 1. Diagnostic criteria for mild cognitive impairment (MCI) used in the study

Petersen's criteria (2)	DSM-5 criteria (5)
(A) Subjective complaint of decline in memory on self- or informant report	(A.1) Concern of the individual, a knowledgeable informant, or the clinician that there has been a mild decline in cognitive function; and (A.2) A modest impairment in cognitive performance, documented by standardized cognitive assessment
(B) Isolated memory impairment on neuropsychological testing (below the standard threshold point)	(B) The cognitive deficits do not interfere with capacity for independence in everyday activities (as measured by ADL scales), but greater effort, compensatory strategies, or accommodation may be required
(C) Intact daily functioning in ADL scales	(C) The cognitive deficits do not occur exclusively in the context of a delirium
(D) Not meeting criteria for a diagnosis of dementia	(D) The cognitive deficits are not better explained by another mental disorder (specifically: psychosis and severe depression)

ADL, activities of daily living.

$P < 0.05$ and all tests were two-tailed. Pearson chi-square test and Student's *t*-test were used to compare demographic features between non-cases and MCI cases (P-MCI and DSM-5- MCI), for categorical and continuous (normally distributed) variables respectively. As the two MCI groups were not mutually exclusive, no statistical differences were calculated between them.

To facilitate comparison with previous studies in the literature, the 'CR' and the 'ACR' to dementia and AD were calculated using the approach by Mitchell et al. (15). The same nomenclature has been used quoted ('CR', and 'ACR'), as the coefficients are not rates *sensu stricto*.

For calculating CR and ACR in P-MCI, all P-MCI cases at baseline were included in the denominator, and the cases converting into dementia (and AD) in both the 2.5- and 4.5-year follow-up were included in the numerator. Identical procedure was followed for calculating conversion in DSM5-MCI and in the 'no-cases'. The overlap of the MCI cases was not considered in the calculations.

For calculating IR in P-MCI, sum of all P-MCI person-years was included in the denominator, and the cases converting into dementia (and AD) in 4.5 year follow-up were included in the numerator. Identical procedure was followed for calculating IR in DSM5-MCI and in the 'no-cases'. Person-years was calculated as the time from the date of first examination (Wave I) to: (i) the end of the follow-up examination (Wave III) for all non-demented individuals; (ii) the date of invitation for refusals; (iii) the date of moving away or death (based on actual data from the official registry in the City of Zaragoza); or, (iv) the time of onset of dementia for cases. The time of onset of dementia was estimated to be the time from the baseline interview to the midpoint between diagnosis and the previous examination. Finally, the incidence rate ratio (IRR) expressed as the ratio between the IR of each MCI group and the IR of 'non-cases' was also calculated.

Results

After excluding 746 prevalent cases or subcases of dementia at baseline, the analytical sample included 3641 dementia-free, non-MCI individuals (non-cases) and 416 MCI cases of which 303 were classified as P-MCI (2) and 139 were classified as DSM5-MCI (5), with an overlap between the two MCI groups. Table 2 shows the demographic

Table 2. Demographic characteristics of non-cases and individuals with MCI according to both Petersen's criteria (P-MCI) (2) and DSM-5 criteria (DSM5-MCI) (5)

	Non-cases $n = 3641$		P-MCI cases $n = 303$			DSM-5-MCI cases $n = 139$		
	N (%)	Mean (SD)	*N* (%)	Mean (SD)	*P*-value*	*N* (%)	Mean (SD)	*P*-value†
Women	1963 (53.9)		185 (61.1)		0.016	96 (69.1)		<0.001
Age (years)		71.7 (9.0)		73.3 (8.7)	0.003		80.7 (8.9)	<0.001
55–64	955 (26.2)		52 (17.2)		<0.001	7 (5.0)		<0.001
65–74	1434 (39.4)		123 (40.6)		0.724	32 (23.0)		<0.001
75+	1252 (34.4)		128 (42.2)		0.007	100 (72.0)		<0.001
Education (years)		7.6 (3.8)		6.5 (3.3)	<0.001		6.5 (3.2)	0.001
Illiterate	273 (7.6)		33 (10.9)		0.044	14 (10.1)		0.336
Primary school	2685 (74.4)		243 (80.5)		0.016	110 (79.1)		0.158
Secondary school or higher	651 (18.0)		26 (8.6)		<0.001	15 (10.8)		0.041

*Non-cases vs. MCI according to Petersen's criteria (P-MCI) (2).

†Non-cases vs. MCI according to DSM-5 criteria (DSM5-MCI) (5).

characteristics of the three groups. Compared to non-cases, individuals with MCI were significantly older and had a higher proportion of women. The proportion of individuals with low educational attainment was higher in both MCI categories, the differences with non-cases being statistically significant in P-MCI cases. While statistical comparisons between P-MCI and DSM5-MCI individuals are not appropriate, the latter were considerably older and the proportion of women, but not the proportion of the illiterate, was higher among them.

During follow-up, 462 (12.6%) non-cases, 29 (9.5%) P-MCI cases and 12 (8.6%) DSM5-MCI cases dropped out at 2.5-year follow-up and 739 (20.3%) non-cases, 65 (21.4%) P-MCI cases and 22 (15.8%) DSM5-MCI cases dropped out at 4.5-year follow-up. Compared with the non-cases, the differences did not reach statistical significance ($P = 0.136$ and $P = 0.198$, at 2.5 years, and $P = 0.685$ and $P = 0.237$ at 4.5 years respectively).

Moreover, 237 (6.5%) non-cases had died at 2.5-year follow-up and 641 (17.6%) at 4.5-year follow-up, the proportions being similar among P-MCI individuals ($n = 22$, 7.2%; and $n = 51$, 16.8% respectively). However, the proportions of individuals who died before the follow-up assessment were almost double among DSM5-MCI individuals ($n = 18$, 12.9%; and $n = 48$, 34.5% respectively) when compared with the non-cases, the differences being statistically significant ($P = 0.005$ and $P < 0.001$ respectively).

'Conversion rate' and 'annual conversion rate'

At 2.5-year follow-up, there was no conversion to dementia or AD in any of the subgroups of individuals aged 55–64 years of age. At 4.5-year follow-up, only five non-cases and one MCI-P case converted to dementia and two non-cases converted to AD in this age stratum. To draw comparisons with previous studies in the literature, we focus the results in the individuals aged 65+ years converting to dementia at each follow-up wave across the three study groups (Table 3). Compared to non-cases, the CR was significantly higher in the MCI-P and DSM5-MCI groups at both follow-up waves. At 2.5-year follow-up, conversion to dementia was observed in 52 (1.9%) non-cases, 13 (5.2%) P-MCI cases, and 14 (10.6%) DSM5-MCI cases, the corresponding numbers and proportions at 4.5-year follow-up being 93 (3.4%), 24 (8.7%), and 20 (15.1%) in each group respectively. Similar results were observed when the outcome was restricted to AD: higher CRs in cases vs. non-cases and in the DSM5- MCI group overall (see Table 3).

Table 3. Conversion rate (CR) to overall dementia and AD in individuals aged 65+ years with MCI diagnosed according to both Petersen's criteria (P-MCI) (2) and DSM-5 criteria (DSM5-MCI) (5) and in non-cases

		Z-II (2.5-years follow-up)					Z-III (4.5-year follow-up)				
65+ years	*n*	Incident dementia cases	CR to dementia*	ACR to dementia†	Incident AD cases	CR to AD*	ACR to AD†	Incident dementia cases	CR to dementia*	ACR to dementia†	Incident AD cases	CR to AD*	ACR to AD†
Non-cases	2686	52	1.9 (1.4–2.4)	0.8	33	1.2 (0.8–1.6)	0.5	93	3.4 (2.7–4.1)	0.8	60	2.2 (1.6–2.8)	0.5
P-MCI cases	251	13	5.2 (2.4–7.9)	2.1	7	2.8 (0.7–4.8)	1.1	24	8.7 (5.3–12.3)	1.9	14	5.6 (2.7–8.4)	1.2
DSM-5-MCI cases	132	14	10.6 (5.3–15.8)	4.2	8	6.1 (2.0–10.1)	2.4	20	15.1 (9.0–21.3)	3.4	13	9.8 (4.7–14.9)	2.2

ACR, annual conversion rate; AD, Alzheimer's disease.
*Expressed as % (95% CI).
†Expressed as %.

The ACRs to dementia in the three study groups are also shown in Table 3. As shown, the results are similar to those observed when comparing the CR to dementia: higher ACRs (all-cause dementia and AD) in the MCI-P and DSM5-MCI groups compared to non- cases and in the DSM5-MCI group overall.

Incidence rate

Incidence rates for both MCI groups of individuals aged 65+ years were significantly higher than for those not meeting these criteria, the IR being almost three times higher (IRR = 2.9) in the MCI-P cases and more than five times higher in the DSM5- MCI cases (IRR = 5.3) (see Table 4). The same pattern was observed in relation to AD.

Discussion

Main results

In line with previous reports (8), in persons aged 65+ years, MCI, operationalized using either the classical Petersen definition or new DSM-5 criteria, was found to be associated with increased CR to dementia (and AD), regardless of the analytical approach used. Further, in comparison with non-MCI individuals, the CR, ACR, and IR were all higher at 2.5 and 4.5 years of follow-up when using the new DSM5-MCI construct, than using the classical P-MCI construct. Moreover, a continued progression to dementia was also observed with an increase in follow-up time. Based on CR at 4.5 years of follow-up, more DSM5-MCI (~15%) than P-MCI individuals (~10%) developed dementia, the corresponding proportions for AD being ~10% and ~5% respectively. Further, the ACR to dementia (and AD) for DSM5-MCI cases was also approximately double that of P-MCI cases. Similar results were observed when the sample was broadened to persons aged 55+ years.

Methods

One strength of the study relates to the sample, which is large, representative of a typical city population in Spain, and includes institutionalized individuals. It has been suggested that studies of elderly populations with cognitive impairment may be challenged by an increasingly high loss to follow-up over time (7). However, the proportion of drop-outs in this study was not high (range 12–16%), and no between-group significant differences were observed. Most researchers report the CR to dementia over the period covered by their studies (13–15), and others calculate the ACR (15–17). We report both analytical approaches, with the additional advantage of calculating the IR, which takes into account the amount of time each individual has been in the measured state (18).

A potential limitation in this study relates to the diagnostic process in the community. While this process has previously been reported to be valid (26), only a limited proportion of cases of dementia identified could complete a hospital diagnostic protocol. However, we expect this does not affect in an important way the main results in the study, as the agreement between the panel and hospital diagnosis was quite substantial. The diagnosis of MCI by the panel of research psychiatrist was careful, all the items used for the diagnosis come from reliable and valid instruments, and the diagnostic criteria were previously operationalized. However, the MCI categories used may merit more careful validity studies before the results are generalizable, as suggested by the instability of the MCI concept itself.

Interpretation

To some extent, the results of an increased probability of developing dementia in individuals who fulfill DSM5-MCI criteria might be expected, in view that signs and symptoms of this construct may be more severe than those captured in the P-MCI definition, which was developed with a

Table 4. Incidence rate (IR) to overall dementia and Alzheimer's disease in individuals aged 65+ years with MCI diagnosed according to both Petersen's criteria (P-MCI) (2) and DSM-5 criteria (DSM5-MCI) (5) and in non-cases

			Overall dementia				Alzheimer's disease			
65+ years	*n*	Person-years	Incident cases	IR (95% CI)	IRR (95% CI)	*P**	Incident cases	IR (95% CI)	IRR (95% CI)	*P**
Non-cases	2686	10 451	93	8.9 (7.3–10.9)			60	5.7 (4.5–7.4)		
P-MCI cases	251	938	24	25.6 (17.1–38.2)	2.9 (1.8–4.5)	<0.001	14	14.9 (8.8–25.2)	2.6 (1.4–4.6)	0.001
DSM-5-MCI cases	132	423	20	47.3 (30.5–73.3)	5.3 (3.3–8.6)	<0.001	13	30.7 (17.8–52.9)	5.3 (2.9–9.7)	<0.001

IRR, incidence rate ratio.

**P*-values related to IRR were from the *z*-test.

different philosophical approach (34). The use of a more restricted set of criteria such as the DSM5-MCI may have special value for the individual (restricted but high performance good), but the higher predictive value may come at only the cost of decreased sensitivity. As a result, the restricted criteria would be not so useful for the population because it would not identify some of the total incident cases in the same population over time.

It might also be argued that the higher conversion in DSM5-MCI cases was mainly a consequence of aging, as DSM5-MCI cases were older. However, a secondary analysis suggests that this is not the only reason for the differences found. While the CRs to dementia were higher on the 'older old' individuals (75+ years) when compared with the 'younger old' (<75 years), the CRs in both age subgroups were higher in the DSM5-MCI cases than in the P-MCI cases. Among the 'older old', 18 (18%) DSM5-MCI cases and 19 (15%) P-MCI cases converted to dementia at 4.5-year follow-up, the corresponding numbers in non-cases being 80 (6%). Among the individuals aged <75 the corresponding numbers were 2 (5%), 6 (3%) and 18 (0.7%). Even more interest may have the comparison of IRs. The IRRs to dementia at 4.5-year follow-up were 3.3 times higher in DSM5-MCI and 2.4 times higher in the P-MCI among the 'older old' individuals, the corresponding values in the 'younger old' individuals being 7.3 and 4.5 respectively. These results are consistent with some previous reviews (7, 35).

Comparison with previous studies

Our finding of the continued progression to dementia with the increase in follow-up time contradicts a study that suggests that the CR is particularly high early in the follow-up period (36), but is consistent with the conclusions of a more recent systematic review (7). In view of diverse follow-up periods in previous studies, we focus on comparisons of IRs in the P-MCI cases, as we have not found similar population studies related to DSM5-MCI. At 4.5-year follow-up, the IR of dementia in our study was 25.6, and the IR of AD was 14.9. Higher rates of IR have been observed in studies such as the one by Solfrizzi et al. (19) (38 and 23, respectively) or Ishikawa, 2006 (20) (161 and 85 respectively). In Ward et al.'s systematic review (7) the IRs of AD (43–115) were also considerably higher than in Zaragoza. Our results may be consistent with a previous study suggesting that the incidence of dementia in Zaragoza was lower than in most studies in Europe and the USA (23).

Implications of the findings

While in this study the proportion of MCI cases progressing to dementia was higher using the DSM5-MCI criteria, than using more classical P-MCI criteria, only ~15% of individuals with DSM5-MCI developed dementia over the 4.5-year follow-up. Nonetheless, the improved predictive power of the DSM5-MCI criteria may come at only the cost of decreased sensitivity. It might be argued that some individuals with dementia die before the follow-up assessment. Yet, more than half the DSM5-MCI cases (n = 78, 56.1%) were alive and non-demented 4.5 years after the baseline assessment. Even in a clinical setting, in primary care, using diagnostic criteria 'very similar to the mild neurocognitive disorder in the DSM-5' the German AgeCoDe study found that only one-quarter of patients with MCI have progression to dementia within the next 3 years (37). Therefore, these results suggest that there is still some way to go for recommending the MCI concept for wider use in population-based settings. It may be unlikely that methods based solely on clinical psychopathology will separate those individuals with MCI susceptible to developing dementia and AD from those who are not.

In conclusion, this study shows that using more stringent DSM5-MCI criteria (5) is associated with an increased rate of conversion to dementia and AD, regardless of how progression to dementia is measured, when compared with the more classical P-MCI criteria (2). Still, most MCI individuals do not develop dementia, and both clinicians and health administrators should be cautious when transferring the concept of MCI into population-based settings as this might create unnecessary concern (37). Incorporation of genetic and biomarker assessments in future studies, in addition to the clinical assessment of MCI, may lend added clarity in the crucial search of early identifiers of individuals at risk of dementia and AD.

References

1. Ganguli M, Chang CC, Snitz BE, Saxton JA, Vanderbilt J, Lee CW. Prevalence of mild cognitive impairment by multiple classifications: the Monongahela-Youghiogheny Healthy Aging Team (MYHAT) project. Am J Geriatr Psychiatry 2010;**18**:674–683.
2. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999;**56**:303–308.
3. Matthews FE, Stephan BC, Bond J, McKeith I, Brayne C, Medical Research Council Cognitive Function and Ageing Study. Operationalization of mild cognitive impairment: a graphical approach. PLoS Med 2007;**4**:1615–1619.

4. Lopez-Anton R, Santabarbara J, De-La-Camara C et al. Mild cognitive impairment diagnosed with the new DSM-5 criteria: prevalence and associations with non-cognitive psychopathology. Acta Psychiatr Scand 2015;**131**:29–39.
5. American Psychiatric Association. DSM-5: diagnostic and statistical manual of mental disorders, 5th edn. Washington, DC: American Psychiatric Publishing, 2013.
6. Petersen RC, Caracciolo B, Brayne C, Gauthier S, Jelic V, Fratiglioni L. Mild cognitive impairment: a concept in evolution. J Intern Med 2014;**275**:214–228.
7. Ward A, Tardiff S, Dye C, Arrighi HM. Rate of conversion from prodromal Alzheimer's disease to Alzheimer's dementia: a systematic review of the literature. Dement Geriatr Cogn Dis Extra 2013;**3**:320–332.
8. Ganguli M, Snitz BE, Saxton JA et al. Outcomes of mild cognitive impairment by definition: a population study. Arch Neurol 2011;**68**:761–767.
9. Gabryelewicz T, Styczynska M, Luczywek E et al. The rate of conversion of mild cognitive impairment to dementia: predictive role of depression. Int J Geriatr Psychiatry 2007;**22**:563–567.
10. Yaffe K, Petersen RC, Lindquist K, Kramer J, Miller B. Subtype of mild cognitive impairment and progression to dementia and death. Dement Geriatr Cogn Disord 2006;**22**:312–319.
11. Di Carlo A, Lamassa M, Baldereschi M et al. CIND and MCI in the Italian elderly: frequency, vascular risk factors, progression to dementia. Neurology 2007;**68**:1909–1916.
12. Lopez OL, Kuller LH, Becker JT et al. Incidence of dementia in mild cognitive impairment in the cardiovascular health study cognition study. Arch Neurol 2007;**64**:416–420.
13. Bennett DA, Wilson RS, Schneider JA et al. Natural history of mild cognitive impairment in older persons. Neurology 2002;**59**:198–205.
14. Saxton J, Snitz BE, Lopez OL et al. Functional and cognitive criteria produce different rates of mild cognitive impairment and conversion to dementia. J Neurol Neurosurg Psychiatry 2009;**80**:737–743.
15. Mitchell AJ, Shiri-Feshki M. Rate of progression of mild cognitive impairment to dementia– meta-analysis of 41 robust inception cohort studies. Acta Psychiatr Scand 2009;**119**:252–265.
16. Wong CH, Leung GT, Fung AW, Chan WC, Lam LC. Cognitive predictors for five-year conversion to dementia in community-dwelling Chinese older adults. Int Psychogeriatr 2013;**25**:1125–1134.
17. Gao S, Unverzagt FW, Hall KS et al. Mild cognitive impairment, incidence, progression, and reversion: findings from a community-based cohort of elderly African Americans. Am J Geriatr Psychiatry 2014;**22**:670–681.
18. Rothman KJ, Greenland S, Lash TL. Modern epidemiology, 3rd edn. Philadelphia, PA: Lippincott, Williams & Wilkins, 2008.
19. Solfrizzi V, Panza F, Colacicco AM et al. Vascular risk factors, incidence of MCI, and rates of progression to dementia. Neurology 2004;**63**:1882–1891.
20. Ishikawa T, Ikeda M, Matsumoto N, Shigenobu K, Brayne C, Tanabe H. A longitudinal study regarding conversion from mild memory impairment to dementia in a Japanese community. Int J Geriatr Psychiatry 2006;**21**:134–139.
21. Stephan BC, Brayne C. Risk factors and screening methods for detecting dementia: a narrative review. J Alzheimers Dis 2014;**42**(Suppl. 4):S329–S338.
22. Roth M, Tym E, Mountjoy CQ et al. CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. Br J Psychiatry 1986;**149**:698–709.
23. Lobo A, Lopez-Anton R, Santabarbara J et al. Incidence and lifetime risk of dementia and Alzheimer's disease in a Southern European population. Acta Psychiatr Scand 2011;**124**:372–383.
24. Copeland JR, Dewey ME, Griffiths-Jones HM. A computerized psychiatric diagnostic system and case nomenclature for elderly subjects: GMS and AGECAT. Psychol Med 1986;**16**:89–99.
25. Copeland JR, Dewey ME, Wood N, Searle R, Davidson IA, McWilliam C. Range of mental illness among the elderly in the community. Prevalence in Liverpool using the GMS-AGECAT package. Br J Psychiatry 1987;**150**:815–823.
26. Lobo A, Saz P, Marcos G, Dia JL, De-La-Camara C. The prevalence of dementia and depression in the elderly community in a southern European population. The Zaragoza study. Arch Gen Psychiatry 1995;**52**:497–506.
27. Dewey ME, Copeland JR. Diagnosis of dementia from the history and aetiology schedule. Int J Geriatr Psychiatry 2001;**16**:912–917.
28. Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;**12**:189–198.
29. Lobo A, Saz P, Marcos G et al. Revalidation and standardization of the cognition mini-exam (first Spanish version of the Mini-Mental Status Examination) in the general geriatric population. Med Clin (Barc) 1999;**112**:767–774.
30. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;**9**:179–186.
31. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. JAMA 1963;**185**:914–919.
32. Hachinski VC, Lassen NA, Marshall J. Multi-infarct dementia. A cause of mental deterioration in the elderly. Lancet 1974;**2**:207–210.
33. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology 1984;**34**:939–944.
34. Sachdev PS, Blacker D, Blazer DG et al. Classifying neurocognitive disorders: the DSM-5 approach. Nat Rev Neurol 2014;**10**:634–642.
35. Bruscoli M, Lovestone S. Is MCI really just early dementia? A systematic review of conversion studies. Int Psychogeriatr 2004;**16**:129–140.
36. Mitchell AJ, Shiri-Feshki M. Temporal trends in the long term risk of progression of mild cognitive impairment: a pooled analysis. J Neurol Neurosurg Psychiatry 2008;**79**:1386–1391.
37. Kaduszkiewicz H, Eisele M, Wiese B et al. Prognosis of mild cognitive impairment in general practice: results of the German AgeCoDe study. Ann Fam Med 2014;**12**:158–165.