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Incidence of Cognitive Decline and Association with Changes in Sociodemographic, Lifestyle, and Health Indicators in Individuals aged 50 years and older: Prospective Cohort

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ABSTRACT

Objectives: To identify the incidence of cognitive decline (CD) in an urban community-dwelling population aged 50 years and older in a 4-year follow-up period and its prospective association with sociodemographic factors, lifestyle and health conditions as well as with changes in these factors. **Methods:** This is a prospective cohort with a representative sample of people aged 50 years and older (n = 206) from Cambé, PR, where baseline data collection occurred in the year 2011 and the follow-up occurred in 2015. The incidence of CD was the outcome of this study, and its evaluation occurred through the Mini-Mental State Examination. **Results:** The incidence of CD was 13.1% over the 4 years of follow-up, and adjusted Poisson regression models (sex, age and age range) showed that this condition was prospectively associated with depression (adjusted relative risk (RR) = 3, 50, 95% CI = 1.65-7.43). When analyzing the effect of sociodemographic factor changes on CD, it was verified that the risk of CD was 2.86 times higher among the group that stopped having a companion in the 4 years of follow-up when compared to the group that maintained a companion in that same period, independent of confounding factors. **Conclusion:** The data suggest that the CD process begins before the age of 60 y and that aggravation is associated with potentially modifiable factors that can be approached by health services from the perspective of promotion, prevention and care.

Keywords: Cognition. Middle age. Mental health. Cohort.

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Introduction

The growing number of cases of cognitive decline (CD) in recent decades has mainly affected low- and middle-income countries, where 58% of global dementia cases were found in 2010, with estimates of 63% for 2030 and 71% for 2050. In turn, less than 10% of studies on this problem are conducted in these countries [1].

In high-income countries, there has been an increase in the number of studies focused on middle-aged individuals, showing concern with the early identification of risk factors and in proposing timely interventions [2,3,4,5,6,7,8,9,10,11,12]. Currently, in South America and especially in Brazil, the epidemiology of CD is a field under construction, and there are still no precise estimates of rates and associated factors. Few studies have been

conducted to examine the course of CD in a longitudinal manner, and those studies are restricted to the elderly, who are more vulnerable to comorbidities and established CD, with less possibility of preventive actions [13,14,15,16,17,18].

Another important aspect is the possibility of quantifying the impact of changes in socioeconomic factors and lifestyle on CD to support more specific, directed and effective strategies for coping with this problem. Thus, the objective of this study was to identify the incidence of CD in individuals aged 50 years and older living in an urban community in a 4-year follow-up and to analyze its prospective association with sociodemographic factors, lifestyle and health conditions as well as with changes in these factors.

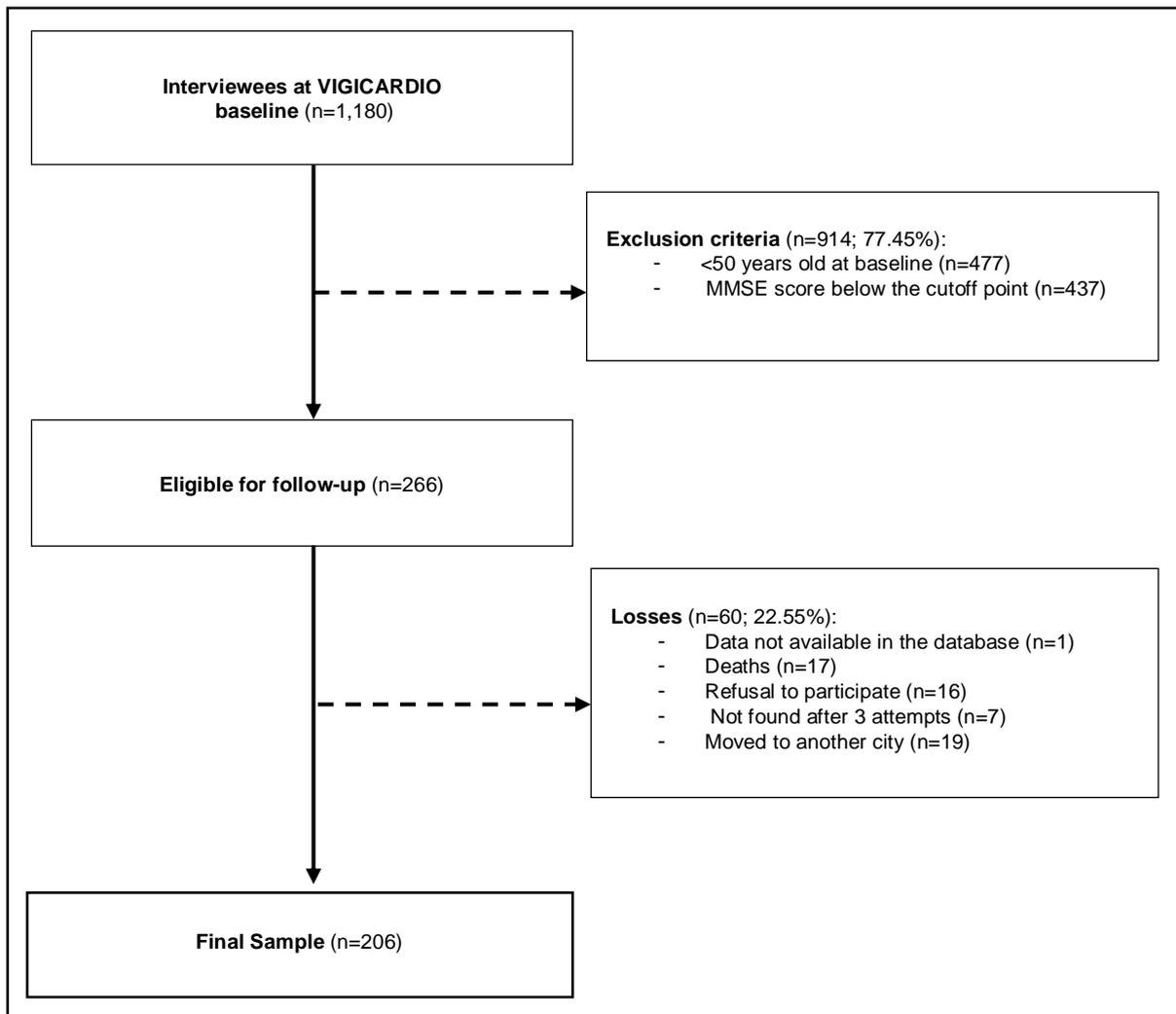


Figure 1. Flowchart of the sampling process. Cambé, Paraná, 2011-2015.

Materials and Methods

a) Design

This observational prospective cohort epidemiological study is part of a population-based study called VIGICARDIO [19], whose data collection occurred at 2 time-points. The first collection occurred in 2011 (baseline), comprising 1,180 individuals aged 40 years and older residing in the city of Cambé, Paraná state, Brazil. The second collection occurred after 4 years and evaluated all the 1,180 individuals interviewed at the first time-point.

For the present study, participants aged 50 years and older who had no CD at baseline were considered eligible for follow-up. Among the 1,180 respondents in 2011, a total of 266 were selected; however, there were 60 losses (22.5%). The final sample in the follow-up period comprised 206 participants (Figure 1).

b) Dependent variable

CD was the outcome of this study. For its estimation, the Mini-Mental State Examination (MMSE) was used [20]. Subjects considered to have CD were those with low scores on the MMSE; the following cutoff points were used: <19 for people with illiteracy; <23 for people with up to 3 complete years of study; <24 for individuals with 4 to 7 complete years of study; and <28 for individuals with more than 7 complete years of study [21].

c) Independent variables

Sociodemographic characteristics

The following variables at baseline and respective categories were selected: gender; age range (50 to 59 years; 60 years old or older); years of study (≤ 3 complete years of study; ≥ 4 complete years of study); marital status (without partner; with partner); work activity (yes; no), socioeconomic condition estimated by the Critério de Classificação Econômica Brasil (Brazilian Economic Classification Criterion; CCEB) of the Brazilian Association of Companies and Research [22], which was classified as the worst economic situation (1st tertile) and other (2nd and 3rd tertiles); and

insufficient consumption of fruits and/or vegetables (frequency less than 5 days per week) (yes; no) [23].

Lifestyle indicators

The use of tobacco was estimated by self-reported smoking: smoker (yes) and nonsmoker (no). Physical activity during free time was identified with the following question: "In a normal (typical) week, did you do some type of physical activity during your free time?"; those who answered "no" were considered inactive, and those who answered "yes" were classified as active.

Health conditions

A brief version of the Geriatric Depression Scale was applied. This scale has 15 items [24,25]; scores between 0 and 5 are considered normal (no), and scores of 6 or more indicate depression (yes). The definition of arterial hypertension was based on the following criteria: mean systolic blood pressure (SBP) ≥ 140 and/or mean diastolic blood pressure (DBP) ≥ 90 mmHg and/or use of prescription medication for hypertension was categorized as (yes); otherwise, the individual was characterized as normotensive (no) [26].

The presence of diabetes mellitus (DM) was defined by fasting blood glucose ≥ 126 mg/dL and/or use of exclusive medication for DM treatment or use of nonexclusive medication with self-reported DM, diagnosed by a healthcare professional [26].

Dyslipidemia was defined based on the following values: triglycerides ≥ 150 mg/dL; high-density lipoprotein (HDL) cholesterol < 40 mg/dL in men and < 50 mg/dL in women; and low-density lipoprotein (LDL) cholesterol ≥ 160 and/or treatment with hypolipidemic drugs [27]. This information was used to classify individuals as those with 1 or more changes and/or use of medication (yes) and noncarriers (no).

Measurement of waist circumference (WC) was considered high when WC > 88 cm for women and WC > 102 cm for men [28].

Changes in sociodemographic and lifestyle factors from baseline to the follow-up period

To explore the effect of change on CD, 6 independent variables (marital status, socioeconomic status, work activity, physical inactivity, smoking, and insufficient consumption of fruits and vegetables) were reclassified into 4 categories: remained in the best condition at both data collection timepoints; progressed from a worse condition at baseline to a better condition at follow-up; remained in the worst condition at both data collection timepoints; and regressed from the best condition at baseline to a worse condition at follow-up.

d) Data processing and statistical analysis

The absolute and relative frequencies, as well as the chi-square test, were used to (a) compare the characteristics of respondents and losses; (b) investigate the association between the incidence of CD and risk factors at baseline; and (c) investigate the association between the incidence of CD and changes in exposure factors. The incidence density of CD was estimated by considering the new cases of CD as the numerator and the exposed population multiplied by the years of follow-up of the study as the denominator. The crude and adjusted relative risk (RR) of incidence of CD according to the different types of sociodemographic factors, lifestyle and health conditions were obtained using Poisson regression with robust adjustment of variance. The statistical analyses were performed using IBM SPSS software, version 19.0 for Windows, adopting a significance level of 5%.

Results

In the sample of 206 individuals, there was a predominance of women (52.4%), the mean age was 59.5 years, and 37.9% of the individuals had a low education level (less than 3 years). When comparing respondents ($n = 206$) and losses ($n = 60$), there was a similar distribution for all variables ($p > 0.05$), except for age group and work activity (Table 1).

After 4 years, CD was detected in 27 participants (13.1%). After adjusting for gender, age, and education, the risk of CD incidence was lower in 60 years and older age group than in those aged 50 to 59 years and higher among individuals classified with depression in 2015 than in those classified without depression (Table 2).

A change in marital status resulted in a higher risk of CD (2.86-fold) among those who no longer had a partner compared to those who remained with a partner, after controlling for confounding variables (Table 3).

Discussion

Over the 4-year follow-up, the present study identified a 13.1% incidence of CD in a sample of individuals aged 50 years and older, and there was a higher risk of CD occurring for those who lost a partner and those who were classified as having depression, after adjustments for the variables gender, age group, and education level.

The 27 new cases of CD among the 206 interviewees resulted in an incidence density of 32.7 per 1,000 person-years of follow-up, similar to that observed in low- and middle-income countries, such as Venezuela (40.1) and China (31.2) [29]. In turn, the incidence density was higher than that of several high-income countries, such as Canada (25.3), France (14.9), the Netherlands (8.1), Spain (12.8), the USA (15.5), and Italy (13.3) [30]. In addition to methodological issues related to the evaluation, it is possible that this difference is related to the sociocultural and economic disparities between Brazil and high-income nations, such as easier access to education, health, leisure, social life and professional fulfillment, given that these factors provide substantial protection against the occurrence of CD, resulting in better brain function by minimizing the effect of neurodegenerative damage due to stress and by increasing the cognitive reserve [31].

The increased risk of CD observed among individuals who lost their spouse/partner corroborates the national [32] and international

Table 1. Comparison between participants and losses in relation to characteristics of the sample at baseline. Cambé, Paraná, 2011.

Factors	Participants (n=206)		Losses (n=60)		Total (n = 266)		p-value ^a
	n	%	N	%	N	%	
Gender							0.74
Female	108	52.4	30	50.0	138	51.9	
Male	98	47.6	30	50.0	128	48.1	
Age range (years)							0.001
50 – 59	121	58.7	21	35.0	142	53.4	
≥60	85	41.3	39	65.0	124	46.6	
Education (years of study)							0.26
≥4	130	63.1	33	55.0	163	61.3	
≤3	76	36.9	27	45.0	103	38.7	
Marital status							0.25
With partner	153	74.3	40	66.7	193	72.6	
Without partner	53	25.7	20	33.3	73	27.4	
Labor activity							0.02
Yes	112	54.4	22	36.7	134	50.4	
Not applicable	94	45.6	38	63.3	132	49.6	
Socioeconomic status							0.62
Higher	124	60.2	34	56.7	158	59.4	
Lower (lower tertile)	82	39.8	26	43.3	108	40.6	
Smoker							0.31
No	173	84.0	47	78.3	220	82.7	
Yes	33	16.0	13	21.7	46	17.3	
Physical inactivity during leisure time							0.30
Yes	140	68.0	45	75.0	185	69.5	
No	66	32.0	15	25.0	81	30.5	
Insufficient consumption of Fruits and vegetables (<5x per week)							0.68
No	92	44.7	25	41.7	117	44.0	
Yes	114	55.3	35	58.3	149	56.0	
Hypertension							0.08
Yes	133	64.6	46	76.7	179	67.3	
No	73	35.4	14	23.3	87	32.7	
Diabetes mellitus							0.81
Yes	30	14.6	8	13.3	38	14.3	
No	176	85.4	52	86.7	228	85.7	
Dyslipidemia							0.08
Yes	122	59.2	28	46.7	150	56.4	
No	84	40.8	32	53.3	116	43.6	
High waist circumference							0.39
Yes	116	56.3	30	50.0	146	54.9	
No	90	43.7	30	50.0	120	45.1	

^aP-value for differences between participants and losses, chi-square test. No multivariate analysis was performed for the factors that had p > 0.20 in the bivariate

Table 2. Incidence and relative risk (RR) of cognitive decline (CD) according to sociodemographic, lifestyle and health factors in individuals aged 50 years and older. Cambé, Paraná, 2011-2015.

	n total	Cases of cognitive decline n (%)	p-value ^a	Crude (CI95%)	RR	Adjusted (CI95%) ^{b, c}	RR
Total	206	27 (13.1)					
Gender			0.19				
Female	108	11 (10.2)		1.00		1.00	
Male	98	16 (16.3)		1.60 (0.78-3.28)		1.75 (0.85-3.62)	
Age range (years)			0.08				
50 – 59	121	20 (16.5)		1.00		1.00	
≥ 60	85	7 (8.2)		0.50 (0.22-1.13)		0.44 (0.20-0.94)	
Education (years of study)			0.38				
≥ 4	130	15 (11.5)		1.00		-	
≤ 3	76	12 (15.8)		1.37 (0.68-2.77)		-	
Marital status			0.98				
With partner	153	20 (13.1)		1.00		-	
Without partner	53	7 (13.2)		1.01 (0.45-2.25)		-	
Work Activity			0.34				
Yes	112	17 (15.2)		1.00		-	
No	94	10 (10.6)		0.70 (0.34-1.46)		-	
Socioeconomic status			0.46				
Higher	124	18 (14.5)		1.00		-	
Lower (lower tertile)	82	9 (11.0)		0.76 (0.36-1.60)		-	
Smoker			0.7				
No	173	22 (12.7)		1.00		-	
Yes	33	5 (15.2)		1.20 (0.49-2.92)		-	
Physical inactivity during leisure time (<1x per week)			0.55				
No	66	10 (15.2)		1.00		-	
Yes	140	17 (12.1)		0.80 (0.39-1.65)		-	
Insufficient consumption of Fruits and vegetables (<5x per week)			0.39				
No	92	10 (10.9)		1.00		-	
Yes	114	17 (14.9)		1.37 (0.66-2.85)		-	
Depression^d			0.03				
No	180	20 (11.1)		1.00		1.00	
Yes	26	7 (26.9)		2.42 (1.14-5.16)		3.50 (1.65-7.43)	
Hypertension			0.81				
No	73	9 (12.3)		1.00		-	
Yes	133	18 (13.5)		1.10 (0.52-2.32)		-	
Diabetes Mellitus			0.53				
No	176	22 (12.5)		1.00		-	
Yes	30	5 (16.7)		1.33 (0.55-3.25)		-	
Dyslipidemia			0.4				
No	84	9 (10.7)		1.00		-	
Yes	122	18 (14.8)		1.38 (0.65-2.92)		-	
High waist circumference			0.93				
No	90	12 (13.3)		1.00		-	
Yes	116	15 (12.9)		0.97 (0.48-1.97)		-	

RR = Relative risk, calculated from the Poisson regression with robust variance adjustment; CI95% = 95% confidence interval; ^a p-value of the chi-square test for heterogeneity between cognitive decline and independent variables; ^b Adjusted for gender, age group and education level; ^c No multivariate analysis was performed for the factors that had p> 0.20 in the bivariate analysis; ^d Data from 2015.

Table 3. Association between risk of cognitive decline and changes in sociodemographic and lifestyle indicators of adults. Cambé, Paraná, 2011-2015.

Factors	n total	Cases of cognitive decline n (%)	Crude RR (CI95%)	Adjusted RR (CI95%) ^{a, c}
Evolution of marital status^b				
Individual remained with a partner	131	15 (11.5)	1.00	1.00
Individual stopped living with partner	21	5 (23.8)	2.08 (0.84-5.12)	2.86 (1.22-6.71)
Individual remained without a partner.	45	6 (13.3)	1.00	1.00
Individual started living with partner	8	1 (12.5)	0.94 (0.13-6.78)	0.97 (0.14-6.79)
Evolution of work activity				
Individual remained working	77	13 (16.9)	1.00	1.00
Individual stopped working	35	4 (11.4)	0.68 (0.24-1.93)	0.83 (0.29-2.37)
Individual remained without work	84	9 (10.7)	1.00	1.00
Individual started to work	10	1 (10.0)	0.93 (0.13-6.62)	0.79 (0.09-6.77)
Evolution of socioeconomic status^b				
Individual remained in the highest condition	110	17 (15.5)	1.00	1.00
Individual went from highest to lowest condition	13	1 (7.7)	0.50 (0.07-3.44)	0.43 (0.05-3.50)
Individual remained in the lowest condition	34	5(14.7)	1.00	1.00
Individual went from the lowest to the highest condition	48	4 (8.3)	0.57 (0.16-1.96)	0.47 (0.14-1.51)
Evolution of smoking				
Individual remained without smoking.	172	22 (12.8)	-	-
Individual started smoking	1	0 (0.0)	-	-
Individual kept smoking.	27	5 (18.5)	-	-
Individual quit smoking	6	0 (0.0)	-	-
Evolution of physical inactivity during leisure time				
Individual kept exercising	30	7 (23.3)	1.00	1.00
Individual stopped exercising	36	3 (8.3)	0.36 (0.10-1.26)	0.36 (0.10-1.27)
Individual remained inactive	113	15 (13.3)	1.00	1.00
Individual started exercising	27	2 (7.4)	0.56 (0.14-2.30)	0.55 (0.14-2.14)
Evolution of insufficient consumption of fruits and vegetables				
Individual kept eating enough fruits and vegetables	84	9 (10.7)	1.00	-
Individual stopped consuming enough fruits and vegetables	8	1 (12.5)	1.17 (0.17-8.07)	-
Individual continued to consume insufficient amount of fruits and vegetables	27	3 (11.1)	1.00	-
Individual began to consume enough fruits and vegetables	87	14 (16.1)	1.45 (0.45-4.67)	-

Note: RR = Relative risk, calculated from the Poisson regression with robust variance adjustment; CI95% = 95% confidence interval.

^a Adjusted for gender, age group and education level; ^b Number of participants less than 206 due to lack of data in the database; ^c No multivariate analysis was performed for the factors that had p > 0.20 in the bivariate

[33,34,35,36,37] literature. Studies focused on changes after the loss of a partner and the social stereotypes that people use to relate to those who remain alone showed that the loss of a partner generates negative changes in the network of social interaction, which is an important component of the cognitive reserve, favoring CD [38,39]. In addition, being alone implies changes in personal interaction and self-reference that can result in stress and social isolation [40]. From this perspective, Thoits (2011) [41] considers that to mitigate the consequences of stressors, in physical and mental health, the most effective strategy is for significant individuals from the social environment to provide emotional support and support to cope with the loss of a partner.

Depression increased the risk of CD in 4 years by 3-fold; however, it should be considered that there is no consensus on how this association is established because, although it is identified as a cause of CD [42], it can be considered a prodromal expression of dementia [43].

Depression is a multifactorial (intrapersonal, social, environmental, etc.) health problem, the causes of which may vary according to stages of life. Therefore, when analyzing this condition in the population aged 50 years and older - the age group in this study - it is important to consider that the changes resulting from aging, such as reduced possibilities of social interaction, worsening health conditions and neuroendocrine and brain neurochemical changes, can trigger depression and promote CD [44]. Another aspect related to the association between depression and CD found in this study is that men (59.3%) were the most affected, corroborating studies that claim that CD associated with depression is more frequent in males, even when women are most affected by depression [45,46,47].

Studies indicate that the CD rates increase as individuals age [48,49,50,29]; however, in this study, when comparing people in the age group of 50 to 59 years with those in the age group of 60 years and older, it was found that the

incidence rates were higher among the youngest. This result may be partly explained by the fact that the population with CD at the study's baseline was excluded, and in this group, individuals aged 60 or older were predominant. Wilkosz et al. (2010) [51] analyzed the trajectory of CD according to subject age and MMSE score and found that individuals with advanced age and a normal MMSE score at baseline declined slower than do younger individuals with a normal MMSE score. From this perspective, it is possible that 4 years of follow-up was adequate to identify CD only among the youngest individuals, i.e., the latency period was not sufficient for the development of CD among older subjects with normal MMSE scores because higher MMSE scores are indicative of greater cognitive reserve. Similarly, a 30-year follow-up cohort observed a decrease in the incidence of CD among participants from advanced age groups compared to younger age groups [52].

In addition, it should be noted that most studies (90%) in this area are conducted in high-income countries and that recent evidence from low- and middle-income countries has indicated that CD seems to start earlier in these countries [53].

Some methodological considerations should be highlighted. The loss of 22% of respondents in the follow-up may be considered a limitation; however, the sample composition of the follow-up was similar to that at baseline, decreasing the possible negative effect of such losses. Another point to be considered is that depression was evaluated only at follow-up, and unlike other independent variables, it was not possible to analyze the effect of changes in this condition on the incidence of CD over the 4 years of follow-up. Another limitation of the study was the assessment of cognitive status only by the MMSE because a broader neuropsychological assessment would have greater sensitivity. However, the MMSE is an easily applied instrument that can be incorporated into clinical assessments in primary care.

In addition to the prospective design, another

positive aspect of this study is the evaluation of a population aged 50 years old and older, an age group that is little explored in cognitive assessment studies in low- and middle-income countries.

Conclusion

The data suggest that the CD process begins before the age of 60; therefore, there is a need for studies on this subject to include middle age individuals because new evidence is necessary for definitive conclusions about the early onset of CD in contexts of social vulnerability. In addition, greater attention is necessary regarding individuals who lose a partner and thus are more vulnerable to the occurrence of CD. This condition has also been associated with situations of potential reversal, such as depression; thus, it is believed that early screening for such a condition will be important to clarify risk factors associated with dementia and consequent policy support aiming to prevent CD. More population studies are needed to monitor cognitive performance in different geographic regions, and ideally, this sample should be followed-up for a longer period of time to identify factors associated with conversion to CD.

Statements

a) Acknowledgments

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b) Ethics Statement

The study was approved by the research ethics committee of the State University of Londrina (UEL), both at baseline (CAAE nº 01920.268.000.10) and in the follow-up period (CAAE nº. 39595614.4.0000.5231), and all the participants signed a free and informed consent form.

c) Disclosure Statement

The authors have no conflicts of interest to declare.

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e) Author Contributions

Conception and planning: M.A.S.C. and M.C.U.V.; Analysis and interpretation of data: D.F.D., A.M.R.S, M.S.S.B and M.C.U.V.; Writing of the manuscript: M.C.U.V. and M.A.S.C. Critical review of the manuscript: D.F.D., A.M.R.S., M.S.S.B and M.A.S.C.

References

1. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement.* 2013;9(1):63-75.
2. Singh-Manoux A, Richards M, Marmot M. Socioeconomic Position across the Lifecourse: How Does it Relate to Cognitive Function in Mid-life? *Ann Epidemiol.* 2005;15(8):572–578.
3. Reynolds CA, Gatz M, Prince JA, Berg S, Pedersen NL. Serum lipid levels and cognitive change in late life. *J Am Geriatr Soc.* 2010;58(3):501–509.
4. Rusanen M, Kivipelto M, Quesenberry CP, Zhou J, Whitmer RA. Heavy Smoking in Midlife and Long-term Risk of Alzheimer Disease and Vascular Dementia. *Arch Intern Med.* 2011;171(4):333–339.
5. Hagger-Johnson G, Sabia S, Brunner EJ, Shipley M, Bobak M, Marmot M, et al. Combined impact of smoking and heavy alcohol use on cognitive decline in early old age: Whitehall II prospective cohort study. *British Journal of Psychiatry.* Cambridge University Press; 2013;203(2):120–5.
6. Then, FS, Luck T, Jacobi F, Berger K, Weyerer S, Grabe HJ, et al. Assessment of mild cognitive impairment and dementia in epidemiologic studies. An overview on the current state of research in Germany. *Psychiatr Prax.* 2013;40(4):183–191.
7. Beydoun MA, Beydoun HA, Gamaldo AA, Teel A, Zonderman AB, Wang Y. Epidemiologic studies of modifiable factors associated with cognition and dementia: systematic review and meta-analysis. *BMC Public Health.* 2014;14:643.
8. Exalto LG, Quesenberry C, Barnes D, Kivipelto M, Biessels G J, Whitmer RA. Midlife risk score for the prediction of dementia four decades later.

- Alzheimers Dement. 2014;10(5):562–570.
9. Gottesman RF, Schneider ALC, Albert M, Alonso A, Bandeen-Roche K, Coker L, et al. Midlife Hypertension and 20-Year Cognitive Change The Atherosclerosis Risk in Communities Neurocognitive Study. *JAMA Neurol.* 2014;71(10):1218–1227.
 10. Girerd X, Hanon O, Pannier B, Mourad JJ, Vaisse B. Hypertension artérielle du sujet âgé en France: caractéristiques du traitement et fréquence de la plainte cognitive selon l'enquête FLAHS 2014. *Ann Cardiol Angeiol (Paris).* 2015;64(3):145–149.
 11. Luchsinger JA, Cabral R, Eimicke JP, Manly JJ, Teresi J. Glycemia, diabetes status, and cognition in middle aged Hispanics. *Psychosomatic medicine.* 2015;77(6):653–663.
 12. Anstey KJ, Ashby-Mitchell K, Peters R. Updating the Evidence on the Association between Serum Cholesterol and Risk of Late-Life Dementia: Review and Meta-Analysis. *Journal of Alzheimer's Disease.* 2016;56(1):215–228.
 13. Herrera E, Caramelli P, Silveira A S B, Nitrini R. Epidemiologic survey of dementia in a community-dwelling Brazilian population. *Alzheimer Dis Assoc Disord.* 2002;16(2):103–108.
 14. Nitrini R, Caramelli P, Herrera Jr E, Bahia VS, Caixeta LF, Radanovic M, Hartmann APJ, et al. Incidence of dementia in a community-dwelling Brazilian population. *Alzheimer Dis Assoc Disord.* 2004;18(4):241-246.
 15. Lebrão ML, Laurenti R. Saúde, bem-estar e envelhecimento: o estudo SABE no Município de São Paulo. *Rev Bras Epidemiol.* 2005;8:127-141.
 16. Chaves LM, Camozzato LA, Godinho C, Piazenski I, Kaye J. Incidence of mild cognitive impairment and Alzheimer disease in Southern Brazil. *J Geriatr Psychiatry Neurol.* 2009;22(3):181-187.
 17. Castro-Costa E, Dewey ME, Uchôa E, Firmo JO, Lima-Costa MF, Stewart R. Trajectories of cognitive decline over 10 years in a Brazilian elderly population: the Bambuí Cohort Study of Aging. *Cad Saude Publica.* 2011;27:s345-s350.
 18. Neri AL, Yassuda MS, Araújo LFD, Eulálio MDC, Cabral BE, Siqueira MEC, et al. Metodologia e perfil sociodemográfico, cognitivo e de fragilidade de idosos comunitários de sete cidades brasileiras: Estudo FIBRA. *Cad Saude Publica.* 2013;29:778-792.
 19. Souza RKTD, Bortoletto MSS, Loch MR, González AD, Matsuo T, Cabrera MAS, et al. Prevalência de fatores de risco cardiovascular em pessoas com 40 anos ou mais de idade, em Cambé, Paraná (2011): estudo de base populacional. *Epidemiol Serv Saude.* 2013;22(3):435-444.
 20. Folstein MF, Robins LN, Helzer JE. The mini-mental state examination. *Arch Gen Psychiatry.* 1983;40(7):812-812.
 21. Brasil. Ministério da saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Envelhecimento e saúde da pessoa idosa. Brasília: Ministério da Saúde, 2007.
 22. Associação Brasileira de Empresas de Pesquisa (ABEP). Critério de classificação econômica Brasil. São Paulo: Associação Brasileira de Empresas de Pesquisa, 2012.
 23. Brasil. Ministério da Saúde. Secretaria de Vigilância de Doenças e Agravos Não Transmissíveis e Promoção da Saúde. VIGITEL Brasil 2012: Vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico. Brasília: Ministério da Saúde, 2013.
 24. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, Leirer VO. Development and validation of a geriatric depression screening scale: a preliminary report. *Journal of psychiatric research.* 1982;17(1):37-49.
 25. Almeida OP, Almeida SA. Confiabilidade da versão brasileira da Escala de Depressão em Geriatria (GDS) versão reduzida. *Arq Neuropsiquiatr.* 1999;57(2B):421-6.
 26. Brandão AA, Rodrigues CIS, Consolim-Colombo F, Plavnik FL, Malachias MVB, Kohlmann J, Ferreira Filho S. VI Diretrizes Brasileiras de Hipertensão. *Arq Bras Cardiol.* 2010;95(4):553-553.
 27. Xavier HT, Izar MC, Faria Neto JR, Assad MH, Rocha VZ, Sposito AC, et al. V Diretriz brasileira de dislipidemias e prevenção da aterosclerose. *Arq Bras Cardiol.* 2013;101(4):1-20.
 28. Associação Brasileira para o Estudo da Obesidade e da Síndrome Metabólica (ABESO). Diretrizes brasileiras de obesidade 2009/2010. Itapéví: AC Farmacêutica, 2010.
 29. Prince M, Acosta D, Ferri CP, Guerra M, Huang Y, Rodriguez JLL, et al. Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: a 10/66 Dementia Research Group population-based cohort study. *The Lancet.* 2012;380(9836):50-58.
 30. Fiest KM, Jetté N, Roberts JI, Maxwell CJ, Smith EE, Black SE, et al. The prevalence and incidence of dementia: a systematic review and meta-

- analysis. *Can J Neurol Sci.* 2016;43(S1):S3-S50.
31. Jones RN, Manly J, Glymour MM, Rentz DM, Jefferson AL, Stern Y. Conceptual and measurement challenges in research on cognitive reserve. *J Int Neuropsychol Soc.* 2011;17(4):593-601.
 32. Ribeiro PCC, Oliveira BHD, Cupertino APFB, Neri AL, Yassuda MS. Desempenho de idosos na bateria cognitiva CERAD: relações com variáveis sociodemográficas e saúde percebida. *Psicologia: Reflexão e Crítica.* 2010;23(1):102-109.
 33. Uchino BN. Social support and health: a review of physiological processes potentially underlying links to disease outcomes. *J Behav Med.* 2006;29(4):377-387.
 34. Feng L, Ng XT, Yap P, Li J, Lee TS, Håkansson K, et al. Marital status and cognitive impairment among community-dwelling Chinese older adults: the role of gender and social engagement. *Dement Geriatr Cogn Dis Extra.* 2014;4(3):375-384.
 35. Fan LY, Sun Y, Lee HJ, Yang SC, Chen TF, Lin KN, et al. Marital status, lifestyle and dementia: a nationwide survey in Taiwan. *PLoS One.* 2015;10(9): e0139154.
 36. Sundström A, Westerlund O, Kotyrlo E. Marital status and risk of dementia: a nationwide population-based prospective study from Sweden. *BMJ open.* 2016;6(1): e008565.
 37. Håkansson K, Rovio S, Helkala EL, Vilksa AR, Winblad B, Soininen H, et al. Association between mid-life marital status and cognitive function in later life: population-based cohort study. *BMJ.* 2009;339:b2462.
 38. Utz RL, Carr D, Ness R, Wortman CB. The effect of widowhood on older adults' social participation: An evaluation of activity, disengagement, and continuity theories. *Gerontologist.* 2002;42(4):522-533.
 39. Cardona AS, Duque MG, Arango DC, Cardona AS. Riesgo de deterioro cognitivo en personas mayores de las subregiones de Antioquia, Colombia. *Rev Bras Estud Popul.* 2016;33(3):613-628.
 40. Cacioppo JT, Hawkley LC, Thisted RA. Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychol Aging.* 2010;25(2):453.
 41. Thoits PA. Mechanisms linking social ties and support to physical and mental health. *J Health Soc Behav.* 2011;52(2):145-161.
 42. Norton S, Matthews FE, Barnes DE, Yaffe K, Brayne C. Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. *Lancet Neurol.* 2014;13(8):788-794.
 43. Almeida OP, Hankey GJ, Yeap BB, Golledge J, Flicker L. Depression as a risk factor for cognitive impairment in later life: the Health In Men cohort study. *Int J Geriatr Psychiatry.* 2016;31(4):412-420.
 44. Ávila R, Bottino CMC. Atualização sobre alterações cognitivas em idosos com síndrome depressiva Cognitive changes update among elderly with depressive syndrome. *Rev Bras Psiquiatr.* 2006;28(4):316-20.
 45. Dal Forno G, Palermo MT, Donohue JE, Karagiozis H, Zonderman AB, Kawas CH. Depressive symptoms, sex, and risk for Alzheimer's disease. *Ann Neurol.* 2005;57(3):381-387.
 46. Ng TP, Niti M, Zaw MH, Kua EH. Depressive symptoms and incident cognitive impairment in cognitively well-functioning older men and women. *J Am Geriatr Soc.* 2009;57(6):1058-1063.
 47. Potvin O, Forget H, Grenier S, Prévaille M, Hudon C. Anxiety, depression, and 1-year incident cognitive impairment in community-dwelling older adults. *J Am Geriatr Soc.* 2011;59(8):1421-1428.
 48. Tervo S, Kivipelto M, Hänninen T, Vanhanen M, Hallikainen M, Mannermaa A, Soininen H. Incidence and risk factors for mild cognitive impairment: a population-based three-year follow-up study of cognitively healthy elderly subjects. *Dement Geriatr Cogn Disord.* 2004;17(3):196-203.
 49. Caracciolo B, Palmer K, Monastero R, Winblad B, Bäckman L, Fratiglioni L. Occurrence of cognitive impairment and dementia in the community A 9-year-long prospective study. *Neurology.* 2008;70(19 Part 2):1778-1785.
 50. Luck T, Riedel-Heller SG, Luppá M, Wiese B, Wollny A, Wagner M, et al. Risk factors for incident mild cognitive impairment—results from the German Study on Aging, Cognition and Dementia in Primary Care Patients (AgeCoDe). *Acta Neurol Scand.* 2010;121(4):260-272.
 51. Wilkosz PA, Seltman HJ, Devlin B, Weamer EA, Lopez OL, DeKosky ST, Sweet RA. Trajectories of cognitive decline in Alzheimer's disease. *Int Psychogeriatr.* 2010;22(2):281-290.
 52. Satizabal CL, Beiser AS, Chouraki V, Chêne G, Dufouil C, Seshadri S. Incidence of dementia over three decades in the Framingham Heart Study. *N*

53. Nitrini R, Bottino CM, Albala C, Capuñay NSC, Ketzoian C, Rodriguez JLL, et al. Prevalence of

dementia in Latin America: a collaborative study of population-based cohorts. *Int Psychogeriatr.* 2009;21(4):622-630.

