

# Association between baseline Mini-Mental State Examination score and dementia incidence in a cohort of oldest old

Associação entre a pontuação inicial do Miniexame do Estado Mental e a incidência de demência em uma coorte de longevos

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## ABSTRACT

**Background:** The Brazilian population has aged rapidly. The oldest old, defined as persons aged 80 years or older, is the fastest growing segment of the Brazilian population. Several instruments have been used to assess the cognitive performance of the older people and predict dementia. One of the most commonly used is the Mini-Mental State Examination (MMSE). **Objective:** The aim of this study was to investigate the relationship between baseline MMSE score and the incidence of dementia in a Brazilian cohort of independent oldest old. **Methods:** Sociodemographic data and serial cognitive assessment of 248 older adults were analyzed. **Results:** Mean follow-up time of subjects was 4.0(±1.9) years, 71.4% were women, and mean MMSE score at entry was 25(±3.5). Mean MMSE scores at baseline were significantly higher ( $p=0.001$ ) in the cognitively intact group than in those who developed dementia. The logistic regression showed that for a one point increase in MMSE score at baseline there was a 10% reduction in the probability of dementia. **Conclusions:** In the Brazilian scenario of a rapidly growing population of oldest old, the extensive use of the MMSE gives rise to the need not only to determine its effectiveness for screening dementia, but also to interpret its score in terms of future conversion to dementia.

**Keywords:** Dementia; Incidence; Aged, 80 and over.

## RESUMO

**Antecedentes:** A população brasileira envelheceu rapidamente. Os longevos, definidos como pessoas com 80 anos ou mais, são o segmento da população brasileira que mais cresce. Diversos instrumentos têm sido usados para avaliar o desempenho cognitivo de idosos e para prever demência. Um dos instrumentos mais utilizados é o Miniexame do Estado Mental (MEEM). **Objetivo:** Nosso objetivo foi investigar a relação entre a pontuação inicial do MEEM e a incidência de demência em uma coorte brasileira de idosos longevos independentes. **Métodos:** Foram avaliados dados de 248 idosos por meio de um questionário sociodemográfico e de avaliações cognitivas seriadas. **Resultados:** O tempo médio de acompanhamento dos participantes foi de 4,0 (±1,9) anos. Eram mulheres 71,4% deles e a pontuação média do MEEM na entrada foi de 25 (±3,5) pontos. As pontuações médias do MEEM no início do estudo foram significativamente maiores ( $p=0,001$ ) no grupo cognitivamente intacto do que naqueles que desenvolveram demência. A regressão logística mostrou que, para cada ponto a mais na pontuação do MEEM no início do estudo, houve redução de 10% na probabilidade de desenvolver demência. **Conclusões:** No cenário brasileiro de rápido crescimento da população de idosos longevos, o uso da ferramenta cognitiva mais amplamente utilizada cria a necessidade de determinar não apenas sua eficácia no rastreamento da demência, mas também de interpretar seu escore considerando-se a futura conversão para demência.

**Palavras-chave:** Demência; Incidência; Idoso de 80 Anos ou mais.

## INTRODUCTION

Demographic changes and the increase in life expectancy have changed the profile of the Brazilian population, making it increasingly important to control risk factors for negative

outcomes, prevent morbidities, and promote early interventions to improve the quality of life of the elderly population<sup>1,2</sup>.

The oldest old, defined as persons aged 80 years or older, is the fastest growing segment of the population and the group with the greatest susceptibility to medical comorbidities,

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**Conflict of interest:** There is no conflict of interest to declare.

**Authors' contribution:** DYH: designed the study, collected and analyzed data; AFJ: analyzed data and wrote the paper; LMQA: revised the paper; CMAF: revised the paper; ABT: collected data and revised the paper; MSC: designed the study, analyzed data and revised the paper.

**Support:** This work was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (2011/12753-8) (2014/04398-1).

Received on November 29, 2020; Received in its final form on February 09, 2021; Accepted on February 15, 2021.



dependence, and mortality<sup>3,4</sup>. Although many oldest old can remain physically and cognitively independent<sup>5</sup>, the risk of dementia increases with age<sup>6</sup>. Dementia is a growing challenge worldwide and the focus of a constant search for effective ways of identifying and controlling its consequences<sup>7,8</sup>, including the high costs associated with the disease<sup>9</sup>.

A number of different models<sup>10,11</sup> and instruments<sup>12</sup> have been developed and used to assess the cognitive performance of older people and to predict dementia. One of the most widely used instruments is the Mini-Mental State Examination (MMSE)<sup>13,14</sup>. The scale has been translated and validated for use in numerous countries, but interpretation of its results is influenced by several factors<sup>15,16</sup>. Education is one of the factors affecting MMSE performance<sup>17,18,19</sup> and should be considered when interpreting the results. In other countries, performance on the MMSE has been shown to be a predictor of dementia and subsequent mortality in the oldest old<sup>20</sup>. In Brazil, there are no studies that confirm these data in oldest old. Therefore, the present study investigated the relationship between baseline MMSE score and dementia incidence in a cohort of independent oldest old.

## METHODS

The “Projeto Longevos” is a cohort study in which functionally independent older people aged 80 years or older living in the community have been invited to participate in an annual global geriatric assessment by the Department of Geriatrics and Gerontology of the Universidade Federal de São Paulo since 2010. They were invited through advertisements on radio, television, magazines, newspapers in the neighborhood or through personal contact (family members, neighbors, and friends)<sup>21</sup>.

For this study, oldest old without suspicion or diagnosis of cognitive impairment after a 1-year follow-up and who had undergone at least two previous annual evaluations were included. Other criteria for inclusion were compensated chronic diseases, no cancer, and no history of cardiovascular events or hospitalizations in the past six months. Individuals diagnosed with cognitive impairment after stroke or who had persistent depression during follow-up were excluded. A total of 248 subjects were selected for analysis. The MMSE<sup>22</sup> was applied systematically by trained geriatricians, and sociodemographic and clinical data were also collected.

A diagnosis of dementia was suspected if the subject presented a decline in performance on the MMSE<sup>22</sup>, the Clock Drawing Test<sup>23</sup>, verbal fluency<sup>24</sup>, and activities of daily living (ADL)<sup>25</sup> and met DSM-V criteria<sup>26</sup>. The diagnosis was confirmed only if two or more trained geriatricians reached consensus after discussion of the data. The tools were applied sequentially and considered together to characterize cognitive decline.

For subjects who died during the study, death was confirmed by death certificate and/or information in medical records.

This study was approved by the Research Ethics Committee of the Universidade Federal de São Paulo and all subjects signed a free and informed consent form.

## Statistical analysis

Categorical variables were expressed as absolute and relative frequencies, while continuous variables were expressed using measures of central tendency. Associations between two categorical variables were assessed using the chi-square or Fisher’s exact test. The comparison of means between two groups was performed using Student’s *t*-test or the Mann-Whitney test depending on the presence of a normal or non-normal distribution, respectively. After checking for mean differences with ANOVA or Kruskal-Wallis test, the identification of groups with different means was performed via multiple comparisons of Duncan and Dunn-Bonferroni, respectively. Logistic regression was used to assess the influence of MMSE on dementia (dependent variable), adjusted for demographic and clinical characteristics (predictor variables). Initially, all predictor variables were included, then the non-significant variables at 5% level were excluded one by one in order of significance (backward method), except history of stroke and transient ischemic attack (TIA) (control variables). In addition, the fit of the final model was assessed using the Hosmer-Lemeshow test.

The final model showed the effect of MMSE adjusted for age, chronic diseases, stroke, and TIA. All statistical analyses were performed using the SPSS software version 20.0. The level of statistical significance of 0.05 was adopted.

## RESULTS

Data on 248 older adults were assessed. Mean follow-up time of subjects was 4.0 years (SD=1.9 years), with a minimum follow-up of 1 year (without dementia) and maximum of 7 years (Table 1).

**Table 1.** Distribution according to sociodemographic and clinical characteristics (n=248).

Gender — females, n (%)		177 (71.4)
Age, n (%)	80–84 years	134 (54.0)
	85–89 years	71 (28.7)
	≥90 years	43 (17.3)
Education — years (mean±SD)		4.9±4.3
Number of chronic diseases, n (%)	0–5	185 (74.6)
	≥6	63 (25.4)
Number of medications at baseline (mean±SD)		5.6±2.7
Use of anti-depressants at baseline, n (%)		58 (23.5)
History of stroke, n (%)		11 (4.4)
History of TIA, n (%)		12 (4.8)
MMSE (mean±SD)		25.0±3.5
Follow-up time (years) (mean±SD)		4.0±1.9

TIA: Transient Ischemic Accident.

In the sample of oldest old, 71.4% were women, 54.0% were aged 80–84 years, 74.6% had 0–5 chronic diseases, less than 5% had a history of stroke or AIT, 5.6 medications (SD=2.7) were taken on average, and 23.5% were taking antidepressants. Mean MMSE score at entry was 25 points (SD=3.5 points) and mean education was 4.9 complete years of formal study (SD=4.3 years).

As shown in Table 2, there was an association only between dementia and age ( $p<0.001$ ), with higher rates of demented individuals than cognitively intact individuals in both the 85–89 age group (45.2 *versus* 25.2% of the 80–84

age group) and  $\geq 90$  years (28.6 *versus* 15.0% of the 80–84 age group). Regarding cognition, there was a higher rate of cognitively intact subjects than demented individuals in the 80–84 age group (59.7 *versus* 26.2%).

Mean MMSE scores at baseline ( $p=0.001$ ) were significantly higher in the cognitively intact group than in the demented group (Table 3).

The MMSE score ( $p=0.034$ ), age ( $p=0.003$ ), and number of chronic diseases ( $p=0.031$ ) remained significant in the final model (Table 4). For every one point increase in the MMSE score at baseline, there was a 10% reduction in the

**Table 2.** Distribution of oldest old by characteristics, according to dementia.

	Cognitive Outcome				Total		p-value*
	Cognitively intact		With dementia		n	%	
	n	%	n	%			
Sex	206	100.0	42	100.0	248	100.0	
Male	59	28.6	12	28.6	71	28.6	0.993
Female	147	71.4	30	71.4	177	71.4	
Age	206	100.0	42	100.0	248	100.0	
80–84 years	123	59.7	11	26.2	134	54.0	<0.001
85–89 years	52	25.2	19	45.2	71	28.6	
$\geq 90$ years	31	15.0	12	28.6	43	17.3	
Number of chronic diseases	206	100.0	42	100.0	248	100.0	
0–5	149	72.3	36	85.7	185	74.6	0.069
$\geq 6$	57	27.7	6	14.3	63	25.4	
Use of antidepressants (baseline)	205	100.0	42	100.0	247	100.0	
Yes	46	22.4	12	28.6	58	23.5	0.393
No	159	77.6	30	71.4	189	76.5	
History of stroke	206	100.0	42	100.0	248	100.0	
Yes	8	3.9	3	7.1	11	4.4	0.404
No	198	96.1	39	92.9	237	95.6	
History of TIA	206	100.0	42	100.0	248	100.0	
Yes	9	4.4	3	7.1	12	4.8	0.433
No	197	95.6	39	92.9	236	95.2	

\*Chi-square or Fisher's exact test; TIA: Transient Ischemic Accident.

**Table 3.** Central tendency measures for education, Mini-Mental State Examination scores and number of medications used at baseline.

	Mean	Standard deviation	Minimum	Maximum	n	p-value*
Education (years)	4.9	4.3	0.0	32.0	248	
Cognitively intact	5.0	4.5	0.0	32.0	206	0.103
Demented	4.1	3.1	0.0	12.0	42	
MMSE	25.0	3.5	11.0	30.0	248	
Cognitively intact	25.4	3.4	14.0	30.0	206	0.001
Demented	23.5	3.6	11.0	29.0	42	
Number of medications (baseline)	5.6	2.7	0.0	14.0	248	
Cognitively intact	5.6	2.8	0.0	13.0	206	0.857
Demented	5.5	2.4	0.0	14.0	42	

\*Student's *t*-test.

probability of dementia, adjusted for the other characteristics in the model. Additionally, the oldest old in the 85–89 age group had a 3.96 times greater probability of having dementia than individuals in the 80–84 age group. This probability was similar to that found in the group aged  $\geq 90$  years (4.01 times higher). Also, the oldest old with  $\geq 6$  chronic diseases had a 68% lower probability of dementia than those with 0–5 chronic diseases. Additionally, the Hosmer-Lemeshow test showed a good fit of the model ( $p=0.077$ ).

## DISCUSSION

In the present study, the association between baseline MMSE score and dementia incidence in an oldest old cohort was investigated. The MMSE is the most commonly used cognitive tool worldwide, both for screening and aiding the clinical diagnosis of dementia<sup>27,28</sup>. The late-life risk models for the general population that included MMSE reached moderate predictive accuracy among the cohorts, but the total MMSE score alone was less strongly associated with dementia<sup>10</sup>. A Cochrane systematic review, published in 2015, also found no evidence that MMSE scores would be a good tool for identifying patients with mild cognitive impairment who could develop dementia<sup>29</sup>. However, in Sweden, a population-based sample showed that the MMSE score was associated with dementia and subsequent mortality even in very older people individuals<sup>20</sup>. In the population aged 60 or over in the city of São Paulo, Brazil, the number of ADL performed was an inverse predictor of cognitive decline, but the MMSE was not included in the model<sup>2</sup>. Hence, the present study is the first to include the MMSE score for diagnosing dementia in an oldest old population in Brazil. The results revealed that low baseline MMSE score, more advanced age, and lower number of chronic conditions were associated with a higher incidence of dementia on a multivariate analysis that included

other important factors (gender, use of antidepressants, and history of stroke or TIA). The association of a single test score with dementia incidence appears to be weaker compared to the association of longitudinal variability of scores. In the Brazilian scenario of a rapidly growing population of oldest old, the common use of the MMSE as a cognitive tool for this age group leads to the need not only to determine its effectiveness for screening dementia, but also to interpret the MMSE score considering future conversion from mild cognitive impairment into dementia states. The association of advanced age with dementia incidence was expected, given that the disease incidence increases exponentially with age. However, the finding of an association between fewer chronic diseases and dementia incidence was intriguing, although it may be explained by the nature of the diseases and not only by their number.

In Brazil, educational level is routinely taken into account as a factor when interpreting MMSE scores, but age is not considered<sup>30</sup>. The MMSE cut-off scores for different educational levels generally used in Brazil are those established in the 2003 study by Brucki et al.<sup>22</sup>. In the study, the age of the sample ranged from 16 to 92 years and mean age was 58.9 years ( $\pm 17.75$ ), although the proportion of oldest old included was relatively small. The strengths of the present study include the oldest old age group investigated, the longitudinal design, and standardization of the study protocols employed. The main limitation concerns the fact that other important variables were not included in the analysis of the association with dementia incidence. Future studies should be conducted to further elucidate these issues.

## ACKNOWLEDGEMENTS

We thank the patients and their families and carers for making this study possible.

**Table 4.** Results of multivariate logistic regression model.

	Initial model (n=247)		Final model (n=248)	
	Adjusted Odds Ratio (95%CI)	p-value	Adjusted Odds Ratio (95%CI)	p-value
MMSE	0.90 (0.81–1.01)	0.084	0.90 (0.82–0.99)	0.034
Female gender (ref.=male)	0.93 (0.40–2.17)	0.873	-	-
Age (ref =80–84 years)		0.001		0.003
85–89 years	4.50 (1.88–10.78)	0.001	3.96 (1.71–9.18)	0.001
$\geq 90$ years	4.84 (1.69–13.88)	0.003	4.01 (1.50–10.74)	0.006
Education (years)	1.02 (0.91–1.13)	0.791	-	-
$\geq 6$ chronic diseases (ref.=0–5)	0.28 (0.10–0.83)	0.022	0.32 (0.11–0.90)	0.031
Number of medications (baseline)	1.00 (0.86–1.15)	0.954	-	-
Use of antidepressants at baseline (ref.=no)	2.17 (0.87–5.40)	0.095	-	-
History of stroke (ref.=no)	2.76 (0.33–22.80)	0.345	2.35 (0.29–19.22)	0.426
History of TIA (ref.=no)	1.42 (0.17–11.88)	0.746	1.49 (0.18–12.30)	0.714

TIA: Transient Ischemic Accident.

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