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Prevalence and Risk of Mild Cognitive Impairment in Low and Middle-Income Countries: A Systematic Review

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Abstract.
Background: Mild cognitive impairment (MCI) is a cognitive state associated with increased risk of dementia. Little research on MCI exists from low-and middle-income countries (LMICs), despite high prevalence of dementia in these settings.
Objective: This systematic review aimed to review epidemiological reports to determine the prevalence of MCI and its associated risk factors in LMICs.
Methods: Medline, Embase, and PsycINFO were searched from inception until November 2019. Eligible articles reported on MCI in population or community-based studies from LMICs and were included as long as MCI was clearly defined.
Results: 5,568 articles were screened, and 78 retained. In total, $n = 23$ different LMICs were represented; mostly from China ($n = 55$ studies). Few studies were from countries defined as lower-middle income ($n = 14$), low income ($n = 4$), or from population representative samples ($n = 4$). There was large heterogeneity in how MCI was diagnosed; with Petersen criteria the most commonly applied ($n = 26$). Prevalence of amnesic MCI (aMCI) (Petersen criteria) ranged from 0.6% to 22.3%. Similar variability existed across studies using the International Working Group Criteria for aMCI (range 4.5% to 18.3%) and all-MCI (range 6.1% to 30.4%). Risk of MCI was associated with demographic (e.g., age), health (e.g., cardio-metabolic disease), and lifestyle (e.g., social isolation, smoking, diet and physical activity) factors.
Conclusion: Outside of China, few MCI studies have been conducted in LMIC settings. There is an urgent need for population representative epidemiological studies to determine MCI prevalence in LMICs. MCI diagnostic methodology also needs to be standardized. This will allow for cross-study comparison and future resource planning.

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INTRODUCTION

Mild cognitive impairment (MCI) defines an intermediate state of cognitive function between normal aging and dementia. Numerous definitions for MCI exist and prevalence estimates vary (range <1% up to 56% across different studies and definitions) depending on population sampling (age, clinical versus population), MCI case definition, and operationalization of the component criterion for an MCI case diagnosis [1–7]. However, the majority of MCI research has been undertaken in high-income countries (HICs), namely North America, Europe, and Australia. This raising questions of generalizability of findings to low-and middle-income countries (LMIC) which vary by wealth, culture, ethnicity, research capacity, and infrastructure to support aging populations.

Studies examining MCI prevalence in LMICs have produced conflicting results. For example, the 10/66 study reported a range of estimates (0.8 to 4.3%) of Petersen defined amnestic MCI (aMCI) [8] across sites in Cuba, the Dominican Republic, Peru, Venezuela, Mexico, China, India, and Puerto Rico [9]. Findings from the World Health Organization's Study on Global Ageing and Adult Health reported an overall MCI prevalence of 15.3% (95%CI: 14.4–16.3) when applying the National Institute of Ageing-Alzheimer's Association (NIA-AA) criteria [10] across sites in China, Ghana, India, Mexico, Russia, and South-Africa [11]; with the individual country prevalence estimates lower (e.g., 8.5% in South Africa [12]). It is not clear what is driving the differences. Within studies, the differences likely reflect variability in the profile of risk and protective factors across sites as well as cultural/ethnic perceptions of cognitive aging and symptom reporting. Across studies, differences are likely due to heterogeneity in methodology, e.g., differences in sample selection and the MCI criteria used for diagnosis.

While some have suggested that MCI as a mode of prodromal classification can have a limited role in clinical and epidemiological settings, others argue that MCI could be a pragmatic tool for identifying individuals who could benefit from risk reduction [13]. There is promising evidence to support dementia risk reduction interventions in HICs [14], with indications of similar opportunities in LMICs [15]. Determining how best to identify individuals with MCI and the prevalence of the condition in LMICs will have important implications for planning intervention trials, treatment strategies, budgeting and public health surveillance. While several reviews on MCI have been conducted [1–7], to our knowledge none have focused specifically on LMIC settings. Therefore, the aim of this systematic review was to report on the population prevalence and risk factors for MCI in these settings.

MATERIALS AND METHODS

This review adhered to standard reporting guidelines [16] and full details of the MOOSE checklist [17] are provided as part of the Supplementary Material. The review protocol can be made available by a member of the research team upon request.

Search strategy

Medline, Embase, and PsycINFO were searched from inception to the 10 January 2018, with updated searches run from 10 January 2018–6 November 2018 and from 6 November 2018–30 November 2019 (CR; See Supplementary Table 1 for the list of search terms).

Inclusion/exclusion criteria

Studies were included if: 1) the sample was from a LMIC at the time of the study, as defined by The World Bank [18]; 2) the study reported population-level or community-based data; and, both cross-sectional and cohort study designs were included; 3) the study described how MCI had been mapped; 4) sample age was $\geq$50 years; and 5) MCI prevalence was reported. No restrictions were placed on the definition of MCI used (as long as it was clearly defined), language or publication date. Randomized controlled trials, case-control studies, unpublished studies, and conference abstracts were excluded. Studies were also excluded if, for analysis, cognitive groups (e.g., dementia and MCI groups) were combined or the sample restricted (e.g., studies investigating MCI in disease specific groups such as diabetics or in illiterate participants only). Reviews were also retained and the reference lists of these interrogated for any missed paper.

Data analysis

Titles/abstracts were first screened, followed by the full text of any identified articles (CR and CVA). Where multiple publications using the same study were identified, these were retained for full text review and kept if they presented original findings. Disagreements were resolved by consensus or a third party (BCMS). Data including study characteristics, operationalization of MCI criteria, MCI prevalence estimates and risk factors for MCI were independently extracted by four investigators (AMG [Chinese Studies], AS, BCMS, and CVA).

Study quality (bias) was assessed using the tool developed by Hoy et al. [19]. Nine items were selected related to representativeness of the study sample, methods for case definition, and the statistical calculation of MCI prevalence. Each risk of bias item was scored '0' (low risk) or '1' (high risk) of bias (total score range: 0 to 9).

Forest plots of the population prevalence estimates of MCI, defined using the most commonly applied criteria across the studies were created using Prism-GraphPad 8 for Windows (GraphPad Software, San Diego, USA). This included plots for MCI defined using Petersen criteria (including all-MCI and aMCI; $n = 26$ studies [9, 20–44]), International Working Group (IWG) criteria ($n = 14$ studies [45–58]), or study specific criteria for Cognitive Impairment no Dementia (CIND; $n = 10$ studies [59–68]). A meta-analysis was not possible due to large heterogeneity in methodology across the studies and the lack of key statistical information (i.e., confidence intervals for the MCI prevalence estimates) in most studies.

Role of the funding source

The review was completed as part of the NIHR Global Health Group: DePEC (Grant number: 16/137/62). AMG and BCMS have full access to the data and final responsibility to submit for publication.

RESULTS

Search yields

The electronic search identified $n = 4{,}548$ studies, with duplicates removed (Fig. 1). Following title/abstract screening, 162 studies were selected for full text review. This included a systemic review on MCI prevalence in China [7], where an additional $n = 48$ studies in Mandarin were identified. From these, 73 studies were selected for inclusion. An updated electronic search in November 2019 yielded 972 studies, and an additional five were included (total $n = 78$ studies). Two studies [66, 67] used the same dataset, but these were retained as they provided MCI prevalence estimates for different age groups.

Study characteristics

Table 1 shows the characteristics of each study. Sample size ranged from $n = 120$ [69] to $n = 32{,}715$ [11]. Most studies included participants aged $\geq$60 years ($n = 46$ studies [22, 25–30, 32, 35–42, 47, 52–56, 58, 60, 61, 65, 67, 68, 70–87]) or $\geq$65 years ($n = 16$ studies [9, 23, 33, 44, 46, 48, 50, 51, 57, 62–64, 69, 88–90]). The remaining studies included participants aged $\geq$50 years ($n = 6$ studies [11, 21, 59, 91–93]), $\geq$55 years ($n = 7$ studies [24, 31, 34, 43, 94–96]), $\geq$70 years ($n = 1$ study [49]), and $\geq$80 years ($n = 2$ studies [20, 66]). One study [92] included only women.

As shown in Table 1, four studies [9, 11, 50, 64] analyzed MCI prevalence for multiple countries. The majority of studies have been conducted in China ($n = 55$ studies [9, 11, 20, 24, 26–45, 48, 51, 52, 54, 56–58, 62, 66–68, 72–84, 86, 87, 89, 90, 94–96]), followed by India ($n = 6$ studies [9, 11, 25, 85, 91, 92]), Mexico ($n = 4$ studies [9, 11, 22, 65]), Brazil ($n = 2$ studies [59, 60]), Malaysia ($n = 2$ studies [47, 53]), the Philippines ($n = 2$ studies [61, 69]), Central African Republic ($n = 2$ studies [50, 64]), South Africa ($n = 2$ studies [11, 93]), Republic of Congo ($n = 2$ studies [50, 64]), and one each in Colombia [21], Nigeria [23], Cuba [9], Dominican Republic [9], Peru [9], Venezuela [9], Georgia [46], Kazakhstan [55], Tanzania [49], Bulgaria [88], Ghana [11], Russia [11], Egypt [70], and Benin West-Africa [63]. Therefore, most studies ($n = 67$ studies [9, 11, 20–22, 24, 26–45, 47, 48, 51–60, 62, 65–68, 71–84, 86–90, 94–96]) were from sites in upper middle-income countries, 14 studies [9, 11, 23, 25, 46, 50, 55, 61, 64, 70, 85, 91–93] were from sites in lower middle-income countries, and four studies [49, 50, 63, 64] were from sites in low-income countries. One study [9] included data collected during 2003–2007 from eight sites, one of which was Puerto Rico. This country was declared high-income by the World Bank in 2002. Therefore, the prevalence data for Puerto Rico has been excluded. Only four studies [11, 44, 65, 93] selected participants from a representative country-wide sample. The remaining studies included a sample of community residents

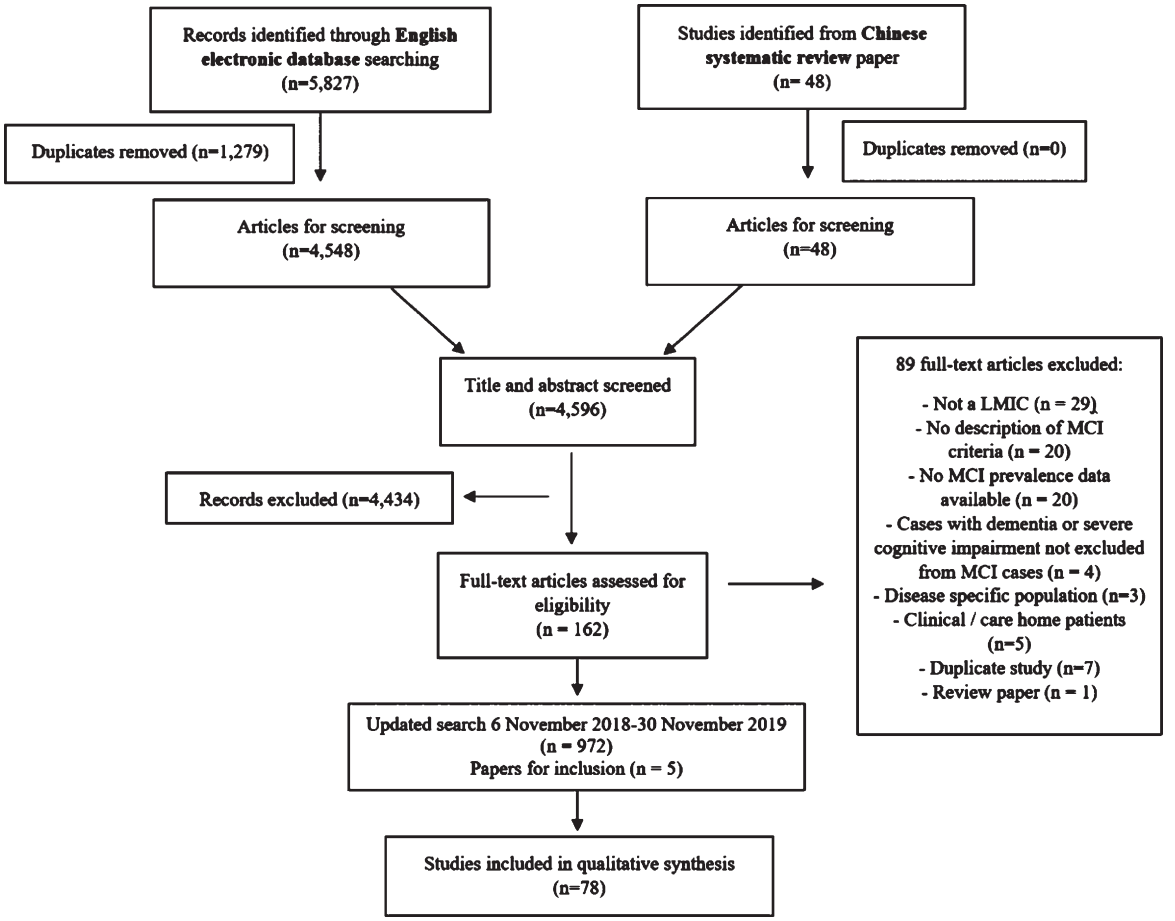

Fig. 1. Study selection.

from a specific region, city or district(s).

Quality assessment

The detailed quality assessment is reported in Supplementary Table 2. Two studies [44, 93] obtained a low risk of bias score across all nine domains assessed, with the majority of studies ($n = 66$ studies) only having high risk scores in 1–3 domains [9, 11, 21–43, 46, 48–51, 53–57, 60, 61, 63, 65–68, 70–73, 75–78, 80–86, 88–91, 94–96]. These were mostly related to a lack of, or unclear use of, randomization procedures and that the study sample was unlikely to be representative of the national population.

MCI criteria

A shown in Table 1, numerous criteria were used to diagnose MCI including: 1) Petersen's criteria [8, 97–102] ($n = 26$ studies [9, 20–44]); 2) IWG criteria [103] ($n = 14$ studies [45–58]); 3) study specific criteria for CIND ($n = 10$ studies [59–68]); 4) study specific criteria for MCI ($n = 13$ studies [30, 70, 74–76, 79, 80, 84, 86, 89, 91, 94, 95]); 5) Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) criteria [104] ($n = 8$ studies [72, 77, 78, 81–83, 90, 96]); 6) MCI based on a score from a neuropsychological assessment tool ($n = 3$ studies [69, 87, 92]); 7) NIA-AA criteria [10] ($n = 2$ studies [11, 93]); or 8) the European Consortium on Alzheimer's Disease criteria [105] ($n = 2$ studies [85, 88]). A full description of the different MCI criteria applied across the studies is in Supplementary Tables 3 and 4.

Operationalizing MCI criteria

Full details of how MCI criteria were operationalized (and any modifications that were made to mapping the original diagnostic criteria) are detailed

Table 1
Study characteristics and MCI prevalence arranged by definition (ordered by age [lowest to highest])

Author	Location	Income Class	Age (y)	Summary population characteristics	Mild cognitive impairment (MCI)			
					MCI definition	Total sample size	Cases	Prevalence % (95% CI)
MCI ACCORDING TO PETERSEN CRITERIA [8, 99, 101, 102] (*n* = 26 studies)								
Henao-Arboleda, 2008 [21]	Columbia	UMIC	≥50	Residents of metropolitan area of Medellin	aMCI	848	82	9.7 (7.6–11.7)
Lao, 2011 [31]	China	UMIC	≥55	Non-demented residents of Hainan province	MCI	7,665	326	4.25 (3.80–4.68)
Li, 2013 [43]	China	UMIC	≥55	Non-demented residents of Beijing with an MMSE ≥24 (The Beijing Ageing Brain Rejuvenation Initiative: BABRI)	All MCI	1,020	160	15.7
					aMCI-SD	1,020	65	6.4
					aMCI-MD	1,020	38	3.7
					naMCI	1,020	57	5.6
Qin, 2014 [34]	China	UMIC	≥55	Non-demented residents of Shanghai	aMCI	4,086	612	14.98 (13.88–16.02)
Qiu, 2003 [24]	China	UMIC	≥55	Non-demented residents of Chengdu	aMCI	3,910	92	2.40 (1.88–2.80)
Gao, 2011 [29]	China	UMIC	≥60	Non-demented residents of a community of Suzhou	aMCI	1,773	243	13.71 (12.1–15.22)
Huang, 2008 [73]	China	UMIC	≥60	Non-demented residents of Guangzhou	aMCI	4,697	257	5.47(4.82–6.09)
Juarez-Cedillo, 2013 [22]	Mexico	UMIC	≥60	Residents, registered with family medicine units (IMSS), of Mexico City	All MCI	2,944	190	6.5 (5.6 – 7.4)
					aMCI-SD	2,944	71	2.4 (1.9 – 3.0)
					aMCI-MD	2,944	75	2.6 (2.0 – 3.1)
					naMCI-SD	2,944	35	1.2 (0.8 – 1.6)
					naMCI-MD	2,944	9	0.3 (0.1 – 0.5)
Liao, 2012 [32]	China	UMIC	≥60	Non-demented residents of Yichun	aMCI	399	41	10.28 (7.30–13.10)
Pan, 2012 [28]	China	UMIC	≥60	Non-demented residents of Jinhua	aMCI	897	154	17.17 (14.7–19.51)
Song, 2012 [35]	China	UMIC	≥60	Non-demented residents of a district of Foshan	aMCI	2,279	167	7.33 (6.26–8.34)
Su, 2013 [36]	China	UMIC	≥60	Non-demented residents of Xian	aMCI	796	145	18.22 (15.53–20.76)
Tang, 2007 [37]	China	UMIC	≥60	Non-demented residents of Beijing	aMCI	1,865	217	11.60 (10.18–13.02)
Tiwari, 2013 [25]	India	LMIC	≥60	Residents of Malihabad and Bakshi Ka Talab of Lucknow district of the State of Uttar Pradesh	All MCI	2,146	98	4.6 (3.7 – 5.5)
Tong, 2013 [38]	China	UMIC	≥60	Non-demented residents of Tangshan	aMCI	1,575	200	12.7
Wang, 2012 [42]	China	UMIC	≥60	Non-demented residents of Tianjin	aMCI	3,678	408	11.1
Wang, 2017 [26]	China	UMIC	≥60	Residents of rural and urban areas in Shanghai	aMCI	1,005	224	22.3
Xu, 2014 [27]	China	UMIC	≥60	Non-demented residents of the Hebei province	All MCI	2,426	526	21.3 (19.2–23.1)‡
Yin, 2011 [39]	China	UMIC	≥60	Non-demented residents of Huzhou	aMCI	2,164	310	14.33 (12.85–15.73)
Zhang, 2011 [41]	China	UMIC	≥60	Non-demented residents of Suzhou	aMCI	5,388	691	12.8
Zhu and Li, 2015 [40]	China	UMIC	≥60	Non-demented residents of some communities of Xinyang	aMCI	1,755	245	13.96 (12.34–15.50)
Jia, 2014 [114]	China	UMIC	≥65	Non-demented residents of 5 city of China	All MCI	10,276	2,137	19.5 (18.8–20.3)¶
					alzMCI	10,276	630	5.6 (5.2–6.0)¶
					cvdMCI	10,276	392	3.4 (3.3–4.1)¶
					vrfMCI	10,276	507	4.6 (4.2–5.0)¶
					otherMCI	10,276	608	5.6 (5.2–6.1)¶
M Guo, 2012 [33]	China	UMIC	≥65	Non-demented residents of Xian	aMCI	264	35	13.26 (9.17–17.14)

Table 1
Continued

Author	Location	Income Class	Age (y)	Summary population characteristics	Mild cognitive impairment (MCI)			
					MCI definition	Total sample size	Cases	Prevalence % (95% CI)
Sosa, 2012 [9]	Cuba	UMIC	≥65	Residents of urban and rural settings	aMCI	2,620	47	1.5 (1.0–1.9)†
	DR	UMIC			aMCI	1,767	25	1.3 (0.7–1.8)†
	Peru	UMIC			aMCI	1,767	55	2.6 (1.9–3.3)†
	Venezuela	UMIC			aMCI	1,820	22	1.0 (0.7–1.4)†
	Mexico	UMIC			aMCI	1,821	58	2.8 (2.0–3.6)†
	China	UMIC			aMCI	2,014	16	0.6 (0.3–0.9)†
	India	LMIC			aMCI	1,802	77	4.6 (3.7–5.4)†
Ogunniyi, 2016 [23]	Nigeria	UMIC	≥65	Residents of the Lalupon community, Oyo State (The IDEA Study)	All MCI	6,613	111	18.4 (14.9–21.9) *
					aMCI-SD	613	47	n/a
					aMCI-MD	613	45	n/a
					naMCI-SD	613	18	n/a
					naMCI-MD	613	1	n/a
Hai, 2012 [20]	China	UMIC	≥80	Non-demented residents of Chengdu	aMCI	202	61	30.2
INTERNATIONAL WORKING GROUP (IWG) ON MCI CRITERIA 2004 [97, 98, 100, 103] (*n* = 14 studies)								
Ding, 2015 [45]	China	UMIC	≥60	Non-demented community residents of Shanghai	All MCI	2,985	601	20.1 (18.7 – 21.5)
					aMCI	2,985	393	13.2 (12.0 – 14.4)
					naMCI	2,985	208	7.0 (6.1 – 7.9)
Fang, 2015 [56]	China	UMIC	≥60	Non-demented residents of a community of Shanghai	aMCI	1,059	137	12.90 (10.9–14.9)
Fang, 2009 [54]	China	UMIC	≥60	Non-demented residents of Hangzhou	MCI	925	195	21.10 (18.45–23.58)
Tsoy, 2019 [55]	Kazakhstan	UMIC	≥60	Residents from Almaty, Kazakhstan	MCI	662	201	30.4 (26.9–33.9)
Vanoh, 2016 [53]	Malaysia	LMIC	≥60	Residents of four different states: Perak, Selangor, Kelantan and Johor (Towards Useful Ageing Study)	aMCI	1,993	315	15.8
Zhang, 2013 [58]	China	UMIC	≥60	Non-demented residents of Taicang	aMCI	2,460	450	18.29 (16.76–19.74)
Su, 2013 [52]	China	UMIC	≥60	Elderly of rural and urban areas in Xi'an	aMCI	796	145	18.2
Lee, 2012 [47]	Malaysia	LMIC	≥60	Residents of Kuala Lumpur	All MCI	318	67	21.1
					aMCI	318	49	15.4
					naMCI	318	18	5.7
Janelidze, 2018 [46]	Georgia	LMIC	≥65	Residents, without moderate to severe cognitive impairment, from urban (Tbilisi) and two rural areas (Kakheti and Imereti)	All MCI§	238	66	27.7
					aMCI	238	38	16.0
					naMCI	238	29	9.9
					aMCI-MD	238	8	3.3
					naMCI-MD	238	12	5.1
Ma, 2016 [48]	China	UMIC	≥65	Non-demented residents of sixteen districts within the Tianjin urban boundary	All MCI	5,067	574	11.3 (8.2–14.4)
					aMCI-SD	5,067	227	4.5 (2.2–6.7)
					aMCI-MD	5,067	106	2.1 (0.8–3.4)
					naMCI-SD	5,067	214	4.2 (1.4–7.1)
					naMCI-MD	5,067	27	0.5 (0.3–0.8)

Table 1
Continued

Author	Location	Income Class	Age (y)	Summary population characteristics	Mild cognitive impairment (MCI)			
					MCI definition	Total sample size	Cases	Prevalence % (95% CI)
Pilleron, 2015 [50]	CAR	LIC	≥65	Residents of Bangui and Nola	All MCI	9,860	62	7.2
	ROC	LMIC		Residents of Brazzaville and Gamboma	All MCI	1,913	56	6.1
Rao, 2018 [51]	China	UMIC	≥65	Residents of Guangzhou	All MCI	2,111	299	14.2
					aMCI	2,111	258	12.2
					naMCI	2,111	41	2.0
Sun, 2016 [57]	China	UMIC	≥65	Non-demented residents of Baotou	MCI	384	40	10.42 (7.36–13.32)
Paddick, 2015 [49]	Tanzania	LIC	≥70	Residents of the Hai district	All MCI	296	46	6.3 (2.9–9.7)[||]
EUROPEAN CONSORTIUM ON ALZHEIMER'S DISEASE CRITERIA 2006 [105] (*n* = 2 studies)								
Mohan, 2019 [85]	India	LMIC	≥60	Residents from Thiruvananthapuram, Kerala	All MCI	426	111	26.1 (22.1–30.4)
Dimitrov, 2012 [88]	Bulgaria	UMIC	≥65	Residents from the city of Varna	All MCI	540	36	6.7 (4.6–8.8)
NIA-AA CRITERIA 2011[10] (*n* = 2 studies)								
Vancampfort, 2017 [11]	South Africa	UMIC	≥50	Nationally representative sample of elderly without severe cognitive impairment (The WHO Study on Global Ageing and Adult Health)	All MCI	32,715	5,005	15.3 (14.4–16.3)[**]
	China	UMIC						
	Ghana	LMIC						
	India	LMIC						
	Mexico	UMIC						
	Russia	UMIC						
Koyanagi, 2019 [93]	South Africa	UMIC	≥50	Nationally representative sample from nine provinces across South Africa	All MCI	3,672	312	8.5 (6.9–10.3)
STUDY SPECIFIC CRITERIA FOR MCI (*n* = 13 studies)								
Das, 2007 [91]	India	LMIC	≥50	Non-demented/non-depressed residents of Kolkata	All MCI	745	111	14.9 (12.2–18.0)
					aMCI (with/without complainers)	745	45	6.0 (4.4–8.1)
					aMCI (complainers only)	745	34	4.6 (3.1–6.3)
					mdMCI	745	66	8.9 (6.8–11.3)
Wang, 2013 [95]	China	UMIC	≥55	Non-demented residents of two cities of Ningxia province	aMCI	1,033	199	19.26 (16.86–21.55)
Wang, 2016 [94]	China	UMIC	≥55	Non-demented residents of Ningxia province	aMCI	2,168	457	21.08 (19.4–22.7)
Huang, 2007 [30]	China	UMIC	≥60	Non-demented residents of Shenzhen	MCI	410	88	21.46 (17.49–25.23)
Khedr, 2015 [70]	Egypt	LMIC	≥60	Residents of Qena governorates in Southern Egypt	aMCI	691	12	1.7 (0.8–2.7)
Li, 2013 [74]	China	UMIC	≥60	Non-demented residents of Jinan	aMCI	1,226	115	9.38 (7.75–10.93)

Table 1
Continued

Author	Location	Income Class	Age (y)	Summary population characteristics	Mild cognitive impairment (MCI)			
					MCI definition	Total sample size	Cases	Prevalence % (95% CI)
Lu, 2019 [86]	China	UMIC	≥60	Residents of Ji County	*In 2010*			
					All MCI		1,278	22.9
					MCI-A	5,581	1,060	19.0
					MCI-VaD		128	2.3
					MCI-O		89	1.6
					In 2015			
					All MCI		1,541	27.8
					MCI-A	5,542	1,019	18.4
					MCI-VaD		377	6.8
					MCI-O		149	2.7
Wang, 2014 [75]	China	UMIC	≥60	Non-demented residents of Zhoushan	MCI	1,906	318	16.68 (15.01–18.27)
Wu, 2012 [76]	China	UMIC	≥60	Non-demented residents of Xian	aMCI	1,583	396	25.02 (22.88–27.04)
Zhao, 2015 [79]	China	UMIC	≥60	Non-demented residents of Jilin province	aMCI	976	171	17.60 (15.14–19.78)
Zhou, 2016[80]	China	UMIC	≥60	Non-demented residents of Changji	MCI	804	223	27.74 (24.64–30.67)
Zhu, 2013 [84]	China	UMIC	≥60	Non-demented residents of Zhejiang province	MCI	1,211	251	20.70 (18.44–22.89)
Chu, 2015 [89]	China	UMIC	≥65	Non-demented residents of a community of Shanghai	MCI	842	180	21.4 (18.6–24.0)
STUDY SPECIFIC CRITERIA FOR CIND/COGNITIVE IMPAIRMENT (*n* = 10 studies)								
Brucki, 2014 [59]	Brazil	UMIC	≥50	The Mamirauá and Amanã Sustainable Development Reserves, Amazonian Basin	CIND	163	10	6.1
Cesar, 2016 [60]	Brazil	UMIC	≥60	Residents of rural and urban areas in the Tremembe area, State of Sao Paulo	CIND	630	135	19.5 (16.6–22.8)
Dominguez, 2018 [61]	Philippines	LMIC	≥60	Residents of Marikina City	CIND	1,367	317	23.2
Lei, 2008 [68]	China	UMIC	≥60	Normal cognitive and MCI residents from urban and rural areas of Guizhou province	CIND	4,323	665	15.4
Mejia-Arango, 2011 [65]	Mexico	UMIC	≥60	Representative sample of elderly in Mexico (Mexican Health and Ageing Study)	CIND	6,847	1,719	28.7‡‡
Zhang, 2014§§ [67]	China	UMIC	≥60	Residents of rural Ji County	CIND	5,550	1,295	23.3
Fei, 2009 [62]	China	UMIC	≥65	Residents of Taiyuan city	CIND	6,192	600	9.7 (9.6–9.8)††
Guerchet, 2009 [63]	Benin, West Africa	LIC	≥65	Residents in the rural commune of Djidja centre	CIND	502	34	6.8
Guerchet, 2010 [64]	CAR	LIC	≥65	Older age residents of Bangui	CIND	496	124	25.0 (21.2–29.0)
	ROC	LMIC		Older aged residents of Brazzaville	CIND	520	98	18.8 (15.6–22.5)
Shi, 2013§§ [66]	China	UMIC	≥80	Residents of rural Ji County	CIND	626	297	47.4 (43.5–51.4)

Table 1
Continued

Author	Location	Income Class	Age (y)	Summary population characteristics	Mild cognitive impairment (MCI)			
					MCI definition	Total sample size	Cases	Prevalence % (95% CI)
CUT-OFF SCORE OF NEUROPSYCHOLOGICAL ASSESSMENT TOOL (*n* = 3 studies)								
Saha, 2010 [92]	India	LMIC	≥50	Non-demented women, without history of neurological disorders, from a village of Singur block of Hoogly district, Kolkata	Cognitive impairment	179	76	42.4
Ruan, 2019 [87]	China	UMIC	≥60	Residents from 20 communities in the Zhoujiaqiao Primary Health Service Area in Changning district, Shanghai,	MCI	5,328	500	9.67
Inocian, 2016 [69]	Philippines	LMIC	≥65	Elderly, with no diagnosed mental health conditions, from Cebu City	All MCI	120	76	63.3
DSM-IV CRITERIA [104] (*n* = 8 studies)								
Hu, 2012 [96]	China	UMIC	≥55	Non-demented residents of Nei Monggol	MCI	9,266	1,782	19.48 (18.43–19.99)
Guo, 2013 [72]	China	UMIC	≥60	Non-demented residents of six towns of rural area of Hunan	aMCI	1,367	139	10.17 (8.57–11.69)
Zhang, 2015 [77]	China	UMIC	≥60	Non-demented residents of Taian	MCI	1,971	651	33.03
Zhang and Zeng, 2014 [78]	China	UMIC	≥60	Non-demented residents of Changsha	aMCI	1,764	229	16.27 (11.41–14.47)
Zhou, 2009 [82]	China	UMIC	≥60	Non-demented residents of Xinjiang	aMCI	2,986	205	10.21 (5.96–7.73)
Zhou, 2011 [81]	China	UMIC	≥60	Non-demented residents of Ningbo	aMCI	1,227	107	10.68 (7.14–10.22)
Zhu, 2009 [83]	China	UMIC	≥60	Non-demented residents of Wulumuqi	aMCI	1,511	148	9.79 (8.3–11.22)
Xiong, 2013 [90]	China	UMIC	≥65	Non-demented residents of Tianjin	aMCI	2,798	339	11.38 (10.91–13.26)

*Weighted prevalence for age using the World Health Organization world population estimates 2015. †Weighted prevalence for age, gender, and education level. ‡Weighted prevalence calculated using reciprocal probability weighting based on the Sixth Nationwide Population Census in China, 2010. §Participants with 'all MCI' could be categorized in more than one MCI subtype. ¶Weighted prevalence using the direct standardization method adjusted by age and sex to the total Chinese population (according to the census conducted in 2005). ||Weighted prevalence for stratification and age according to the WHO standard population. **Weighted prevalence according to the population structure as reported by the United Nations Statistical Division. ††Weighted prevalence to account for selection probabilities and controlling for age and sex. ‡‡Weighted prevalence to represent the total Mexican population. §§The study from Shi, 2013 and Zhang, 2014 used data from the same cohort study. 95%CI, confidence interval; alzMCI, MCI caused by prodromal Alzheimer's disease; aMCI, amnestic MCI; CAR, Central African Republic; CIND, cognitive impairment no dementia; cvdMCI, MCI resulting from cerebrovascular disease; DR, Dominican Republic; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; LIC, low income country; LMIC, lower middle income country; MCI, mild cognitive impairment; MCI-A, MCI with significant memory impairment; MCI-MD, multi domain MCI; MCI-O, non memory/nonvascular related types of mild cognitive impairment; MCI-SD, single domain MCI; MCI-VaD, significant executive function impairment and relationship with cerebral vascular disease; naMCI, non-amnestic MCI; NIA-AA National Institute on Aging and Alzheimer's Association; otherMCI, MCI caused by other diseases; ROC, Republic of Congo; UMIC, upper middle income country; vrfMCI, MCI with vascular risk factors.

below and outlined in Supplementary Table 5. Overall, MCI was diagnosed using one or more of the following criteria: 1) subjective/informant cognitive or memory complaint; 2) global cognitive performance; 3) domain specific cognitive performance; 4) physical functioning; 5) no dementia; and 6) other factors (e.g., disease related co-mobility). Additional assessments were used in 7/78 studies [24, 27, 45, 47, 51, 62, 70]. In four studies, a Clinical Dementia Rating (CDR) score between 0 and 0.5 [27], or a score of 0.5 was needed for diagnosis of MCI [24, 45, 51]. In four studies [24, 47, 62, 70], it was required that cognitive impairment was independent of other factors such as depression.

Domain specific MCI

Based on the cognitive domain test scores, 17 studies [9, 20–24, 26, 43, 45–48, 51–53, 70, 91] stratified MCI into different subtypes. This included non-amnestic MCI (naMCI; $n = 8$ studies [22, 23, 43, 45–48, 51]), aMCI single domain (aMCI-SD; $n = 4$ studies [22, 23, 43, 48]), multi-domain aMCI (aMCI-MD) ($n = 5$ studies [22, 23, 43, 46, 48]), multi-domain non-amnestic MCI (naMCI-MD; $n = 4$ studies) [22, 23, 46, 48], and single domain naMCI (naMCI-SD; $n = 3$ studies [22, 23, 48]).

Subjective cognitive/memory complaint

Cognitive/memory complaints were included as part of the MCI diagnosis in 57/78 studies [9, 11, 20–24, 26–29, 31–34, 36–43, 45, 47–56, 58–60, 62, 70, 72–76, 78–83, 85, 88, 90, 91, 93–95]. Complaint was typically required to be subjective and focused on memory ($n = 43$ studies [9, 11, 20–22, 24, 26–28, 31–34, 36–43, 47, 48, 52, 53, 58–60, 62, 70, 72–74, 76, 78, 79, 81–83, 90, 95]) or cognition in general ($n = 11$ studies [23, 45, 49–51, 54, 56, 75, 80, 85, 88]). In 25 studies, complaints could also be reported by an informant [22, 23, 27, 28, 44, 45, 47, 48, 51, 52, 54–56, 60, 62, 70, 72, 73, 75, 76, 80, 85, 91, 94, 95]. Thirty studies did not specify how cognitive/memory complaints were assessed or the information was not reported [20, 24–26, 29, 30, 43, 44, 46, 49, 50, 55, 57, 61, 63–69, 77, 84, 87–89, 92, 93, 96].

Global cognitive function

Global cognitive function was assessed in 61/78 studies [21–23, 25–34, 36–44, 46, 47, 50, 52–54, 57–70, 72–76, 78–83, 88–92, 95, 96]. In 33 studies [23, 25, 29, 32, 39–41, 50, 57–70, 74, 75, 79–83, 88, 90, 92, 95], global cognitive function was required to be impaired, while in 28 studies [21, 22, 26–28, 30, 31, 33, 34, 36–38, 42–44, 46, 47, 52–54, 72, 73, 76, 78, 89, 91, 94, 96], it was required to be preserved or within normal limits. In total, 10 different neuropsychological assessment tools were used to assess global cognitive function including the Mini-Mental State Examination (MMSE; $n = 40$ studies [20, 22, 25–27, 30, 31, 33, 34, 36, 43, 47, 52–54, 57, 59, 60, 62, 66–69, 72, 74–76, 78, 80–83, 88–92, 95, 96]), the Montreal Cognitive Assessment (MoCA; $n = 10$ studies [27, 29, 32, 39–41, 46, 58, 79, 89]), the CDR ($n = 5$ studies [44, 61, 66, 67, 70]), the Community Screening Instrument for Dementia (CSI-D; $n = 3$ studies [50, 63, 64]), the Consortium to Establish a Registry for Alzheimer's Disease battery (CERAD; $n = 2$ studies [21, 91]), the Five Word Test ($n = 2$ studies [63, 64]), the Cambridge Examination for Mental Disorders-Revised (CAMDEX-R; $n = 1$ study [20]), the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen ($n = 1$ study [23]), The Memory Impairment Screen (MIS; $n = 1$ study [88]), and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; $n = 1$ study [65]). Of the studies using the MMSE, and with reported cut-off scores, 22 studies [26, 27, 30, 31, 33, 57, 59, 60, 62, 67, 72, 73, 75, 80–83, 89, 90, 94–96] used education specific cut-off scores, and 16 studies used a mixture of the following:

1) To demonstrate normal cognitive function: MMSE ≥ 24 ($n = 4$ studies [43, 54, 76, 78]), MMSE one standard deviation (1SD) from norm ($n = 1$ study [68]), MMSE ≥ 19 ($n = 2$ studies [47, 53]), MMSE ≥ 23 ($n = 1$ study [22]) and MMSE range 24–26 ($n = 1$ study [36]); and,
2) To demonstrate cognitive impairment: MMSE ≤ 24 ($n = 2$ studies [25, 92]), MMSE ≤ 26 ($n = 2$ studies [34, 74]), MMSE ≤ 25 ($n = 1$ study [88]), MMSE ≤ 27 ($n = 1$ study [66]), and MMSE range 20–25 ($n = 1$ study [69]).

Domain specific cognitive function: Memory

Memory was individually assessed for impairment in 41 studies [9, 11, 20–24, 26–29, 37–53, 55, 56, 59, 60, 62, 65, 70, 73, 78, 88, 90, 91, 93]. Some studies used neuropsychological assessment tools to assess memory impairment. The MMSE ($n = 3$ studies [20, 26, 52]), and the Wechsler Memory Scale (WMS; $n = 3$ studies [27, 48, 62]) were the most frequently

used, followed by the MIS ($n = 2$ studies [22, 88]), the CSI-D ($n = 1$ study [9]), the Cross-Cultural Cognitive Examination (CCCE; $n = 1$ study [65]), and the CAMDEX ($n = 1$ study [20]). The remaining studies used individual memory tests, of which the Auditory-Verbal Learning Test ($n = 6$ studies [43–45, 51, 53, 62]) was most often used followed by the CERAD 10 word learning test ($n = 5$ studies [9, 11, 21, 49, 93]), the digit span test ($n = 4$ studies [11, 12, 47, 53]), the Brief Cognitive Screening Battery delayed recall task ($n = 2$ studies [59, 60]), the Fuld Object Memory Evaluation ($n = 1$ study [45]), the stick test ($n = 1$ study [45]), the Renminbi test ($n = 1$ study [45]), the IDEA 10 word learning test ($n = 1$ study [23]), the MoCA free delayed recall test ($n = 1$ study [46]), the Rey-Osterrieth complex figure test ($n = 1$ study [43]), Rey Auditory Verbal Learning Test (RAVLT) total learning ($n = 1$ study [47]), RAVLT delayed recall ($n = 1$ study [47]), the MMSE memory subtask ($n = 1$ study [48]), WMS-III local memory test ($n = 1$ study [70]), CDR memory score ($n = 1$ study [70]), CCCE verbal memory ($n = 1$ study [65]), and the free and cued selective reminding test ($n = 1$ study [50]). Nineteen studies describe cut-off scores for impairment including: < 1.5 SDs adjusted for age and education ($n = 8$ studies [9, 21, 22, 43, 45, 48, 51, 78]), < 1.5 SDs below norms ($n = 6$ studies [27, 44, 46, 53, 62, 91]), < 1 SD below norms ($n = 2$ studies [47, 70]), < -1 SD adjusted for age, education, and country ($n = 2$ studies [11, 93]), and 1.5–2 SDs below the overall mean adjusted for age and education ($n = 1$ study [56]).

Domain specific cognitive function: Other domains

Non-memory cognitive test performance was assessed in 25 studies [11, 22, 23, 25, 27, 43–51, 55, 56, 59, 60, 62, 65, 79, 85, 88, 91, 93]. Nine different test batteries were used including: the Wechsler Adult Intelligence Scale ($n = 3$ studies [27, 48, 62]), CERAD ($n = 1$ study [88]), CSI-D ($n = 1$ study [49]), the Alzheimer's Disease Assessment Scale Cognitive Subscale ($n = 1$ study [22]), IDEA cognitive screen ($n = 1$ study [23]), CAMCOG ($n = 1$ study [25]), MOCA ($n = 1$ study [46]), Malayalam version of Addenbrooke's Cognitive examination ($n = 1$ study [85]), and the CCCE ($n = 1$ study [65]). In addition, domain-specific tests (e.g., attention and executive function) were used, with the four most common being the verbal fluency test ($n = 10$ studies [11, 43, 44, 50, 51, 59, 60, 62, 91, 93]), the Trail Making Test ($n = 7$ studies [27, 43–46, 51, 62]), the Clock Drawing Test ($n = 5$ studies [43, 44, 46, 47, 51]), and the Boston Naming Test ($n = 2$ studies [43, 62]). Two studies [56, 79] stated that non-memory domains were assessed, however they did not describe which tests were used.

Dementia

Criteria used to exclude dementia included the DSM-IV ($n = 27$ studies [20, 23, 25, 27, 34, 37, 44–46, 48–51, 55, 59, 61–64, 66–68, 70, 85, 88, 91, 92]), performance on a neuropsychological assessment battery ($n = 8$ studies [22, 43, 47, 52, 56, 69, 87, 89]), a combination of cognitive test performance and evaluation of Activities of Daily Living (ADL)/Instrumental Activities of Daily Living (IADL; $n = 4$ studies [11, 21, 65, 93]), National Institute of Neurological and Communicative Diseases and Stroke - Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria ($n = 3$ studies [23, 37, 62]), ICD-10 criteria ($n = 1$ study [25]), the 10/66 dementia algorithm ($n = 1$ study [9]), diagnoses by a doctor ($n = 1$ study [53]) or NIA-AA criteria ($n = 1$ study [60]).

Functional performance

Fifty-six studies reported that physical functioning, including ADL/IADL, were part of the assessment for MCI [9, 11, 20–28, 31–33, 36–38, 42–56, 59, 60, 62, 65–67, 72–76, 79–83, 85, 88, 90, 91, 93–95]. However, 26 of these studies did not report the method used to determine physical functioning status [24–26, 28, 32, 34, 36–38, 42, 43, 46, 48, 49, 56, 72, 73, 75, 76, 79–83, 94, 95]. Thirty-six studies [9, 11, 20, 21, 24–27, 31–33, 37, 38, 42, 45–50, 52–54, 62, 65–67, 73, 74, 88, 90, 95] exclusively assessed either ADL or IADL. The majority of studies required persevered ADL/IADL for a diagnosis of MCI, with only 13 studies [9, 11, 22, 41, 46, 53, 72, 75, 80–83, 91] allowing for subtle changes/mild functional impairment. In 26 studies, impairment in ADL/IADL was assessed using previously developed tools, of which the Katz ADL scale was the most often used ($n = 8$ studies [11, 20, 22, 27, 47, 52, 53, 93]), followed by the Lawton and Brody scale ($n = 5$ studies [21, 45, 47, 52, 53]), the Functional Activities Questionnaire ($n = 4$ studies [44, 51, 55, 60]), the CDR ($n = 2$ studies [45, 51]), the CSI-D informant interview ($n = 2$ studies [9, 50]), the Everyday Ability Scale for India ($n = 2$ studies [85, 91]), the Barthel scale ($n = 1$ study

[21]), the Clinician Home Based Interview to assess Function ($n = 1$ study [23]), and the IQCODE ($n = 1$ study) [60].

MCI prevalence

The prevalence estimates reported in this review were all determined at the time of the study. However, one study [86] reported MCI prevalence at two time points (2010 and 2015). Across the different definitions used, 31 studies [11, 22, 23, 25, 27, 30, 31, 43–51, 55, 57, 69, 71, 75, 80, 84–89, 91, 93, 96] calculated overall MCI prevalence, 47 studies [9, 20–24, 26, 28, 29, 32, 34–43, 45–48, 51–53, 56, 58, 70, 72–74, 76, 78, 79, 81–83, 90, 91, 94, 95] calculated aMCI prevalence, eight studies [22, 23, 43, 45–48, 51] calculated naMCI prevalence, and 10 studies [59–68] calculated CIND prevalence. Two studies [44, 86] subtyped MCI by etiology as defined by: MCI caused by prodromal Alzheimer's disease [44], MCI resulting from cerebrovascular disease [44], MCI with vascular risk factors [44], MCI with significant memory impairment [86], MCI with significant executive function impairment and relationship with cerebral vascular disease [86], and MCI caused by other factors [86]. As shown in Table 1, MCI prevalence ranged from 0.3% (95% CI: 0.1–0.5) in a sample from Mexico ($n = 2{,}944 \geq 60$ years; naMCI multiple domain, Petersen criteria) [22] to 63.3% in a sample from the Philippines ($n = 120 \geq 65$ years; MCI defined as an MMSE score 20–25 out of 30) [69]. Specifically, for Petersen criteria, prevalence of aMCI ranged from 0.6% (95%CI: 0.3–0.9) [9] to 22.3% [26]. Similar variability was seen across studies using the IWG Criteria for aMCI (range 4.5% [48] to 18.3% [58]; $n = 9$ studies); IWG criteria for all-MCI (range 6.1% [50] to 30.4% [55]; $n = 10$ studies); studies using CIND criteria (range 6.1% [59] to 47.4% [66]; $n = 10$ studies), studies using study specific criteria to diagnose MCI (range 1.6% [86] to 27.7% [80]; $n = 13$ studies); DSM-IV criteria (range 9.8% [83] to 33.0% [77]; $n = 8$ studies); studies using neuropsychological tests (range 9.7% [87] to 63.3% [69]; $n = 3$ studies); NIA-AA criteria (range 8.5% [93] to 15.3% [106]; $n = 2$ studies) and European Consortium of AD criteria (range 6.7% [88] to 26.1% [85]; $n = 2$ studies).

The forest plots in Fig. 2 show the MCI prevalence estimates for Petersen defined all-MCI (Fig. 2A) and aMCI (Fig. 2B), the IWG criteria (Fig. 2C), and criteria for CIND (Fig. 2D). The plots show there is large variability in MCI prevalence across studies even when the same criteria are applied in the same country *albeit* in different samples. In contrast, prevalence estimates are generally, although not always, more consistent across countries in multi-site studies ($n = 4$ studies [9, 11, 50, 64]) when the same methods are used (0.6%–4.6% [9]; 6.1%–7.2% [50]; 18.8%–25.0% [64]).

Associated risk factors

Risk factors for prevalent MCI were investigated in 64/78 studies [20–24, 26–45, 47, 48, 51–60, 62, 67–69, 72–76, 78–87, 89–93, 95, 96]. Two studies [53, 67] did not report risk factor information in the original article; however, risk factor data for the same cohort were later published [107, 108]. In this scenario, we have added the risk factor information as documented in the most recent publication. One paper [27] reported additional vascular risk factor information in a separate article [109] and we have also included this data. Significant risk factors for MCI included increased age ($n = 46/64$ studies [22, 23, 26–42, 44, 45, 48, 51, 54–58, 62, 67, 72–76, 78–82, 84, 89, 90, 92, 94, 96]), sex ($n = 41/64$ studies; in 37 studies [22–24, 26, 28–30, 33, 34, 36, 38–42, 45, 48, 51, 54, 58, 62, 67–69, 72, 73, 76, 78, 81, 84, 86, 89, 90, 93–96] women had higher risk and in four studies [21, 27, 44, 87] men had higher risk), and low level of education ($n = 44/64$ studies [20–23, 27–37, 39–45, 48, 51, 54–57, 62, 67, 72–76, 78–82, 84, 89, 90, 94]). Other significant risk factors included the presence of disease related co-morbidities (e.g., hypertension, stroke, coronary heart disease) [12, 20, 22, 34, 41–44, 48, 56, 60, 67, 84, 86, 89–91, 94], low monthly income/low economic status [27–29, 33, 36, 39–42, 62, 79, 90, 92], marital status (without spouse) [28, 33, 34, 41, 54, 62, 68, 75, 76, 78, 80, 84, 87, 90, 92], occupation (physical labor) [27, 28, 34, 37, 41, 44, 58, 74–76, 78, 81, 83], geographic area (rural location) [37, 51, 68], diabetes [34, 41–44, 48, 84, 86, 90, 91], alcohol consumption [20, 39, 72, 81, 85, 93, 94], high body mass index [22, 48, 86, 89, 94], living alone [28, 29, 32, 34, 36, 38, 72, 78, 79, 81], Apolipoprotein E4 (APOE E4) carrier [32, 94], low physical activity [28, 38, 39, 41, 54, 84], current or a history of smoking [26, 34, 39, 48, 72, 75, 84, 90, 91], sleep (poor) [26, 28, 38, 84], depression [22, 41, 90], and an introverted personality [29, 40, 58]. Protective factors included maintaining social contact with others [29, 43, 58, 76, 78] and following a healthy diet/consuming healthy dietary components [35, 40, 43, 81] or specifically drinking tea

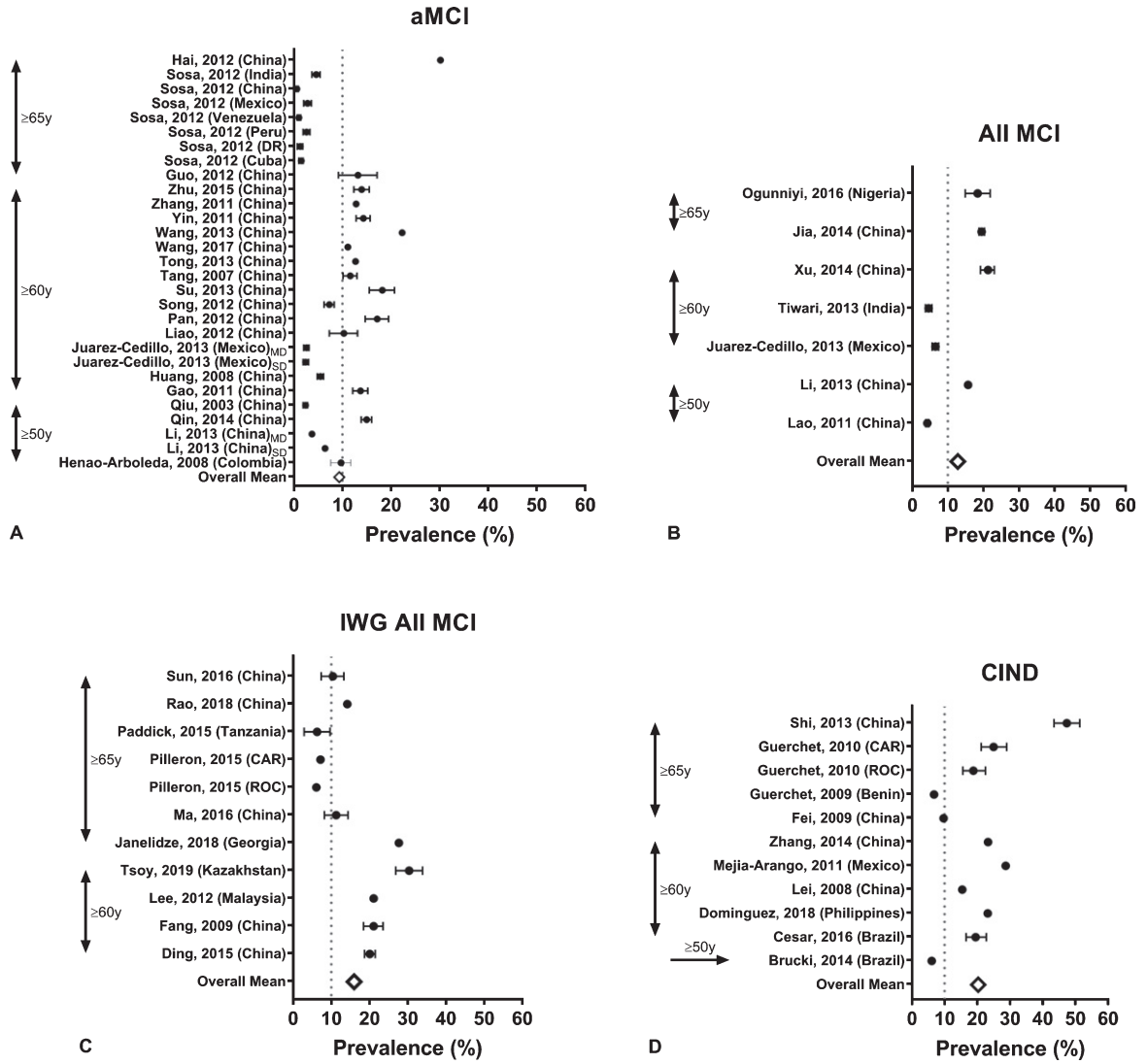

Fig. 2. A. Forest plot of MCI prevalence from studies using Petersen's criteria for Amnestic MCI (ordered by age). Note: red dotted line indicates 10% prevalence. 95%CI, 95% confidence interval; aMCI, amnesic mild cognitive impairment; DR, Dominican Republic. B. Forest plot of MCI prevalence from studies using Petersen's criteria for All MCI (ordered by age). Note: red dotted line indicates 10% prevalence. 95%CI, 95% confidence interval; MCI, mild cognitive impairment. C. Forest plot of MCI prevalence from studies using the International Working Group criteria (ordered by age). Note: red dotted line indicates 10% prevalence. 95%CI, 95% confidence interval; IWG, International Working Group; CAR, Central African Republic; ROC, Republic of Congo. D. Forest plot of MCI prevalence from studies using definition of Cognitive Impairment No Dementia criteria (ordered by age). Note: red dotted line indicates 10% prevalence. 95%CI, 95% Confidence Interval; CAR, Central African Republic; ROC, Republic of Congo; CIND, Cognitive Impairment No Dementia.

[26, 35, 43, 89]. See Supplementary Table 6 for full details of all risk factors reported across the different studies.

DISCUSSION

This is the first systematic review, to our knowledge, that has focused on MCI prevalence and its risk factors specifically in LMICs. The results highlight that MCI research in LMICs is largely restricted to upper-middle income countries, namely China. Further, MCI research is characterized by wide variation in population sampling, the case definition used for an MCI diagnosis, operationalization of the component criterion and prevalence estimates. These differences make cross-study comparison extremely difficult and highlight the urgent need for consensus in how MCI is defined across different settings.

MCI prevalence ranged from 0.3% [22] to 63.3% [69]. This variability was not reduced when grouping prevalence estimates by case definition. However, as shown in Fig. 2, there was a general pattern. Similar to what is observed in HICs [110], we found that diagnostic criteria that are more restrictive and capture a single impairment (e.g., Petersen aMCI criteria; range 0.6% (95%CI: 0.3–0.9) [9] to 22.3% [26]) have generally lower prevalence estimates compared to more general criteria that capture broader dysfunction (e.g., CIND where the majority of studies $n = 7/10$ reported a prevalence >15%). Although it is important to note that estimated prevalence for specific criteria did vary considerably. In relation to age, across all definitions, MCI appears to be rare in the very young, i.e., people <50 years. Furthermore, aMCI (Petersen Criteria) and IWG generally have a lower prevalence in studies where people are aged ≥65 versus people aged ≥60 with the opposite trend observed for all MCI (Petersen Criteria) and CIND.

Regarding definition, across studies, the most widely applied criteria were Petersen defined aMCI ($n = 26$ studies [9, 20–44]) requiring subjective/informant memory complaint, normal global cognitive function, impaired memory, preserved (or relatively preserved in later definitions) physical function and no dementia. Prevalence of aMCI ranged from 0.6% (95%CI: 0.3–0.9) [9] to 22.3% [26]. Similar variability was seen across studies using the IWG Criteria for aMCI (range 4.5% [48] to 18.3% [58]) and IWG criteria for all-MCI (range 30.4% [55] to 6.1% [50]). These results are in line with previous systematic reviews of MCI incorporating studies predominately from HICs [111]. Variability in prevalence is likely due to differences in sample characteristics (e.g., age, educational attainment, and distribution of risk and protective factors) and methodology (e.g., test batteries used to assess cognitive and physical function, cut-off scores for impairment and whether the analyses were adjusted for factors such as age, sex, and education) across studies. Indeed, all of the studies that included multiple sites demonstrated that when the same methods were used to diagnose MCI, prevalence estimates were generally (although not always) more comparable across countries [9, 11, 50, 64].

Similar to findings in high-income countries, both modifiable and non-modifiable risks factors were identified for MCI. Key socio-demographic risk factors included increased age, sex (usually, but not always, female) and low educational attainment. Modifiable health and lifestyle risk factors included, but were not limited to, smoking, presence of cardiovascular related diseases, social contact, occupation, physical activity, and dietary related factors. These findings support the development of novel public health interventions to reduce risk of cognitive impairment targeting education, cardio-metabolic health, and lifestyle factors that are applicable to the specific context of LMIC settings. However, a key knowledge gap highlighted by the review is the lack of research into context specific risk factors. Indeed, compared to HICs factors such as lifelong disadvantage, food insecurity, poverty, and absence of robust health and social care services might also be important in increasing risk of MCI and dementia in these settings.

Of note, is the scarcity of studies on MCI from countries classified as low-income (only $n = 4$ studies [49, 50, 63, 64]). Further, no studies were identified from LMICs in the Middle East, with the exception of one study from Egypt [70]. As shown in Fig. 3, most MCI research in LMICs has come from cohorts in the Far East (e.g., China and parts of Asia and South-Asia including Malaysia, Philippines, and India), South America and the Caribbean (including Cuba, Dominican Republic, Mexico) and an increase in research in Africa (Tanzania, Nigeria, Central African Republic, Republic of Congo) only in the last five years (i.e., from 2015 onwards). Few studies have also been conducted in European LMICs with the exception of Bulgaria [88], Russia [106], and Georgia [46]. This lack of research into MCI could reflect the more recent demographic transition and population ageing in LMICs, highlighted by an increase in dementia-specific research in the past 10 years [112]. Also, across different LMIC settings there are high levels of low educational attainment/illiteracy in older people and there are often no norms for cognitive testing making MCI diagnosis challenging. Furthermore, there are typically very few specialist clinicians able to supervise this type of work in LMIC settings, with the exception of some countries like China.

Strengths and weaknesses

The study has a number of strengths. We undertook a wide literature search capturing many of the different definitions of MCI. This allowed for a more comprehensive synthesis of the types of criteria used to diagnose MCI across the many different LMICs. Some studies, however, could still have been missed if they defined MCI outside the scope of the

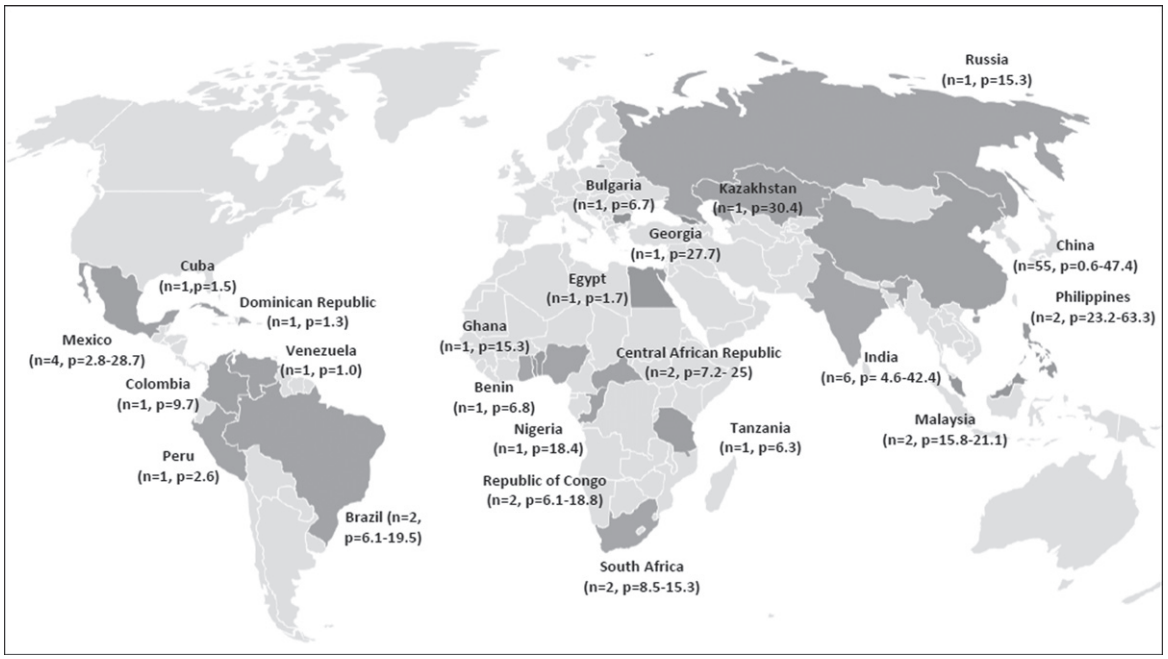

Fig. 3. World map showing each study site, number of studies in each site (n) and the reported MCI prevalence estimate(s).

search. There are some weaknesses. First, the electronic search was undertaken in English and therefore studies published in other languages, including those common in LMICs such as Spanish, Portuguese, and French could have been missed if they were not recorded in EMBASE, Pubmed, or PsycInfo. We minimized the risk of not capturing Chinese articles by including findings from a recent systematic review on MCI prevalence in China [7]. Structuring the search this way could possibly explain the large number of MCI studies captured from China compared to other LMICs. This difference could also be due to variability in research investment into aging and dementia. Second, we focused only on cross-sectional studies that reported MCI prevalence estimates. Therefore, we did not investigate whether MCI is predictive of future dementia in LMICs or what the risk factors for incident MCI are. As such, we are unable to make recommendations as to which criteria are the most "useful". This was beyond the scope of the review. Last, given the paucity of research into aging and dementia in LMIC settings we included any population-based study in the review; and only four were population-representative [11, 44, 65, 93]. MCI prevalence results in non-representative samples must be viewed with caution as they may be biased for example by sampling (e.g., difference in location such as urban versus rural) and differences in the profile of risk/protective factors (e.g., demographic, health, and socio-economic status).

CONCLUSION

Numerous definitions of MCI have been proposed [113]. Determining which, if any, are suitable for application in LMICs will require an in-depth evaluation of not only how well they capture people with cognitive impairment, but also whether the condition is predictive of future dementia in these settings. To achieve this, consensus on how MCI is defined will be required, particularly in settings with varying educational levels amongst older people, varying cultural milieu and expectations resulting in challenges in MCI case identification. Nevertheless, given the high burden of dementia now seen in LMICs, identification of these higher risk individuals at a stage where intervention could take place is likely to have a high impact on the burden of disease associated with cognitive impairment and dementia in these settings. Thus, to further understand MCI prevalence in these settings there is an urgent need for more high quality, population representative MCI prevalence studies, particularly in countries classified as low income.

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SUPPLEMENTARY MATERIAL

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