

Title: Is loneliness associated with mild cognitive impairment in low- and middle-income countries?

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ABSTRACT

Background: Loneliness may be a risk factor for mild cognitive impairment but studies on this topic are scarce, particularly from low- and middle-income countries (LMICs).

Therefore, the aim of the present study was to investigate the association between loneliness and MCI in six LMICs (China, Ghana, India, Mexico, Russia, South Africa).

Methods: Cross-sectional, community-based, nationally representative data from the WHO Study on global AGEing and adult health (SAGE) were analyzed. The definition of MCI was based on the National Institute on Ageing-Alzheimer's Association criteria. Multivariable logistic regression analysis and meta-analysis were conducted to assess associations.

Results: The final analytical sample consisted of 19092 and 13623 individuals aged 50-64 years (middle-aged adults) and ≥ 65 years (older adults), respectively. Among the middle-aged, overall, loneliness was associated with a non-significant 1.43 (95%CI=0.93-2.21) times higher odds for MCI although significant associations were observed in China (OR=1.51; 95%CI=1.08-2.09) and South Africa (OR=3.87; 95%CI=1.72-8.71). As for older adults, overall, there was a significant association between loneliness and MCI (OR=1.52; 95%CI=1.12-2.07).

Conclusion: In this large representative sample of middle-aged and older adults from multiple LMICs, findings suggest that loneliness is associated with MCI. It may be prudent to consider reducing loneliness in low-economic settings to aid in the prevention of MCI and ultimately dementia.

Key Words: Loneliness, Low- and middle- income countries, Mild cognitive impairment, Multi-country

1 INTRODUCTION

2 Dementia is defined as a syndrome characterized by deterioration in cognitive function
3 beyond what might be expected from normal ageing¹. The global prevalence of dementia is
4 expected to increase to 82 million in 2030 and 152 million in 2050¹. Since dementia is more
5 likely to affect older adults, this increase is predominantly driven by more people now living
6 into older age. Dementia is one of the main causes of disability and dependency in older
7 adults and has profound detrimental psychological, social, physiological, and economic
8 impact on people living with the disease, their families, other care providers, and society as a
9 whole². However, there is currently no cure for dementia and thus, there is an increasing
10 emphasis on the identification of modifiable risk factors for conditions known to predict the
11 ultimate emergence of dementia in order to develop interventions aiming to prevent or delay
12 the onset of dementia. Specifically, mild cognitive impairment (MCI) is a preclinical state of
13 dementia with a high conversion rate to dementia (annual conversion rates ranging from 10%
14 to 15% in clinical samples and 3.8% to 6.3% in community-based samples⁴⁻⁶), and is
15 increasingly being recognized as an important “target” for the prevention of dementia.

16
17 Several correlates of MCI have been identified. For example, in one study from China, older
18 age and comorbidity were associated with a higher risk of MCI whereas having a high school
19 degree or a high family-capita monthly income was associated with a lower risk⁷. Other
20 research has identified mental health correlates (e.g., depression)⁸ and behavioral correlates
21 (e.g., moderate exercise)⁹. However, inter-personal correlates of MCI including loneliness
22 (i.e., the perception of being alone and isolated) are studied to a lesser extent. Loneliness is
23 plausibly associated with MCI through several mechanisms. For example, loneliness may
24 trigger neural responses that may directly influence the development of neurodegenerative

25 conditions¹⁰. Furthermore, loneliness has been shown to be associated with unhealthy
26 behaviors including low levels of physical activity, substance abuse and poor nutrition, and
27 such behaviors can negatively affect cognition either directly or via increased risk of
28 cardiometabolic disease¹⁰.

29

30 One recent review on the effect of loneliness on MCI by Lara and colleagues, which included
31 three longitudinal studies [all from high-income countries (i.e., Singapore, USA, Spain)],
32 suggested a potential effect of loneliness on MCI although evidence was limited¹⁰.

33 Specifically, Rawter and colleagues found in a sample of 1601 participants from Singapore
34 that loneliness was associated with MCI-dementia (HR 1.26 [95% CI 0.86-1.84]), but did not
35 investigate the association between loneliness and MCI per se¹¹. Lobo and colleagues
36 investigated in a sample of 1654 Spanish adults the association between loneliness and
37 incident MCI, and found that those who suffer from loneliness were over two times more
38 likely to develop MCI¹². Finally, Wilson and colleagues found in a sample of 529 adults from
39 the US that loneliness was associated with a higher risk of developing MCI (HR 1.53 [95%
40 CI 1.13-2.07])¹³. Other recent studies have also found similar findings in Europe

41 https://onlinelibrary.wiley.com/doi/full/10.1002/gps.5304?casa_token=8Wt_SzO2jx0AAAA

42 [A%3Aa0fCu1MoqKtFA-3yg_p0lFQaoJb6sK-](https://doi.org/10.1002/gps.5304?casa_token=8Wt_SzO2jx0AAAA)

43 [DpBUu1KmWCJeWX73LNt2ygTXhLaoaWu8_PpkCRJOhST3f](https://doi.org/10.1002/gps.5304?casa_token=8Wt_SzO2jx0AAAA) and China

44 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6721226/>

45 <https://academic.oup.com/ageing/article-abstract/49/4/599/5799038>

46 <https://pubmed.ncbi.nlm.nih.gov/27073010/> However, in the Cambridge City Over-75s

47 Cohort Study (n=3713), it was found that loneliness does not exert long-term harmful effects
48 on cognitive function among the oldest old.

49 https://www.tandfonline.com/doi/full/10.1080/13607863.2019.1655704?casa_token=3DNhk

50 [T6hlzUAAAAA%3AQbKx79Sr2DIqDnFdRISUfbqetAxL48d1c79oW7xUnx5JIpgQQFWmu](https://www.cambridge.gov.uk/media/1261/cambridge_at_a_glance.pdf)
51 [st5RIRZRxegaQ-pvhYefg](https://www.cambridge.gov.uk/media/1261/cambridge_at_a_glance.pdf) It is important to consider the context of this study to understand
52 differing results. First, the study included only the oldest old and it is possible that in the
53 absence of dementia, individual cognitive impairment reached a ceiling effect prior to joining
54 the cohort. Moreover, Cambridge City is classed as one of the most affluent areas in the UK
55 with one of the highest average salaries
56 https://www.cambridge.gov.uk/media/1261/cambridge_at_a_glance.pdf. Indeed, even among
57 the oldest old, it is unlikely that the studied population is representative of the general UK
58 population, and the present association may be unique to this location. Given this, it is clear
59 that more research is required to further elucidate the association between loneliness and MCI
60 from more diverse settings and in larger samples; indeed, this was one of the key conclusions
61 of the discussed review by Lara and colleagues¹⁰.

62

63 In particular, it is important to investigate the association between loneliness and MCI in low-
64 and middle-income countries (LMICs) since almost 60% of those with dementia live in such
65 settings. Moreover, literature suggests that rates of loneliness are also high in LMICs¹⁴.
66 Despite this, there are very limited studies on loneliness and MCI from LMICs. Therefore,
67 the aim of the present study was to investigate the association between loneliness and MCI in
68 13,623 middle-aged and older adults from six LMICs (China, Ghana, India, Mexico, Russia,
69 South Africa) that broadly represent different geographical locations and levels of socio-
70 economic and demographic transition.

71

72 **METHODS**

73 *The survey*

74 Data from the Study on Global Ageing and Adult Health (SAGE) were analyzed. These data
75 are publicly available through <http://www.who.int/healthinfo/sage/en/>. This survey was
76 undertaken in China, Ghana, India, Mexico, Russia, and South Africa between 2007 and
77 2010. Based on the World Bank classification at the time of the survey, Ghana was the only
78 low-income country, and China and India were lower middle-income countries although
79 China became an upper middle-income country in 2010. The remaining countries were upper
80 middle-income countries.

81 Details of the survey methodology have been published elsewhere¹⁵. Briefly, in order
82 to obtain nationally representative samples, a multistage clustered sampling design method
83 was used. The sample consisted of adults aged ≥ 18 years with oversampling of those aged
84 ≥ 50 years. Trained interviewers conducted face-to-face interviews using a standard
85 questionnaire. Standard translation procedures were undertaken to ensure comparability
86 between countries. The survey response rates were: China 93%; Ghana 81%; India 68%;
87 Mexico 53%; Russia 83%; and South Africa 75%. Sampling weights were constructed to
88 adjust for the population structure as reported by the United Nations Statistical Division.
89 Ethical approval was obtained from the WHO Ethical Review Committee and local ethics
90 research review boards. Written informed consent was obtained from all participants.

91

92 *Mild cognitive impairment (MCI)*

93 MCI was ascertained based on the recommendations of the National Institute on Aging-
94 Alzheimer's Association¹⁶. We applied the identical algorithms used in previous SAGE
95 publications to identify MCI^{17,18}. Briefly, individuals fulfilling all of the following conditions
96 were considered to have MCI:

97 (a) Concern about a change in cognition: Individuals who replied ‘bad’ or ‘very bad’ to the
98 question “How would you best describe your memory at present?” and/or those who
99 answered ‘worse’ to the question “Compared to 12 months ago, would you say your memory
100 is now better, the same or worse than it was then?” were considered to have this condition.

101 (b) Objective evidence of impairment in one or more cognitive domains: was based on a <-1
102 SD cut-off after adjustment for level of education and age. Cognitive function was assessed
103 through the following performance tests: word list immediate and delayed verbal recall from
104 the Consortium to Establish a Registry for Alzheimer's Disease¹⁹, which assessed learning
105 and episodic memory; digit span forward and backwards from the Weschler Adult
106 Intelligence Scale²⁰, that evaluated attention and working memory; and the animal naming
107 task, which assessed verbal fluency.

108 (c) Preservation of independence in functional abilities: was assessed by questions on self-
109 reported difficulties with basic activities of daily living (ADL) in the past 30 days²¹. Specific
110 questions were: “How much difficulty did you have in getting dressed?” and “How much
111 difficulty did you have with eating (including cutting up your food)?” The answer options
112 were none, mild, moderate, severe, and extreme (cannot do). Those who answered either
113 none, mild, or moderate to both of these questions were considered to have preservation of
114 independence in functional activities. All other individuals were deleted from the analysis
115 (935 individuals aged ≥ 50 years).

116 (d) No dementia: Individuals with a level of cognitive impairment severe enough to preclude
117 the possibility to undertake the survey were not included in the current study.

118

119 ***Loneliness***

120 As in a previous publication using the same dataset¹⁴, loneliness was assessed with the
121 question “Did you feel lonely for much of the day yesterday?” with answer options ‘yes’ or
122 ‘no’.

123

124 ***Control variables***

125 The control variables were selected based on past literature²² and included age, sex, wealth
126 quintiles based on income, education (years), physical activity, alcohol use in the past 30
127 days, smoking (never, past, current), social cohesion, depression, diabetes, hypertension, and
128 stroke. Levels of physical activity were assessed with the Global Physical Activity
129 Questionnaire and were classified as low, moderate, and high based on conventional cut-
130 offs²³. As in a previous SAGE publication²⁴, a social cohesion index was created based on 9
131 questions on the participant’s involvement in community activities in the past 12 months
132 (e.g., attended religious services, club, society, union etc) with answer options ‘never
133 (coded=1)’, ‘once or twice per year (coded=2)’, ‘once or twice per month (coded=3)’, ‘once
134 or twice per week (coded=4)’, and ‘daily (coded=5)’. The answers to these questions were
135 summed and later converted to a scale ranging from 0-100 with higher scores corresponding
136 to higher levels of social cohesion (Cronbach’s $\alpha=0.79$). The actual questions can be found in
137 **Table S1** of the supplementary material. Questions based on the World Mental Health
138 Survey version of the Composite International Diagnostic Interview²⁵ were used for the
139 endorsement of DSM-IV depression²⁶. Diabetes and stroke were based solely on lifetime self-
140 reported diagnosis. Hypertension was defined as having at least one of: systolic blood
141 pressure ≥ 140 mmHg; diastolic blood pressure ≥ 90 mmHg; or self-reported diagnosis.

142

143 ***Statistical analysis***

144 The statistical analysis was performed with Stata 14.1²⁷. The analysis was restricted to those
145 aged ≥ 50 years as MCI is an age-related condition. We included the middle-aged in this
146 analysis as assessment of cognitive function and its risk factors at earlier ages is crucial for
147 the prevention of dementia owing to the fact that cognitive dysfunction can emerge up to 10
148 years before a dementia diagnosis²⁸, and there is burgeoning evidence that intervening in
149 mid-life is important²⁹⁻³². We stratified all analyses by age groups (i.e., middle-aged 50-64
150 years and ≥ 65 years) as it has been previously reported that the risk factors of MCI may differ
151 between these age groups³³. We conducted country-wise multivariable logistic regression
152 analysis to assess the association between loneliness (exposure) and MCI (outcome). The
153 regression analysis was adjusted for age, sex, wealth, education, physical activity, alcohol
154 consumption, smoking, social cohesion, depression, diabetes, hypertension, and stroke.
155 Furthermore, in order to assess the between-country heterogeneity that may exist in the
156 association between loneliness and MCI, we calculated the Higgins's I^2 based on estimates
157 from each country. The Higgins's I^2 represents the degree of heterogeneity that is not
158 explained by sampling error with a value of $<40\%$ often considered as negligible and 40-60%
159 as moderate heterogeneity³⁴. A pooled estimate was obtained by random-effect meta-
160 analysis. All variables were included in the models as categorical variables with the
161 exception of age, years of education, and the social cohesion index (continuous variables).
162 The sample weighting and the complex study design were taken into account in the analyses.
163 Results from the regression analyses are presented as odds ratios (ORs) with 95% confidence
164 intervals (CIs). The level of statistical significance was set at $p < 0.05$.

165

166

167

168 **RESULTS**

169 The final analytical sample consisted of 19092 and 13623 people with preservation in
170 functional abilities aged 50-64 years (middle-aged adults) and ≥ 65 years (older adults),
171 respectively. The sample characteristics are provided in **Table 1**. The prevalence of MCI
172 ranged from 5.5% (Ghana) to 23.0% (China) among the middle-aged, while the range was
173 9.7% (Ghana) to 26.4% (China) among older adults. The ranges for loneliness were 4.1%
174 (China) to 15.2% (India) and 7.2% (China) to 20.4% (India) for middle-aged and older
175 adults, respectively. Among the middle-aged, the prevalence of MCI was higher among those
176 who claimed to be lonely in all countries with the exception of Mexico (**Figure 1**). For
177 example, in South Africa, the prevalence of MCI among lonely individuals was 19.2% while
178 this was only 5.9% among those who were not lonely. Among older individuals, the
179 prevalence of MCI was higher in lonely individuals (vs. not lonely) in all countries with the
180 most pronounced contrast being observed in Russia (30.5% vs. 11.6%) (**Figure 2**). The
181 country-wise association between loneliness and MCI estimated by multivariable logistic
182 regression among the middle-aged is shown in **Figure 3**. Overall, loneliness was associated
183 with a non-significant 1.43 (95%CI=0.93-2.21) times higher odds for MCI with a moderate
184 level of between-country heterogeneity ($I^2=63.0\%$). In terms of individual countries,
185 significant associations were observed in China (OR=1.51; 95%CI=1.08-2.09) and South
186 Africa (OR=3.87; 95%CI=1.72-8.71). As for older adults, based on the pooled estimate, there
187 was a significant association between loneliness and MCI (OR=1.52; 95%CI=1.12-2.07) with
188 a moderate level of between-country heterogeneity ($I^2=52.3\%$). In terms of individual
189 countries, significant association were found in China (OR=1.41; 95%CI=1.05-1.91), Mexico
190 (OR=1.81; 95%CI=1.06-3.09), South Africa (OR=2.48; 95%CI=1.12-5.51), and Russia
191 (OR=2.86; 95%CI=1.46-5.61).

192

193 **DISCUSSION**

194 ***Main findings***

195 In this large representative sample of adults aged ≥ 50 years from six LMICs, an overall non-
196 significant positive association between loneliness and MCI was found among middle-aged
197 adults (i.e., 50-64 years). However, at the country level, significant associations were
198 observed in China and South Africa. In older adults (i.e., ≥ 65 years) overall, loneliness was
199 associated with a significant 1.52 times higher odds for MCI, and significant associations
200 were observed in China, Mexico, South Africa, and Russia. Taken together, these findings
201 suggest that those who suffer from loneliness in LMICs may be at increased odds for MCI.

202 ***Interpretation of the findings***

203 The findings from the present study support and add to the findings of the limited existing
204 literature on this topic.

205 https://onlinelibrary.wiley.com/doi/full/10.1002/gps.5304?casa_token=8Wt_SzO2jx0AAAA

206 [A%3Aa0fCu1MoqKtFA-3yg_p0lFQaoJb6sK-](https://onlinelibrary.wiley.com/doi/full/10.1002/gps.5304?casa_token=8Wt_SzO2jx0AAAA)

207 [DpBUu1KmWCJeWX73LNt2ygTXhLaoaWu8_PpkCRJOhST3f](https://onlinelibrary.wiley.com/doi/full/10.1002/gps.5304?casa_token=8Wt_SzO2jx0AAAA)

208 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6721226/>

209 <https://pubmed.ncbi.nlm.nih.gov/30914351/> <https://academic.oup.com/ageing/article->

210 [abstract/49/4/599/5799038](https://pubmed.ncbi.nlm.nih.gov/27073010/) <https://pubmed.ncbi.nlm.nih.gov/27073010/> It supports the

211 existing literature by further identifying an association between loneliness and MCI across

212 multiple LMICs with this association being more consistent among older adults. As

213 previously described, there are likely several mechanisms that explain a higher odds of MCI

214 among those who suffer from loneliness, including loneliness triggering neural responses that

215 may directly influence the development of neurodegenerative conditions. Furthermore,

216 perceived social isolation (a lack of social connections and a risk factor for loneliness) can

217 induce augmented stress reactivity, which is associated with prolonged activation of the

218 hypothalamic-pituitary-adrenal axis and the sympathoadrenal system. This disrupted brain
219 response may further lead to sleep deprivation, dysregulation of the immune system,
220 increased levels of oxidative stress and over-expression of proinflammatory genes, which
221 may all lead to the development of MCI¹⁰. Moreover, loneliness is associated with health-
222 behavioral factors implicated directly and/or indirectly with MCI via cardiometabolic
223 disease¹⁰. Finally, loneliness may be a result of limited social interactions and this may lead
224 to cognitive decline via limited intellectual stimulation³⁵. For example, one systematic review
225 investigated the impact of social activities, social networks and social support on the
226 cognitive functioning of healthy older adults (50 years and over) and examined the influence
227 of different aspects of social relationships on various cognitive domains. A total of 39 studies
228 were included in the review and findings suggested a relationship between (1) social activity
229 and global cognition and overall executive functioning, working memory, visuospatial
230 abilities and processing speed but not episodic memory, verbal fluency, reasoning or
231 attention; (2) social networks and global cognition but not episodic memory, attention or
232 processing speed; and (3) social support and global cognition and episodic memory but not
233 attention or processing speed.

234 <https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-017-0632-2>

235

236 It is important to note some nuanced findings in the present analyses, specifically, a more
237 consistent association between loneliness and MCI in older adults than middle-aged adults.
238 This may be explained by the possibility that older adults may have been exposed to
239 loneliness for a greater length of time than middle-aged adults and prolonged exposure to a
240 “health correlate” is likely to have a greater impact on health outcomes. However, future
241 research is needed to test this hypothesis. Second, older adults are more likely to have fewer
242 social networks than middle-aged adults^{36,37} and thus may experience loneliness to a greater

243 extent than middle aged adults. Indeed, the prevalence of loneliness was higher among those
244 aged ≥ 65 years than in those aged 50-64 years in our study.

245

246 Furthermore, we found a moderate level of between-country heterogeneity in the association
247 between loneliness and MCI. Although the reasons for this between-country heterogeneity is
248 unknown, several hypotheses may be proposed. For example, given that loneliness may lead
249 to higher risk for MCI via unhealthy behaviors, it is possible that lonely individuals in some
250 countries may be more prone to engage in unhealthy behaviors as a coping strategy against
251 loneliness. Furthermore, some of these unhealthy behaviors may increase risk for
252 cardiovascular diseases which is a known risk factor for cognitive decline.

253 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3245189/> In countries such as South Africa
254 where the prevalence of obesity and hypertension have been reported to be extremely high,
255 <https://pubmed.ncbi.nlm.nih.gov/29169587/> it is possible that unhealthy behavior as a result
256 of loneliness may act synergistically with pre-existing cardiovascular risk factors and lead to
257 a particularly increased risk for MCI via cardiovascular diseases. Indeed, in our study, we
258 found that the association between loneliness and MCI was particularly strong in South
259 Africa. However, these hypotheses are purely speculative and thus, further studies on the
260 reasons underlying the between-country heterogeneity should be conducted.

261

262 ***Policy implications***

263 Considering the present findings and those of other research, it may be prudent to implement
264 policy and intervention to reduce loneliness to aid in the prevention of MCI and ultimately
265 dementia. Four primary intervention strategies have been identified to reduce loneliness
266 including: 1) improving social skills, 2) enhancing social support, 3) increasing opportunities
267 for social contact, and 4) addressing maladaptive social cognition³⁸. It would be prudent for

268 any intervention or policy change aiming to reduce loneliness to focus on one or more of
269 these tenants.

270

271 ***Strengths and limitations***

272 The use of large representative samples across multiple LMICs and the stratification by age
273 are clear strengths of the present study. However, findings must be interpreted in light of the
274 study limitations. First, since the study was not designed to generate clinical diagnoses of
275 dementia, our analytical sample could have included some individuals with mild dementia.
276 However, it is reassuring that the prevalence of MCI in our study was within previously
277 reported figures³⁹. Second, loneliness was measured utilizing a single item and data on the
278 duration of this condition was not available. Finally, the study was cross-sectional in nature,
279 and thus, it is not known whether loneliness increased the odds for MCI or vice versa. For
280 example, it is possible for people with MCI to have difficulties socializing, and this may lead
281 to loneliness.

282

283 ***Conclusions***

284 In this large representative sample of middle-aged and older adults, we found that older
285 adults who suffer from loneliness have a significantly higher odds for MCI in LMICs overall.
286 An overall significant association was not found among the middle-aged but at the individual
287 country level, significant associations were found in China and South Africa. It may be
288 prudent to consider reducing loneliness in LMICs to aid in the prevention of MCI and
289 ultimately dementia.

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291

292

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407

Table 1 Sample characteristics by age group

Characteristic		China	Ghana	India	Mexico	Russia	South Africa
Age 50-64 years		N=7721	N=2297	N=3980	N=891	N=1946	N=2257
Mild cognitive impairment	Yes	23.0	5.5	8.2	17.8	5.9	7.1
Loneliness	Yes	4.1	8.2	15.2	13.7	6.8	9.2
Age (years)	Mean (SD)	56.6 (7.3)	56.2 (7.6)	56.0 (6.0)	56.0 (6.0)	56.0 (5.2)	56.0 (7.8)
Sex	Male	51.5	52.8	51.1	48.0	44.4	46.4
Education (years)	Mean (SD)	6.2 (7.3)	5.5 (10.2)	4.1 (7.5)	5.6 (6.6)	12.2 (3.7)	6.4 (9.3)
Physical activity	High	50.7	68.9	61.2	49.5	70.4	32.8
	Moderate	25.9	12.3	21.4	20.8	13.8	11.8
	Low	23.4	18.8	17.4	29.6	15.8	55.4
Alcohol consumption	Yes	26.4	34.1	7.6	33.3	42.0	15.6
Smoking	Never	62.0	76.6	46.6	60.8	61.5	66.1
	Current	32.9	9.8	49.7	22.0	30.5	25.6
	Former	5.1	13.6	3.7	17.3	8.0	8.4
Social cohesion index ^a	Mean (SD)	18.8 (18.3)	46.0 (35.3)	26.5 (22.0)	17.7 (21.0)	21.5 (15.5)	35.3 (30.8)
Depression	Yes	1.1	5.5	11.6	12.5	2.8	3.2
Diabetes	Yes	4.8	3.6	6.7	16.8	5.5	7.8
Hypertension	Yes	55.3	58.8	34.4	54.5	64.3	76.8
Stroke	Yes	2.0	1.4	1.4	2.4	2.6	3.2
Age ≥65 years		N=5094	N=1904	N=2211	N=1179	N=1820	N=1415
Mild cognitive impairment	Yes	26.4	9.7	12.5	17.3	14.8	11.3
Loneliness	Yes	7.2	13.4	20.4	17.8	15.2	10.7
Age (years)	Mean (SD)	72.1 (10.6)	74.0 (13.8)	71.2 (9.3)	73.9 (14.0)	73.8 (9.8)	72.7 (14.8)
Sex	Male	46.8	52.5	53.2	45.6	32.4	39.0
Education (years)	Mean (SD)	4.7 (9.2)	2.7 (8.7)	3.2 (7.1)	4.1 (8.9)	9.8 (6.2)	5.3 (10.8)

Physical activity	High	32.2	54.4	38.2	26.5	43.0	19.4
	Moderate	30.7	12.7	26.5	25.1	18.9	14.8
	Low	37.1	32.9	35.4	48.4	38.1	65.8
Alcohol consumption	Yes	17.2	27.0	5.9	12.0	21.8	10.7
Smoking	Never	67.9	73.6	42.6	59.3	80.2	67.7
	Current	23.4	11.8	51.8	17.8	9.6	20.0
	Former	8.7	14.6	5.6	22.9	10.3	12.3
Social cohesion index ^a	Mean (SD)	16.0 (19.7)	40.0 (37.5)	22.6 (21.8)	17.7 (29.5)	15.7 (17.0)	31.4 (34.2)
Depression	Yes	1.0	8.8	12.4	5.9	3.7	2.4
Diabetes	Yes	9.3	3.7	6.9	17.7	8.6	12.1
Hypertension	Yes	69.2	59.8	41.3	74.3	82.0	82.3
Stroke	Yes	4.4	3.1	2.2	6.2	6.8	3.9

Abbreviation: SD Standard deviation

Data are % unless otherwise stated.

^aThe social cohesion index ranged from 0 to 100 with higher scores representing higher levels of social cohesion.

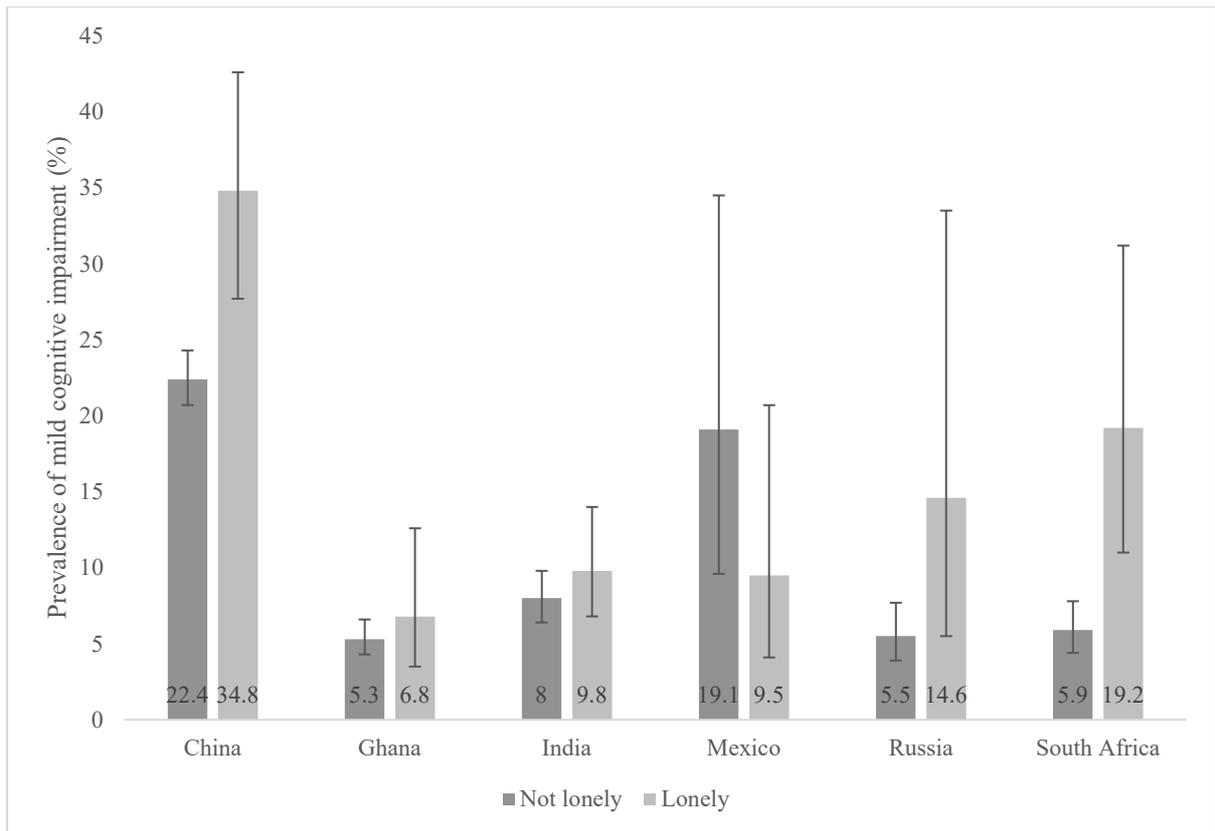


Figure 1 Prevalence of mild cognitive impairment by presence or absence of loneliness by country among adults aged 50-64 years
 Bars denote 95% confidence interval.

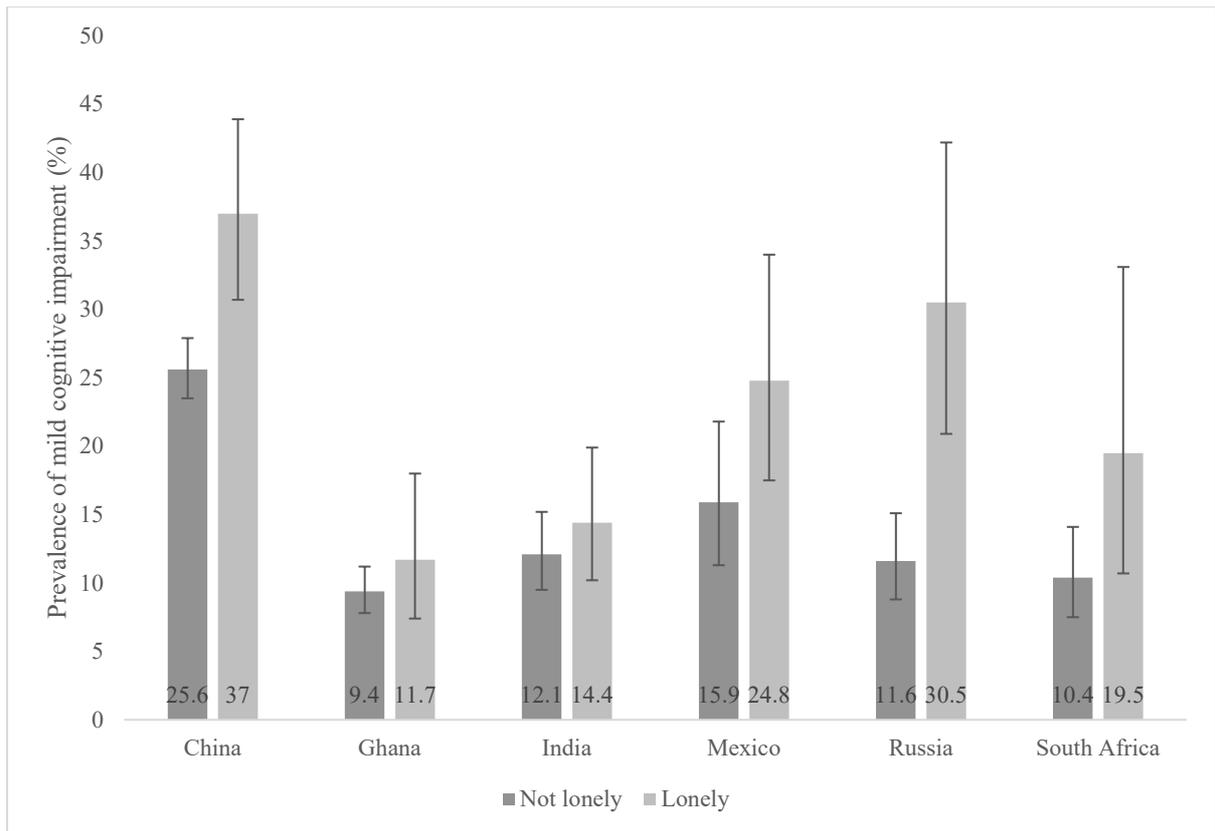


Figure 2 Prevalence of mild cognitive impairment by presence or absence of loneliness by country among adults aged ≥ 65 years
 Bars denote 95% confidence interval.

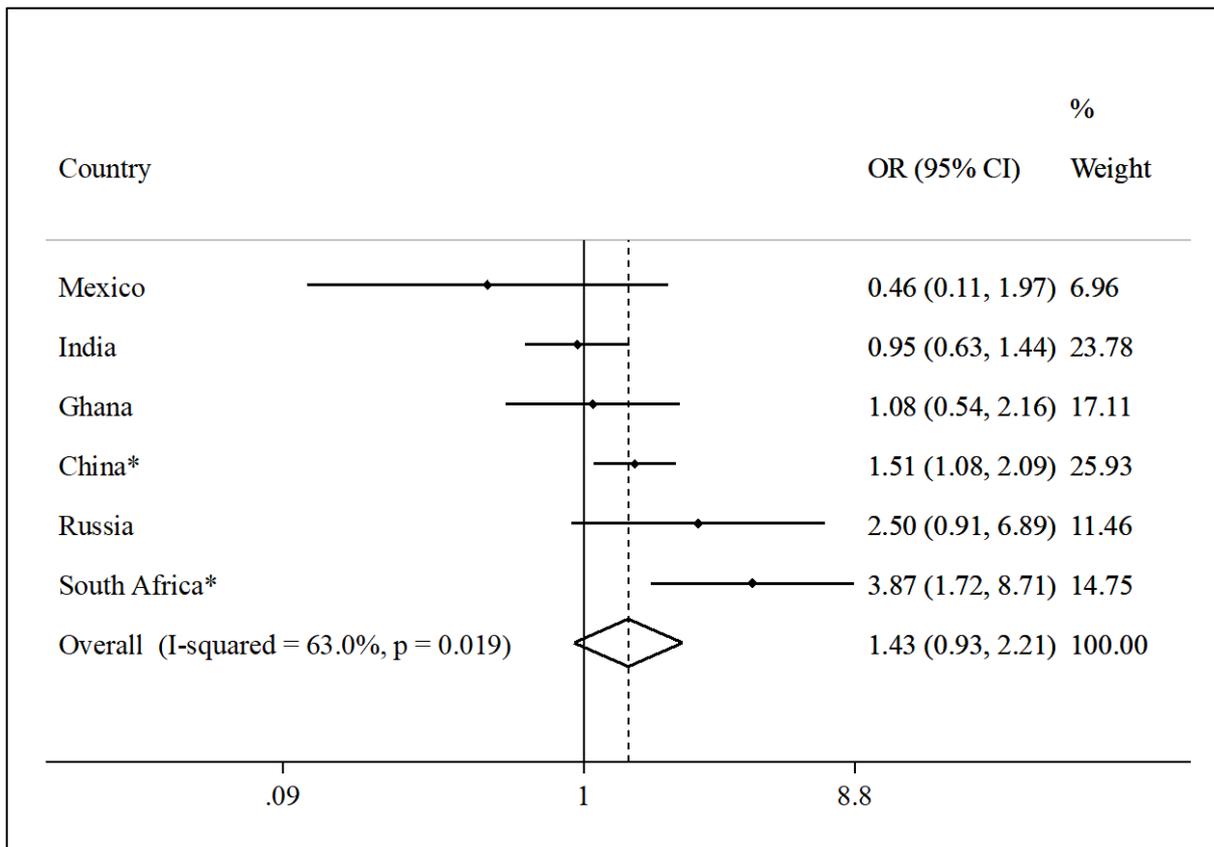


Figure 3 Country-wise association between loneliness and mild cognitive impairment (outcome) among adults aged 50-64 years estimated by multivariable logistic regression
Abbreviation: OR Odds ratio; CI Confidence interval
Models are adjusted for age, sex, wealth, education, physical activity, alcohol consumption, smoking, social cohesion, depression, diabetes, hypertension, and stroke.
Overall estimate was obtained by meta-analysis with random effects.
* p<0.05

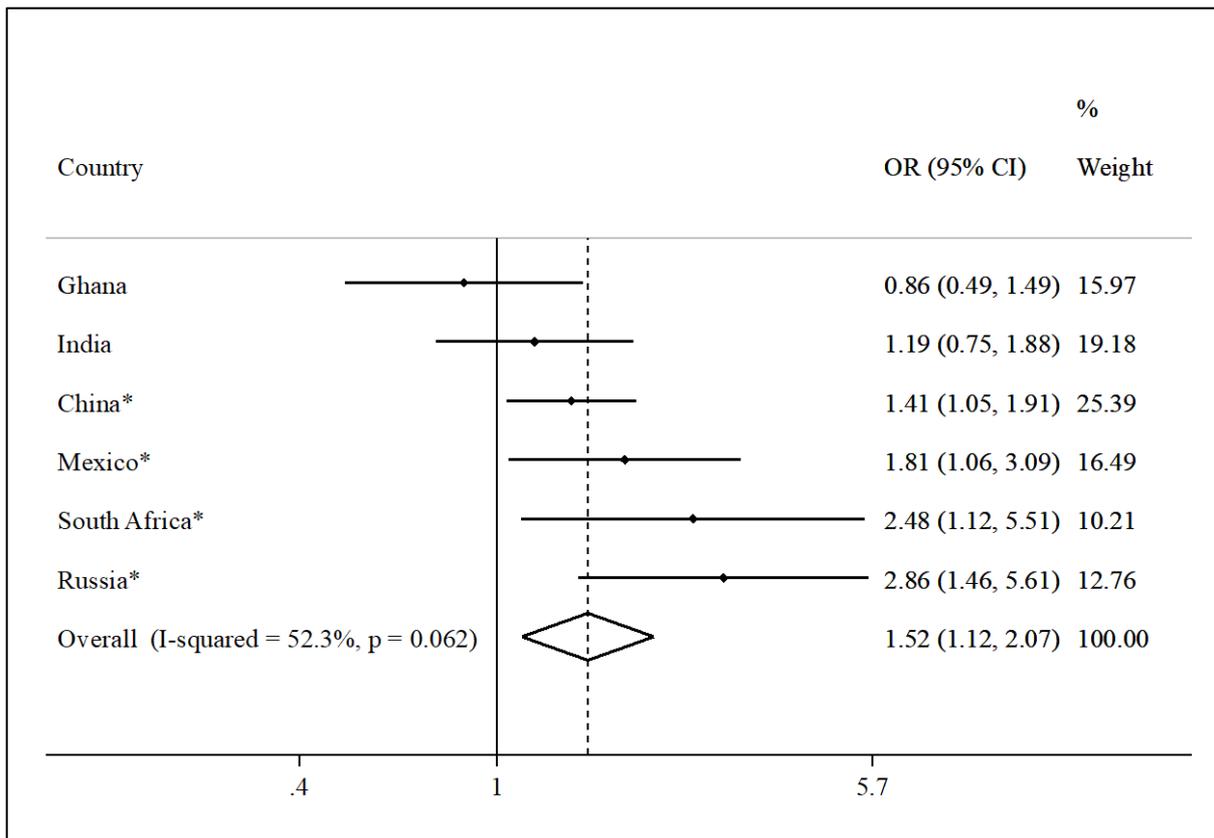


Figure 4 Country-wise association between loneliness and mild cognitive impairment (outcome) among adults aged ≥ 65 years estimated by multivariable logistic regression
 Abbreviation: OR Odds ratio; CI Confidence interval
 Models are adjusted for age, sex, wealth, education, physical activity, alcohol consumption, smoking, social cohesion, depression, diabetes, hypertension, and stroke.
 Overall estimate was obtained by meta-analysis with random effects.
 * $p < 0.05$

APPENDIX

Table S1 Questions used to assess social cohesion

How often in the last 12 months have you ...

- (1) attended any public meeting in which there was discussion of local or school affairs?
 - (2) met personally with someone you consider to be a community leader?
 - (3) attended any group, club, society, union or organizational meeting?
 - (4) worked with other people in your neighborhood to fix or improve something?
 - (5) had friends over to your home?
 - (6) been in the home of someone who lives in a different neighbourhood than you do or had them in your home?
 - (7) socialized with coworkers outside of work?
 - (8) attended religious services (not including weddings and funerals)?
 - (9) gotten out of the house/your dwelling to attend social meetings, activities, programs or events or to visit friends or relatives?
-