Memory complaint in a middle-income country: a four-year longitudinal study in a cohort with low-education

Queixa de memória na comunidade em um país de renda média: um estudo longitudinal de quatro anos em uma coorte de baixa escolaridade

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Arq. Neuro-Psiquiatr. 2024;82(5):s00441787138.

Abstract

Background Memory complaints are frequent in older adults and are associated with higher risk of cognitive decline.

Objective To investigate the functional outcome of individuals with memory complaints followed up at primary care centers.

Methods Data were collected between 2016 e 2020 in primary health care centers in Brazil. Patients underwent the Brief Cognitive Screening Battery, and the Functional Activities Questionnaire.

Results The initial sample (2016) comprised 91 individuals classified into those with subjective cognitive decline (SCD, $n = 15$), mild cognitive impairment (MCI, $n = 45$), or dementia ($n = 31$). During follow-up, 8 individuals (8.8% of the initial sample) died and 26 (28.5% of the initial sample) were not found. Fifty-seven participants underwent clinical reassessment. Of 15 individuals with SCD, 7 were not found (46.7%), 4 (26.7%) progressed to MCI, and 4 (26.7%) remained stable. Of 45 individuals with MCI, 11 were not found (24.4%), 2 (4.4%) died, 6 (13.4%) progressed to dementia, 12 (26.7%) regressed to SCD, and 14 (31.1%) remained stable. Of 31 individuals with dementia, 8 were not found (25.8%), 6 (19.4%) died, 2 (6.5%) regressed to SCD, 7 (22.6%) regressed to MCI, and 8 remained stable (25.8%). Clinical improvement was due to the treatment

Keywords
- Cognitive Dysfunction
- Primary Health Care
- Dementia
- Memory Disorders

received
August 7, 2023
Received in its final form
March 04, 2024
accepted
March 23, 2024

DOI https://doi.org/10.1055/s-0044-1787138.
ISSN 0004-282X.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

of reversible causes, such as B12 hypovitaminosis and mood disorders. Older age, lower Mini-Mental State Examination, and higher scores of memory complaint, but not the use of benzodiazepines and of proton pump inhibitors, were predictors of functional status.

Conclusion Despite their limits (short sample size, missing data), these results support the idea that adequate screening, follow-up, and treatment of reversible causes of dementia in primary care are essential.

Resumo

Antecedentes Queixas de memória são frequentes em idosos e estão associadas ao maior risco de declínio cognitivo.

Objetivo Investigar o desfecho funcional de indivíduos com queixas de memória acompanhados em centros atenção primária.

Métodos Os dados foram coletados entre 2016 e 2020 em centros de atenção primária à saúde no Brasil. Os pacientes foram submetidos à Bateria Cognitiva Breve e ao Questionário de Atividades Funcionais.

Resultados A amostra inicial (2016) foi composta por 91 indivíduos, classificados como tendo declínio cognitivo subjetivo (DCS, $n = 15$), comprometimento cognitivo leve (CCL, $n = 45$), ou demência ($n = 31$). Durante o seguimento, 8 indivíduos (8,8% da amostra inicial) faleceram e 26 (28,5% da amostra inicial) não foram encontrados. Cinquenta e sete participantes foram submetidos à reavaliação clínica. Dos 15 indivíduos com DCS, 7 não foram encontrados (46,7%), 4 (26,7%) declinaram para CCL e 4 (26,7%) permaneceram estáveis. Dos 45 indivíduos com CCL, 11 não foram encontrados (24,4%), 2 (4,4%) morreram, 6 (13,4%) declinaram para demência, 12 (26,7%) evoluíram para DCS e 14 (31,1%) permaneceram estáveis. Dos 31 indivíduos com demência, 8 não foram encontrados, (25,8%), 6 (19,4%) morreram, 2 (6,5%) evoluíram para DCS e 7 (22,6%) para CCL; e 8 permaneceram estáveis (25,8%). A melhora clínica deveu-se ao tratamento de causas reversíveis, como hipovitaminose B12 e transtornos de humor. A idade avançada, a baixa pontuação no Mini-Exame do Estado Mental e os escores de queixa de memória mais altos, mas não o uso de benzodiazepínicos e inibidores da bomba de prótons, foram preditores de declínio funcional.

Conclusão Apesar de suas limitações (amostra pequena, dados ausentes), esses resultados corroboram que a triagem adequada, o acompanhamento e o tratamento de causas reversíveis de demência na atenção primária são essenciais.

Palavras-chave
- Disfunção Cognitiva
- Atenção Primária à Saúde
- Demência
- Transtornos da Memória

INTRODUCTION

Cognitive decline is common in older adults and follows a syndromic continuum, ranging from the individual's subjective perception of change in a cognitive domain (memory, language, visuospatial expression, among others) to the most advanced stages of dementia.[1] This continuum comprises the concept of subjective cognitive decline (SCD) and mild cognitive impairment (MCI).

Subjective cognitive decline is a cause of memory complaints and is defined as a self-perception of progressive cognitive decline, in comparison with the individual's preceding status, associated with normal performance on standardized neuropsychological tests.[2] Epidemiological studies indicate that SCD may represent a predementia stage of Alzheimer disease (AD),[3,4] with an increased risk of conversion to MCI and dementia, thus being considered a risk factor for objective cognitive disorders.[5] A meta-analysis has suggested that the annual progression rates of SCD to MCI and dementia are 7% and 2%, respectively.[4] A recent meta-analysis[6] found that the mean prevalence of SCD in community-based studies was 46% and confirmed that patients with SCD have an increased risk of developing MCI and dementia. The higher the level of education, income, and leisure activities, the lower the risk of conversion.[7] Interestingly, in this same series, 9.6% of SCD cases had functional decline but did not meet criteria neither for MCI nor for dementia.[7] Taken together, these data show that older adults with normal cognition or with SCD are at increased risk of subsequent development for MCI or dementia.[8]

Individuals with MCI present cognitive complaints associated with abnormal neuropsychological exams and

preserved independence for functional activities of daily life.[9] Mild cognitive impairment may be considered as a prodromal stage of AD, as subjects with memory deficits and biological evidence of AD pathophysiology with cerebrospinal fluid (CSF) biomarkers or amyloid imaging are prompt to develop AD dementia during follow-up.[10]

Several other risk factors have been associated with possible progression from MCI to dementia, such as older age, low education, previous history of stroke, cardiovascular risk factors (e.g., hypertension, diabetes), depression, and *Apolipoprotein E* genotype, among others.[8,11] The cognitive profile of MCI is also a risk factor, as individuals with amnestic MCI or multiple domain MCI have greater risk to convert to dementia.[12] In a Chinese study[13] with 245 individuals with MCI, 29.0% converted to dementia during the follow-up. In a recent longitudinal cohort,[7] 12.9% of MCI individuals progressed to dementia after 2 years. A meta-analysis demonstrated that the annual progression rate of MCI individuals to dementia was estimated at 12%.[4] In sum, MCI individuals are at increased risk of progressing to dementia over time.[14]

Few studies analyzed the outcome of individuals with memory complaints followed up at primary health care centers in low- and middle-income countries.[15] Most of the studies in the field were conducted in populations from high-income countries, with high educational level[16–18] and better control of cardiovascular risk factors, which may influence the rate of cognitive decline and conversion to dementia. This is a critical issue, as most of the global population at-risk to dementia live in low- and middle-income countries.[15,19] Moreover, these countries are facing a marked increase of aged populations. It is, therefore, essential to investigate which risk factors are associated with cognitive and functional decline in this scenario.

In Brazil, primary health care is performed by family health teams. Primary health care is a gateway to the public health service, facilitating and assuring the population's access to the health care network. Based on the principles of comprehensive health care, family health teams are responsible for health promotion, risk reduction, early detection, screening of preventable diseases, and also for treatment and rehabilitation.[20] From this perspective, the primary health care is the ideal setting for detecting and preventing cognitive decline, and thus contributing to the development of strategies targeting on the prevention of dementia. This is of particular interest in Brazil, as recent data show that the potential of dementia prevention is higher in Brazil than in high-income countries,[21,22] thus highlighting the need of strict control of risk factors at the primary health care.

The present study aimed to investigate the cognitive/functional outcome of a convenience sample of older individuals with amnestic complaints in primary health care, in a medium-sized municipality in Brazil. Individuals were followed longitudinally over four years, and we aimed to investigate the conversion of individuals into the following categories: SCD, MCI, and dementia. We also aimed to investigate the potential factors associated with cognitive/functional decline in the sample.

METHODS

Study design and ethical aspects

This is a longitudinal and observational study, conducted at Patos de Minas, a medium-sized municipality located in the state of Minas Gerais, southeastern Brazil. It has an estimated population of 154,641 inhabitants and a human development index of 0.765 (2021). This study was approved by the local Ethics Committee (number 1.733.241) and all participants or their legal representants signed the informed consent after clarification, prior to the enrolment in the study.

Inclusion and exclusion criteria

All patients were recruited at the Lagoa Grande basic health unit, in Patos de Minas; all of them were assessed by the same investigator (MLP). In the first phase of this study (March–September 2016),[23] we consecutively collected clinical and cognitive data from individuals of both sexes, aged 50 years or older, who presented inquired or spontaneous memory complaints during a general practice consultation. As a required inclusion criterion, all participants had to have a family member or close contact for independent assessment of functional abilities. Participants with previous established diagnosis of dementia, amyotrophic lateral sclerosis, multiple sclerosis, epilepsy, or stroke were not included. We did not include patients with antecedents of severe psychiatric disorders (schizophrenia or bipolar disorder). Patients who were not from the territory assigned to the family health unit were not included.

Procedures

Participants answered a semi-structured questionnaire, describing sociodemographic and clinical information. The following neuropsychological tests were applied: Memory Assessment Clinics Questionnaire - MAC-Q[24] (normal score: < 25); Mini-Mental State Examination – MMSE;[25] Figure Memory Test from the Brief Cognitive Screening Battery;[26] Semantic Verbal Fluency (animals/minute);[27] Clock Drawing Test;[28] and the scale of Instrumental Activities of Daily Living – IADL.[29]

All participants underwent the Neuropsychiatric Inventory Questionnaire (NPI-Q)[30] and a clinical interview with a general practitioner. Patients with a consistent history of symptoms of depression and/or anxiety persisting for 6 months or more were diagnosed with depression and/or anxiety, respectively (Diagnostic and Statistical Manual of Mental Disorders, fourth edition - DSM-IV).

Subjects underwent standard laboratory tests and brain computerized tomography to investigate reversible causes of cognitive impairment, in line with current guidelines.[31]

In the second phase of the study (February 2019–December 2020), we contacted by phone all the patients from the initial sample ($n = 91$) and invited them for a new clinical, cognitive, and functional reassessment, with the above-mentioned tools.

Sample classification

Based on clinical and neuropsychological data, participants were clinically re-classified into three main clinical categories:

- SCD: MAC-Q $\geq$ 25, normal scores on neuropsychological tests and preserved functional capacity;
- MCI: MAC-Q $\geq$ 25, abnormal score in the MMSE and/or in the semantic fluency test and alteration in another neuropsychological test (Figure Memory Test or Clock Drawing Test) and preserved functionality;
- Dementia: MAC-Q $\geq$ 25, abnormal score in the MMSE and/or in the semantic fluency test and deficit in another neuropsychological test (Figure Memory Test or Clock Drawing Test) and altered IADL ($>$ 5).

Of note, we adopted the same classification criteria from the first study.[27] For all tests, we considered the normative values for the Brazilian population, according to educational level.[25,27]

Statistical analyses

All statistical analyses were performed using the IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, United States) software, version 26.0. The normality of the sample was verified with the Shapiro-Wilk test. When necessary, we used the Mann-Whitney and Chi-square tests to compare continuous and categorical variables between independent groups, respectively.

We conducted a multivariate analysis with a multiple linear regression model to investigate the potential predictors of functional status, considering the second (longitudinal) score on the instrumental activities of daily living (IADL) as a dependent variable.

We computed a composite global cognition z-score,[32,33] by averaging standardized scores on the MMSE (total score), the delayed (5 minutes) recall on the figure memory test (FMT), and semantic fluency (animals). Taken that there is no maximum score for the semantic fluency, we considered two standard deviations above the mean as the maximum, as described elsewhere.[33]

We included the following factors as independent variables on the multiple linear regression model: age, schooling, and the baseline (2016) scores on the IADL, Global Cognition Z-score, MAC-Q, and the NPI-Q (total score).

Finally, we also calculated the relative risk (odds ratio) of MCI and of dementia associated with the following factors: use of proton-pump inhibitors or benzodiazepines, and diagnoses of arterial hypertension or diabetes.

RESULTS

The initial sample (2016) consisted of 91 individuals,[23] who were classified according to their clinical status into SCD (n = 15, 16.5%), MCI (n = 45, 49.4%), or dementia (n = 31, 34.1%).

Here, we present the detailed results from the second phase of the study, which was conducted between March and September 2020. Participants from the previous study were invited to undergo a new clinical assessment, that is, the population included in 2016 was re-evaluated after a mean follow-up of 44.5 $\pm$ 6.8 months, using the same initial protocol. Of these, 26 individuals (28% of the initial sample; 7 SCD, 11 MCI, and 8 dementia) were not found and, therefore, were not reassessed. Eight individuals (2 MCI individuals and 6 with dementia) died during the follow-up (2016–2020). The total loss in the follow-up was of 37.3% (n = 34; being 8 deaths and n = 26 loss of contact). The mortality rates for individuals with MCI and dementia were 4.4% (1%/year) and 19% (4.8%/year), respectively. Finally, 57 participants (therefore comprising the final sample of the present study) underwent new clinical and cognitive assessments. ►**Figure 1** presents the flowchart of the study.

►**Table 1** presents the sociodemographic data of the sample in the follow-up. Of note, reassessed patients (n = 57) did not differ from patients who died or were lost during follow-up (n = 34) in terms of age (p = 0.549), schooling (p = 0.159), sex distribution (p = 0.054), MAC-Q (p = 0.465), and MMSE (p = 0.77).

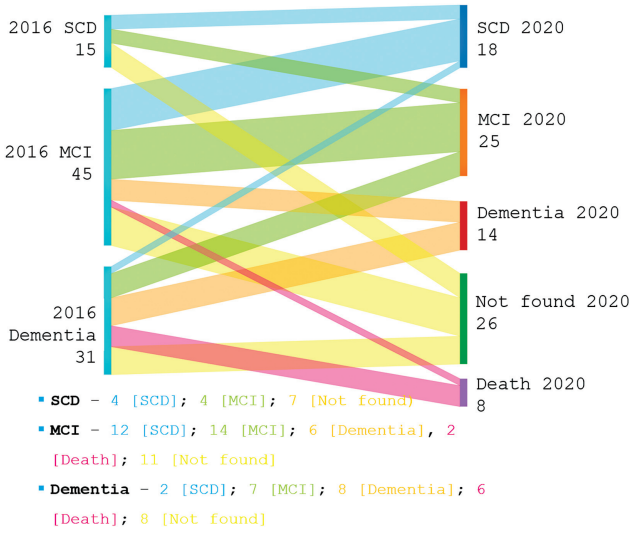
►**Table 2** describes the comorbidities of the participants. Descriptive data regarding the neuropsychological tests are shown in ►**Table 3**.

In 2016, 15 individuals were classified as SCD, and 8 of them were re-examined on follow-up (7 not found, 46.7%). After the reassessment of these individuals, 26.7% (n = 4) remained as SCD and 26.7% (n = 4) evolved to MCI.

Thirty-two out 45 individuals initially (2016) classified as MCI were assessed on the follow-up (11 not found, 24.4%; 2 died, 4.4%). Twelve (26.7%) regressed to SCD (of these, 5 had high blood pressure, 2 had diabetes, 4 had dyslipidemia, 5 had hypothyroidism, 4 had anxiety, and 3 had depression). These individuals were treated after the initial clinical evaluation, in 2016, and then 31.1% (n = 14) remained as MCI, while 13.3% (n = 6) converted to dementia during the follow-up. The annual rate of conversion to dementia was 3%.

The initial dementia group (2016) was composed of 31 individuals and 17 of them were re-examined (8 were not found, 25.8%; 6 died, 19.4%). Two individuals (6.4%) regressed to SCD. Both individuals presented anxiety and depression; one of them also had decompensated hypothyroidism and hypovitaminosis B12. Seven individuals (22.6%) regressed to MCI. All of them had anxiety and depression; 2 of them had hypothyroidism, and 2 had B12 hypovitaminosis. The comorbidities were diagnosed and treated after baseline assessment (2016). Eight individuals with dementia (25.8%) remained within this category. The data are shown in ►**Table 4**.

We conducted multiple linear regression to investigate the potential predictors of functional status, considering the score on the IADL (second measure) as a dependent variable. The model was statistically significant (R^2 = 0.56, F (6, 50) = 10.47, $p < 0.0001$). The following factors were retained as predictors of functional status: age (β = 0.34, 95% confidence interval [95%CI] 0.71–0.44; $p < 0.008$), MAC-Q score (β = 0.26, 95%CI 1.09–1.13; p = 0.018), Global Cognition Z-score (β = -0.25, 95%CI -25.5 to -0.17; p = 0.047), and the baseline score on the IADL (β = 0.26, 95%CI 0.009–0.57; p = 0.044) (see ►**Supplementary Material Table S1** for



Abbreviations: MCI, mild cognitive impairment; SCD, subjective cognitive decline.
Figure 1 Flowchart of the study.

details - https://www.arquivosdeneuropsiquiatria.org/wp-content/uploads/2024/03/ANP-2023.0179-Supplementary-Material.docx).

We calculated the relative risk (odds ratio) of MCI or dementia associated with the use of medications (proton-pump inhibitors and benzodiazepines), and with the diagnosis of hypertension or diabetes. None of these factors was associated with higher risk of MCI or dementia in our cohort.

DISCUSSION

Cognitive complaints are common in older adults and are a frequent cause of medical consultation at primary health care. The functional outcome of individuals with memory complaints is variable, as a subgroup of these individuals converts to dementia over time, while others remain stable or improve. The present study investigated the predictive factors associated with functional decline among individuals with memory complaints. Of note, our sample was composed of individuals with less education, in contrast with previous investigations conducted in populations with high education level.[16–18] This naturalistic longitudinal study found that older age, low MMSE scores, and the severity of memory complaints are strong predictors of functional status. We also identified that reversible causes of dementia are frequent, thus providing a window for treatment of patients, and improving their cognitive status. These are relevant results for clinical practice at primary health care, especially in low- and middle-income countries.

In our sample, 26.7% of SCD individuals converted to MCI, while 26.7% remained stable. There are three main groups of SCD: reversible SCD, stable SCD, and converters.[2] The small sample size and the high number of SCD individuals not found (46.7%) preclude a comparative analysis of risk factors specifically associated with functional decline among SCD individuals.

In the present study, 13.3% of MCI individuals converted to dementia during the follow-up, and the annual rate of conversion to dementia was 3%. The progression to dementia

Table 1 Sociodemographic data of the population ($n = 57$)

		Population ($n = 57$)
Sex (male/female)		11/46
Age (mean ± standard deviation)		71.1 ± 9.4
Schooling (in years; mean ± standard deviation)		5.49 ± 4.0
Family income (in Brazilian minimum wages): n (%)	1–2	42 (3.3%)
	3–5	12 (26.7%)
	6–10	3 (0.0%)
	> 10	0 (0.0%)
Marital status: n (%)	Unmarried	5 (20.0%)
	Married	29 (66.7%)
	Widow	4 (13.3%)
	Divorced	19 (0.0%)
Tests	Score (mean ± standard deviation)	Frequency of altered results (%)
MAC-Q	29.6 ± 4.0	49 (86%)
MMSE	23.0 ± 4.4	26 (45.6%)
Figure test (recall 5')	7.5 ± 1.9	16 (28.1%)
Verbal fluency (animals)	10.8 ± 4.1	29 (50.9%)
Clock drawing test	3.5 ± 1.5	22 (38.6%)
FAQ	4.9 ± 7.3	15 (26.3%)

Abbreviations: FAQ, Functional Activity Questionnaire; MAC-Q, Memory Assessment Clinics Questionnaire; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination.

Table 2 Clinical comorbidities, medication, and lifestyle habits

Variables		Total ($n = 57$)	%
Clinical comorbidities	Arterial hypertension	39	68.4
	Diabetes mellitus	23	40.3
	Dyslipidemia	16	28.1
	Hypothyroidism	16	28.1
	Anxiety	21	36.8
	Depression	13	22.8
Drugs in use	Proton pump inhibitors	12	21.1
	Antidepressants	23	40.4
	Typical antipsychotics	2	3,.5
	Statin	24	42.1
	Benzodiazepines	17	29.8
Life habits	Alcohol use	7	12.3
	Smokers	5	8.8
	Practice of physical activity	18	31.6

Table 3 Neuropsychological data for the final sample of the population ($N = 57$ participants)

	SCD		MCI		Dementia	
	Score (mean ± SD)	Frequency of altered results (%)	Score (mean ± SD)	Frequency of altered results (%)	Score (mean ± SD)	Frequency of altered results (%)
MAC-Q	28.7 ± 3.6	16 (88.9%)	29.3 ± 4.2*	21 (84%)	31.1 ± 4.2	12 (85.7%)
MMSE	26.2 ± 2.1*§	0 (0%)	22.6 ± 4.1*	15 (60%)	19.6 ± 4.7	11 (78.6%)
Figure test (recall 5′)	8.7 ± 1.1	0 (0%)	7.2 ± 1.6	9 (36%)	6.5 ± 2.6	7 (50%)
Verbal fluency (animals)	14.5 ± 3.3*§	0 (0%)	10.0 ± 3.1	17 (68%)	7.5 ± 3.0	12 (85.7%)
Clock drawing test	4.2 ± 1.1	0 (0%)	3.8 ± 1.4	8 (32%)	2.2 ± 1.5	11 (78.6%)
FAQ	0.7 ± 1.0*	0 (X%)	2.0 ± 2.0*	0 (0%)	15.6 ± 7.6	14 (100%)

Abbreviations: FAQ, Functional Activity Questionnaire; MAC-Q, Memory Assessment Clinics Questionnaire; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; SCD, Subjective cognitive decline; SD, standard deviation.
§$p < 0.05$ (Mann-Whitney test) vs MCI.
Notes: *$p < 0.05$ (Mann-Whitney test) vs Dementia.

in people with MCI is variable, and it is estimated at 2 to 18% per year.[34–37] While most studies reported higher annual rates of progression to dementia among MCI individuals, our results are similar to data from a recent north-American community-based study, which reported that 12.9% of MCI individuals progressed to dementia, while 29.6% remained stable during a follow-up of 2.4 years.[7]

Some methodological points should be considered when analyzing the low conversion rate to dementia in our MCI sample. First, due to its naturalistic design, our study included MCI individuals due to reversible causes of cognitive decline, such as hypovitaminosis B12 and hypothyroidism.[23] Therefore, it is possible that individuals with MCI due to neurodegenerative causes are underrepresented in our sample. The lack of biomarkers of AD hampers the verification of the underlying biological processes in our sample. Another issue is the high proportion of individuals that could not be reassessed on the follow-up, in terms of clinical, cognitive, and functional profile. Indeed, 28% of the initial sample was not found, including 11 individuals with MCI. It is possible that the inclusion of these individuals could affect the rate of conversion to dementia.

One of the most striking results of our study is the significant number of individuals who improved their cognitive and functional status during the follow-up period. Indeed, 12 individuals with MCI and 9 with dementia ($n = 21$, that is, 23% of the baseline sample) had reversible causes of cognitive decline (hypothyroidism, hypovitaminosis B12, anxiety, and depression) and improved after appropriate medical treatment. Indeed, we have previously reported the high frequency of reversible causes of cognitive impairment in this population,[23] in line with other studies in the field.[38] For instance, a German study identified reversible causes of cognitive impairment in 31.1% individuals with

Table 4 Progression of cognitive decline

Baseline category (2016)	Longitudinal (2020)	n	%
SCD ($n = 15$)	SCD	4	26.7
	MCI	4	26.7
	Dementia	0	0
	Death	0	0
	Not located	7	46.7
MCI ($n = 45$)	SCD	12	26.7
	MCI	14	31.1
	Dementia	6	13.3
	Death	2	4.4
	Not located	11	24.4
Dementia ($n = 31$)	SCD	2	6.4
	MCI	7	22.6
	Dementia	8	25.8
	Death	6	19.4
	Not located	8	25.8

Abbreviations: MCI, mild cognitive impairment; SCD, subjective cognitive decline.

dementia, with depressive pseudodementia and hypovitaminosis B12 being the most frequent causes.[38] The present findings highlight the benefit of appropriate medical treatment of reversible causes of dementia,[39] with a clear impact on the outcome of individuals with memory complaints. These results emphasize the need for the screening of non-degenerative causes of dementia, in line with the United Nations Decade of Healthy Aging (2021–2030). In this scenario, primary health care has an essential role in the diagnosis, treatment, and prevention of dementia.

Interestingly, we did not find correlations between educational level and vascular risk factors and risk of cognitive or functional decline. Previous studies found that individuals with hypertension or diabetes,[38] and also those with low schooling, have higher risk to develop dementia.[40] The small sample size of our study may account for these unexpected results. Moreover, there is low dispersion of schooling in our population, thus rendering it difficult to detect significant correlations with cognitive and functional impairment. More studies, with larger sample sizes and more heterogeneous educational level, are warranted to investigate the complex relations between education, vascular risk factors and functional decline among individuals with memory complaints in the primary health care system.

The use of benzodiazepines and of proton pump inhibitors was not associated with cognitive or functional status in our cohort. While some papers have previously reported higher risk of dementia in individuals under treatment with benzodiazepines[41,42] or proton pump inhibitors,[43,44] others did not.[45,46] The association of these drugs with dementia risk remains a controversial issue and should be addressed in further studies.

We found that older age, lower MMSE, and higher MAC-Q scores were predictors of cognitive and functional decline during the follow-up. Aging is a well-established risk factor for dementia. While some studies found that the severity of memory complaints was a predictor of dementia,[47,48] others did not.[49,50] Our data suggest that older individuals with memory complaints associated with abnormal MMSE scores are at increased risk of cognitive and functional decline and should undergo careful follow-up for medical assistance.

This study has limitations, the main one being the small number of participants. The unbalanced proportion of women in our sample hinders analyzing sex as a risk factor for cognitive decline. Another major issue is the high number of participants from the baseline that could not be contacted (28% of the initial sample), thus precluding their reassessment. This may be explained by the difficulties of conducting clinical research in low- and middle-income countries, and also by the coronavirus disease 2019 (COVID-19) pandemia, which disrupted health care team, thus hampering the contact with patients from the original sample. Eight patients from the initial sample died during the follow-up. It is possible that the patients who died and those with whom we lost contact were at increased social and medical vulnerabilities. We acknowledge that missing data represent a substantial inclusion bias in the follow-up, as individuals with worse outcome may have been underscored in total calculations. The exclusion of individuals with a previous diagnosis of dementia is also a bias, with possible selection of patients toward earlier phases of cognitive decline. Due to the absence of biomarkers for AD, we could not describe individuals in terms of the underlying AD pathophysiological status, according to the AT(N) criteria.[51] Moreover, neuroimaging with magnetic resonance imaging (MRI) was not available for our individuals, which hampers the analysis of different patterns of brain atrophy and of subcortical vascular lesions as potential predictive factors of cognitive and functional decline.

In conclusion, despite the aforementioned caveats, this study brings relevant findings in the context of the assistance of individuals with less education with memory complaints at primary health care in low- and middle-income countries, highlighting the importance of careful clinical assessment and follow-up of individuals, and treating reversible causes of cognitive decline, when present. Our data suggest that these strategies improved the cognitive performance of a subgroup of individuals. Public health policies should encourage the screening of memory complaints in primary care, to minimize the impact of potentially reversible causes of cognitive and functional decline. More studies are warranted to investigate how the complex interactions among demographic, clinical, cognitive, and neurobiological factors affect the cognitive and functional outcome of patients with memory complaints.

Authors' Contributions

MLP: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, and writing – original draft; PC: conceptualization, data curation, investigation, methodology, resources,

validation, visualization, and writing – review & editing; VMS: data curation, investigation, and resources; PHMR: conceptualization, data curation, funding acquisition, investigation, and resources; JPGO: conceptualization, data curation, formal analysis, funding acquisition, investigation, and resources; RPA: conceptualization, formal analysis, funding acquisition, and resources; EVS: conceptualization, data curation, funding acquisition, investigation, and resources; VSD: conceptualization, formal analysis, funding acquisition, and resources. MTB: formal analysis, methodology, validation, visualization, and writing – review & editing; LFJRM: conceptualization, formal analysis, investigation, methodology, project administration, resources, supervision, validation, visualization, and writing – review & editing; LCS: conceptualization, data curation, formal analysis, methodology, project administration, supervision, validation, visualization, writing – original draft, and writing – review & editing.

Support
We are thankful to Secretaria Municipal de Saúde de Patos de Minas and to Centro Universitário de Patos de Minas (UNIPAM) for supporting the present study.

Conflict of Interest
The authors have no conflict of interest to declare.

Acknowledgments
The authors would like to thank the Municipal Health Department of Patos de Minas and Centro Universitário de Patos de Minas (UNIPAM) for supporting this study.

LCS and PC are supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) through a productivity in research grant.

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