



## Social participation and mild cognitive impairment in low- and middle-income countries

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**Title:** Social participation and mild cognitive impairment in low- and middle-income countries

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## **ABSTRACT**

Social participation may theoretically decrease risk for mild cognitive impairment (MCI). However, to date, no study has specifically investigated the association between social

participation and MCI in LMICs, while the mediating role of loneliness is unknown. Thus, we investigated this association in a sample of adults aged  $\geq 50$  years from six low- and middle-income countries (LMICs; China, Ghana, India, Mexico, Russia, South Africa) using nationally representative datasets. We analyzed cross-sectional, community-based data from the Study on Global Ageing and Adult Health. A social participation score (range 0-10 with higher scores corresponding to greater levels of social participation) was created based on nine questions about involvement in community activities in the last 12 months. The National Institute on Ageing-Alzheimer's Association criteria were used to define MCI. Multivariable logistic regression and mediation analysis was performed. The analytical sample consisted of 32,715 individuals aged  $\geq 50$  years with preserved functional abilities [mean (SD) age 62.1 (15.6) years; 51.7% females]. In the overall sample, after adjustment for potential confounders, a one-unit increase in the social participation score was associated with a 13% decrease in odds for MCI (OR=0.87; 95% CI=0.82-0.93). Loneliness only explained 3.0% of the association. Greater levels of social participation were associated with a reduced odds for MCI, and this was not largely explained by loneliness. It may be prudent to implement interventions in LMICs to increase levels of social participation to aid in the prevention of MCI and ultimately dementia.

**Key Words:** cognition, social engagement, interpersonal relationships, epidemiology, adults, older adults

## **INTRODUCTION**

Dementia is a syndrome associated with an ongoing decline of brain functioning (National Health Service, 2020). Globally, dementia is one of the major causes of disability and impaired autonomy among older people, while it leads to significant burden to economic and social systems (Wimo, et al, 2017). Approximately, 55 million people live with dementia worldwide, with over 60% living in low- and middle-income countries (LMICs). Moreover, there are nearly 10 million new cases of dementia every year (World Health Organization, 2021). As the number of older people in the global population is rising, this number is predicted to increase to approximately 78 million in 2030, and 139 million in 2050 (World Health Organization, 2021). As there are no existing treatment methods to cure dementia, identification of risk factors known to predict the onset of dementia are of upmost importance.

Specifically, mild cognitive impairment (MCI) is a preclinical transitional state of dementia (Petersen, et al, 1999), for which targeted interventions may be possible.

MCI is defined as an early stage of memory loss or other cognitive ability loss (such as language or visual/spatial perception) in individuals who maintain the ability to independently perform most activities of daily living (Alzheimer's Association, 2021), and is associated with an increased conversion rate to dementia (Solfrizzi, et al, 2004). Importantly, the prevalence of MCI has been observed to be high in LMICs, and particularly in older adults (McGrattan, et al, 2021). Although several potential risk factors for MCI (e.g., low physical activity, stroke, depression) have been identified (Lara, et al, 2016), one potentially important but understudied risk factor for MCI is that of social participation.

Social participation is defined as a person's involvement in activities that provide interaction with others in the society or the community, and represents interpersonal interactions outside the home (Aroogh and Shahboulaghi, 2020). Social participation may lead to lower risk for MCI via increased mental stimulation and strategic thinking, as well as better synaptic density and neural growth (Zunzunegui, et al, 2003, Tomioka, et al, 2018). Furthermore, social participation may lead to reduction in loneliness (Zhang, et al, 2018), and loneliness in turn, may lead to MCI by triggering neural responses that may directly influence the development of neurodegenerative conditions. Indeed, loneliness has been identified as a risk factor for MCI (Lara, Martín-María, et al, 2019), also in LMICs (Smith, et al, 2021).

However, to date, no research has specifically examined the association between social participation and MCI in LMICs, while the potential mediating role of loneliness in this relationship is unknown. Therefore, the aim of the present study was to investigate the association between social participation and MCI, as well as the potential mediating role of loneliness, in a sample of 32,715 individuals aged  $\geq 50$  years from six LMICs. We hypothesized that lower levels of social participation will be associated with higher odds for MCI, with the association being partly mediated by loneliness.

## **METHODS**

The Global Ageing and Adult Health (SAGE) database was used for the present study. The survey methodology has been previously published elsewhere in detail (Kowal, et al, 2012). The survey was undertaken between 2007 and 2010 in six countries (China, Ghana, India, Mexico, Russia, South Africa). Importantly, these countries represent varying levels of socioeconomic and demographic transition. According to the World Bank classification when the survey was carried out, Ghana was the sole low-income country, whereas China and India were classified as lower middle-income countries. All other countries were upper middleincome countries. SAGE utilized a multistage clustered sampling design to ensure that the sample was nationally representative. The sample consisted of adults aged  $\geq 18$  years, and people aged  $\geq 50$  years were oversampled. A standardized questionnaire was utilized by trained interviewers, and face-to-face interviews were conducted (mean interview duration 2.5 hours). To achieve comparability between countries, standardized survey translation procedures were implemented. The survey response rates in each country were as follows: China 93%; Ghana 81%; India 68%; Mexico 53%; Russia 83%; and South Africa 75%. To take into account of the population structure as reported by the United Nations Statistical Division and non-response, sampling weights were created. Ethical approval was obtained from the WHO Ethical Review Committee as well as local ethics research review boards: China (Shanghai Municipal Centre for Disease Control and Prevention, Shanghai); Ghana (Ghana Medical School, Accra); India (International Institute of Population Sciences, Mumbai); Mexico (National Institute of Public Health, Cuernavaca); Russia (School of Preventive and Social Medicine, Russian Academy of Medical Sciences, Moscow); South Africa (Human Sciences Research Council, Pretoria). All participants provided written informed consent prior to participation in the survey.

### ***Mild cognitive impairment***

The National Institute on Aging-Alzheimer's Association recommendations were utilized to determine MCI (Albert, et al, 2011). Algorithms to identify MCI employed in previous SAGE publications were used in the present study (Koyanagi, et al, 2018, Koyanagi, et al, 2019). Those fulfilling all of the following criteria were categorized as having MCI: (a) Concern regarding change in cognition: This referred to answering 'bad' or 'very bad' to the question "How would you best describe your memory at present?" and/or answering 'worse' to the question "Compared to 12 months ago, would you say your memory is now better, the same or worse than it was then?"

(b) Impairment in at least one cognitive domains based on objective evidence: Objective cognitive function tests included the following: the Consortium to Establish a Registry for Alzheimer's Disease word list immediate and delayed verbal recall (Morris, et al, 1989), which measures both learning and episodic memory; the animal naming task (Morris, et al, 1989), which assesses verbal fluency; Weschler Adult Intelligence Scale forward and backwards digit span (Tulsky and Ledbetter, 2000), which examines working and attention memory. A result of under -1 SD cut-off after adjustment for level of education, age, and country, for any of these tests corresponded to fulfilling this criterion.

(c) Preserved independence in functional abilities: This was examined by utilizing questions on self-reported difficulties in basic activities of daily living (ADL) over the last 30 days (Katz, et al, 1963). The actual questions were: "How much difficulty did you have in getting dressed?" and "How much difficulty did you have with eating (including cutting up your food)?" Response categories were 'none', 'mild', 'moderate', 'severe', and 'extreme (cannot do)'. Those who reported either 'none', 'mild', or 'moderate' to both of these questions were categorized as having preservation of independence in functional activities. All other individuals were removed from the analysis (935 people aged  $\geq 50$  years).

(d) Absence of dementia: Individuals who were unable to undertake the survey due cognitive impairment were not included in the study.

### ***Social participation***

Following a protocol from previously published SAGE literature, a social participation score was derived utilizing nine questions relating to participant's involvement in community activities over the previous 12 months (e.g., attended religious services, society, club, union

etc.). Response options included ‘never (coded=1)’, ‘once or twice per year (coded=2)’, ‘once or twice per month (coded=3)’, ‘once or twice per week (coded=4)’, and ‘daily (coded=5)’ (Ma, et al, 2021). Responses were added and transformed to a scale ranging from 0-10 (Cronbach’s  $\alpha=0.79$ ) with 10 corresponding to the highest level of social participation and 0 the lowest (See **Table S1** of the supplementary material for all questions). The variable on social participation was also divided into quartiles and used as such in some analyses.

### ***Control variables***

Previous literature was consulted to select control variables (Lara, Caballero, et al, 2019, Smith, et al, 2021). The following variables were included as controls: age, sex, wealth quintiles based on income, education (years), physical activity, alcohol use in the last 30 days, smoking status (never, past, current), depression, diabetes, hypertension, and stroke. Levels of physical activity were derived from the Global Physical Activity Questionnaire and were classified as low, moderate, and high using conventional cut-offs, which are provided in **Table S2** of the Appendix (Bull, et al, 2009). Questions derived from the World Mental Health Survey version of the Composite International Diagnostic Interview (Kessler and Üstün, 2004) were used to identify DSM-IV depression (American Psychiatric Association, 2013) (full details are provided in **Table S3** of the Appendix). The presence of diabetes and stroke were based on self-reported diagnosis. Hypertension was defined as having either a systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg; or self-reported diagnosis.

### ***Statistical analysis***

Statistical analyses were performed in Stata 14.2 (Stata Corp LP, College station, Texas). MCI is an age-related condition, and thus, the analysis was only carried out on those aged  $\geq 50$  years. The difference in sample characteristics by level of social participation was tested by Chi-squared tests and Student’s *t*-tests for categorical and continuous variables, respectively. Multivariable logistic regression analysis was used to assess the association between social participation (exposure) and MCI (outcome). In order to gain an understanding of the extent to which loneliness may explain the relation between social participation and MCI, we conducted mediation analysis. Loneliness was assessed with the question “Did you feel lonely for much of the day yesterday?” with answer options ‘yes’ or ‘no’. The mediation analysis was conducted using the *khb* (Karlson Holm Breen) command in Stata (Breen, et al, 2013). This method is applicable in logistic regression models and

decomposes the total effect of a factor into direct and indirect effects (i.e., the mediational effect). This method allows for the calculation of the mediated percentage, which is the percentage of the main association explained by the mediator. These analyses were also stratified by age groups (i.e., 50-64 and  $\geq 65$  years) and sex, and these stratified analyses were decided to be undertaken *a priori* as previous studies have shown that the correlates or risk factors of MCI differs by age or sex (Lara, et al, 2016, Lindgren, et al, 2019).

Country-wise analysis was also conducted, and to assess the degree of between-country heterogeneity in the association between social participation and MCI, we calculated the Higgins's  $I^2$  based on country-wise estimates. This corresponds to the degree of heterogeneity that is not due to sampling error, with values of 25%, 50%, and 75% frequently considered as heterogeneity levels of low, moderate, and high, respectively (Higgins, et al, 2003). Overall estimates were calculated based on country-wise estimates by fixed effects meta-analysis.

All regression analyses including the mediation analysis were adjusted for age, sex, wealth, education, physical activity, alcohol consumption, smoking, depression, diabetes, hypertension, stroke, and country, with the exception of the sex-stratified and country-wise analyses, which were not adjust for sex and country, respectively. To adjust for country, we included dummy variables for each country in the model, as has been done in previous SAGE publications (Koyanagi, et al, 2018, Koyanagi, et al, 2014). The sample weighting and the complex study design were accounted for in all analyses. Results from the regression analyses are shown as odds ratios (ORs) with 95% confidence intervals (CIs). The level of statistical significance was set at  $P < 0.05$ .

## RESULTS

The final analytical sample consisted of 32,715 individuals [China  $n=12,815$  (6812 females and 6003 males); Ghana  $n=4201$  (1999 females and 2202 males); India  $n=6191$  (3033 females and 3158 males); Mexico  $n=2070$  (1234 females and 830 males); Russia  $n=3766$  (2429 females and 1337 males); South Africa  $n=3672$  (2099 females and 1573 males)] aged  $\geq 50$  years with preservation in functional abilities. The mean (SD) age was 62.1 (15.6) years and 51.7% were females. The overall prevalence (95%CI) of MCI was 15.3% (14.4%-16.3%). The sample characteristics are provided in Table 1. Low levels of social participation were associated with higher prevalence of MCI, female sex, low levels of wealth and physical



activity, never smoking, hypertension, stroke, and loneliness, while they were also associated with older age and less years of education. The mean social participation scores (range 0-10) by sample characteristics are provided in Table S4 of the Appendix. The prevalence of MCI decreased with increasing levels of social participation in the overall sample, and also in the samples stratified by age groups and sex (Figure 1). For example, in the overall sample, among those in the lowest quartile, the prevalence of MCI was 20.9% but this decreased to 10% among those in the highest quartile. After adjustment for potential confounders, a one unit increase in the social participation score was associated with a 13% decrease in odds for MCI in the overall sample (OR=0.87; 95%CI=0.82-0.93) (Table 2). Estimates were similar for those aged 50-64 years and  $\geq 65$  years as well as males and females. The univariable association between the social participation score or potential confounders and MCI are shown in **Table S5** of the Appendix. Country-wise analysis showed that social participation is negatively associated with MCI (i.e., OR<1) in all countries although statistical significance was not reached in all countries (**Figure 2**). The overall estimate was OR=0.90 (95%CI=0.86-0.94) with a low level of between-country heterogeneity ( $I^2=22.9\%$ ). Finally, mediation analysis showed that loneliness only explained a very small proportion of the association between social participation and MCI (**Table 3**). Specifically, loneliness explained 3.0% of the association in the overall sample, 4.2% in those aged  $\geq 65$  years, and 5.9% among females.

## **DISCUSSION**

### ***Main findings***

This present large multi-country study among middle-aged and older aged adults from multiple LMICs found that after controlling for potential confounders, a one-unit increase in the social participation score (range 0-10) was associated with a 13% decrease in the odds for MCI in the overall sample (OR=0.87; 95%CI=0.82-0.93), and a low level of between-country heterogeneity was observed. Interestingly, loneliness explained just 3.0% of the association in the overall sample. However, it is important to note that the present study was cross sectional in nature, and thus, the direction of the association could not be determined.

### ***Interpretation of the findings***

To the best of the authors' knowledge, this one of the first studies to demonstrate an association between higher levels of social participation and a reduced odds for MCI. There

are several plausible pathways that likely explain this association. While loneliness can theoretically be a mediator, we found that it only explained a very small proportion of this association. Therefore, other mechanisms are likely to be more important. First, social engagement may result in preservation of or improvement in cognitive function via increased mental stimulation and strategic thinking, as well as better synaptic density and neural growth (Zunzunegui, et al, 2003, Tomioka, et al, 2018). Second, social participation may increase levels of social support (Cohen, 2004), and social support in turn, may increase disease resistance owing to improved physiological function (e.g., immune and neuroendocrine systems) (Skoog, et al, 1996), consequently reducing the risk of developing cardiovascular diseases, which may increase risk for MCI (Roberts, et al, 2013). Finally, perceived social isolation (a lack of social connections), which may be the consequence of lack of social participation, can induce augmented stress reactivity, which is associated with prolonged activation of the hypothalamic-pituitary-adrenal axis and the sympathoadrenal system. This represents a disrupted brain response and likely induces sleep deprivation, dysregulation of the immune system, increased levels of oxidative stress and over-expression of proinflammatory genes, and these all have the potential to increase risk of MCI (Lara, Martín-María, et al, 2019).

### ***Implications of the study findings***

Findings from the present study suggest that interventions to increase social participation in LMICs may be a useful strategy to aid in the prevention of MCI and ultimately dementia. To achieve this, multidimensional initiatives should be considered. For example, those focusing on social (e.g., cultural recreation, volunteering opportunities), psychosocial (e.g., well-being, quality of life), and material (e.g., access to public transportation) aspects could be broadly introduced, all of which could be significant contributors to increasing social participation (Ma, et al, 2021). Findings from this study also suggest that interventions should look beyond subjective experiences of loneliness and aim to promote broader social participation in communities.

Finally, interventions that aim to increase group physical activity participation may be particularly beneficial to promote social participation, and to prevent MCI. Such interventions have been shown to increase interpersonal interactions and connections (Franke, et al, 2021), while physical activity itself may lead to reduction in risk for MCI or dementia (Gallaway, et al, 2017).

### ***Strengths and limitations***

The use of large representative datasets of middle-aged and older adults from six LMICs are clear strengths of this study. However, the results should be interpreted in light of the study's limitations. First, the majority of variables were self-reported, potentially introducing recall and social desirability bias into the findings. Second, the study was cross-sectional in nature and thus, it is not possible to determine the direction of the association. For example, it is possible that MCI reduces social participation (Amano, et al, 2020), such that cognitive problems make it difficult to organize, find, and attend social events. Third, the sample did not include institutionalized individuals, and therefore, the results are not generalizable to this population. Finally, the 'MCI' group was not identified using clinical assessment but through proxy measures. Thus, it is possible for people with mild forms of dementia to have been included in our study sample. Finally, the variable on loneliness only referred to feelings of loneliness in the day prior to the survey. Thus, it is possible for the results to differ if a different timeframe was used.

### ***Conclusions***

Higher levels of social participation were associated with reduced odds for MCI in a sample of middle-aged and older adults in LMICs, but this association was only minimally explained by loneliness. Future studies of a longitudinal nature are now required to determine the direction of the observed association, and to provide insight into potential causality. If confirmed by longitudinal studies, interventions in LMICs to increase levels of social participation may aid in the prevention of MCI and ultimately dementia.

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