Prognostic value of disability on mortality: 15-year follow-up of the Bambuí Cohort Study of Aging

Clarissa de M. Nascimento, PhD [1], Cesar de Oliveira, PhD [2], Josélia O. A. Firmo, PhD [1], Maria Fernanda Lima-Costa, MD, PhD [1], Sérgio V. Peixoto, PhD [1,3]*

1 Oswaldo Cruz Foundation, René Rachou Research Institute, Belo Horizonte, Brazil.

2 University College London, Department of Epidemiology and Public Health, London, UK

3 Federal University of Minas Gerais, Nursing School, Belo Horizonte, Brazil

*Corresponding author:

Dr. Sérgio Viana Peixoto

Av. Augusto de Lima, 1715 - Belo Horizonte, Brazil, 30190-009

Telephone: +55 31 33497846; Fax: +55 31 32953115; Email: sergio@cpqrr.fiocruz.br

ABSTRACT

Background: Disability is a concern in the context of population ageing. The extent of an individual's disability is a major determinant of whether or not they require long-term care or survival time. We investigated the effect of three disability domains as predictors of all-cause mortality over 15-year follow-up in a Brazilian socioeconomically disadvantaged and multiracial older adult population.

Methods: We estimated Cox proportional hazards models using data from 1,333 community-dwelling individuals aged 60 and older from the Bambuí Cohort Study of Ageing. Disability was defined as a great difficulty or not being able to perform one and two or more activities in each domain: mobility, instrumental activities of daily living (IADL) and basic activities of daily living (BADL).

Results: The overall mortality rate was 46.1 per 1,000 person-years at risk (pyrs) and it was higher in men. Among men, the fully adjusted Hazard Ratios (HRs) were 1.92 (95%CI: 1.43-2.58), 2.07 (95%CI: 1.53-2.79) and 1.65 (95%CI: 1.11-2.45), and among women 1.75 (95%CI: 1.38-2.21), 1.43 (95%CI: 1.11-1.84) and 1.43 (95%CI: 1.05-1.95), for two or more disability in mobility tasks, IADLs and BADLs, respectively, compared to those with no difficulty or some difficulty to perform all the tasks.

Conclusion: A similar risk of death for mobility, IADL and BADL in both genders was found, suggesting that any of these domains can be used to identify risk of all-cause mortality among older adults. The number of activities with limitations in each domain was an important factor.

Keywords**:** Mortality, Disability, Cohort Studies, Brazil

Highlights

- Any domain of disability can be used to identify mortality risk among older adults

- The mortality risk for mobility and IADL was independent of BADL disability

- The mortality risk was strongly associated to the number of limitations for all domains

1. Introduction

Population aging, which is happening very fast in Brazil and in other developing countries, is associated with an increased number of older adults with disabilities (Kinsella & He, 2009). This scenario leads to depression, reduction in social participation (Stuck, Walthert, Nikolaus, Büla, Hohmann, & Beck, 1999), institutionalization, hospitalization (Gill, Gahbauer, Murphy, Han, & Allore, 2012) and risk of death (Hennessy et al., 2015; Majer, Nusselder, Mackenbach, Klijs, & van Baal, 2011; Tiainen, Luukkaala, Hervonen, & Jylhä, 2013). Previous evidence showed a wide range of results about the prognostic value of disability on mortality among older adults, with important differences, especially on the strength of the association between different types of disability and sex (Doblhammer & Hoffmann, 2009; Hardy, Kang, Studenski, & Degenholtz, 2011; Majer, Nusselder, Mackenbach, Klijs, & van Baal, 2011; Nybo et al., 2003; Pongiglione, De Stavola, Kuper, & Ploubidis, 2016; Pudaric, Sundquist, & Johansson, 2003; Stineman et al., 2012; Takata et al., 2013; Tiainen, Luukkaala, Hervonen, & Jylhä, 2013; Tsuji et al., 1995).

Disability is often measured by a difficulty or inability to perform Basic Activities of Daily Living (BADLs) (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963), Instrumental Activities of Daily Living (IADLs) (Lawton & Brody, 1969) and mobility tasks (Nagi, 1976). These domains are part of a hierarchical model of developing disabilities in older adults. The first domain to be compromised is mobility, followed by IADL and then BADL (Barberger-Gateau, Rainville, Letenneur, & Dartigues, 2000; Chen, Wang, Lee, Tang, Chu, & Suen, 2010; Harris, Kovar, Suzman, Kleinman, & Feldman, 1989).

Previous research conducted in developed countries showed the effect of disability on mortality rates (Hardy, Kang, Studenski, & Degenholtz, 2011; Hennessy et al., 2015; Nybo et al., 2003; Pudaric, Sundquist, & Johansson, 2003; Stineman et al., 2012; St Johon, Tyas, Menec, & Tate, 2014; Takata et al., 2013; Tiainen, Luukkaala, Hervonen, & Jylhä, 2013). However, most of these studies evaluated just one specific domain of disability (Nybo et al., 2003; Hardy, Kang, Studenski, & Degenholtz, 2011; Pudaric, Sundquist, & Johansson, 2003; Stineman et al., 2012; Takata et al., 2013; Tsuji et al., 1995) and few studies have included two disability measures (Hennessy et al., 2015; Majer, Nusselder, Mackenbach, Klijs, & van Baal, 2011; Tiainen, Luukkaala, Hervonen, & Jylhä, 2013; van Houwelingen

et al., 2014). Therefore, the possible differences in the effects of these domains on mortality are not clear. Furthermore, BADL is the most exploited domain, with few studies including IADLs and mobility tasks (Hardy, Kang, Studenski, & Degenholtz, 2011; Hennessy et al., 2015; Majer, Nusselder, Mackenbach, Klijs, & van Baal, 2011; Pudaric, Sundquist, & Johansson, 2003; Stineman et al., 2012; Takata et al., 2013; van Houwelingen et al., 2014), which are domains affected earlier and, therefore, with greater potential for intervention (Barberger-Gateau, Rainville, Letenneur, & Dartigues, 2000; Chen, Wang, Lee, Tang, Chu, & Suen, 2010). To our knowledge, just one community-based study among elderly living in France showed that a disability hierarchical scale, including BADL, IADL and mobility, was significantly associated with mortality rate at 3 and 5 years follow-up, (Barberger-Gateau, Rainville, Letenneur, & Dartigues, 2000). However, this analysis did not consider potential confounders. In addition, it is also important to note that some previous findings indicated that the mortality risk associated with disability were stronger among men than women (Doblhammer & Hoffmann, 2009; Drumond Andrade, Guevara, Lebrão, de Oliveira Duarte, & Santos, 2011; Majer, Nusselder, Mackenbach, Klijs, & van Baal, 2011; Tiainen, Luukkaala, Hervonen, & Jylhä, 2013), although women report a higher prevalence and incidence of disability (Murtagh & Hubert, 2004; Oksuzyan, Juel, Vaupel, & Christensen, 2008; Pongiglione, De Stavola, Kuper, & Ploubidis, 2016).

Most of the studies mentioned were performed in developed countries and there is no consistent evidence among older adults living in low and middle-income countries, characterized by high racial miscegenation and social inequality. Brazil, the largest Latin American country, offers a valuable opportunity to explore this issue. To our knowledge, only two population-based studies among older adults were conducted in Brazil, which included just BADL, and showed a significant association between baseline disability and mortality (Lima-Costa, Peixoto, Matos, Firmo, & Uchôa, 2011; Ramos, Simões, & Albert, 2001). Another study was conducted among elderly enrolled in the Family Health Program, who used the primary care services, and found an association between inability to perform BADL and IADL and mortality (Ferreira, Coimbra, Falsarella, Costallat, & Coimbra, 2016). Therefore, this study aimed to investigate the effect of three domains of disability on all-cause mortality over 15-year of follow-up in a Brazilian socioeconomically disadvantaged and multiracial older adult population.

Additionally, we evaluated the potential differences in the magnitude of risk between different domains and sex.

2. Methods

2.1 Study population

Data came from the Bambuí Cohort Study of Ageing, which is ongoing in Bambuí, a city of approximately 15,000 inhabitants, located in the southeastern Brazil. This cohort study was designed and developed to investigate predictors of adverse health outcomes in an elderly Brazilian population with low schooling and income levels and in epidemiological transition (Lima-Costa, Firmo & Uchoa, 2011; de Oliveira, Marmot, Demakakos, Mambrini, Peixoto, & Lima-Costa, 2016). Brazil has transitioned from a low-income, primarily rural country in the mid-1950s, to one of the largest economies in the world, with 84% of the population living in urban areas by 2010. However, cohort participants were born before 1960, and they have experienced dramatic political and social changes during their lifetime, leading to low levels os schooling (Lima-Costa, De Oliveira, Macinko & Marmot, 2012; IBGE, 2011).

The baseline cohort population were identified by the census conducted in the community in 1996. All residents aged 60 years and over on January 1st 1997 were eligible to participate in the baseline survey. Of the 1,742 inhabitants, 1,606 (92.2%) were interviewed and 1,496 (85.8%) were examined. Baseline data collection included interviews, physical examination and blood collection. The cohort participants were visited annually and had a face-to-face interview and verification of deaths. Detailed information on this cohort can be found elsewhere. (Lima-Costa, Firmo, & Uchoa, 2011) The Bambuí Project was approved by the Ethics Research Committee of the Oswaldo Cruz Foundation. Written informed consent was obtained from all participants at baseline and at all follow-up interviews.

2.2 Mortality data source

Deaths occurring from study enrollment to December 31, 2011, were considered in this analysis. Deaths were reported by next of kin during the annual follow-up interview and were ascertained through the Brazilian mortality information system from the Brazilian Ministry of Health. The death certificates were obtained for 98.9% of the individuals.

2.3 Disability Measures

Disability was assessed using three domains: mobility, IADL and BADL. Self-reported limitations in any activity of each disability domain were collected at baseline. The following mobility tasks were considered: walking about two or three blocks; climbing steps; stooping, crouching and kneeling; and lifting or carrying weights (5kg) (Nagi, 1976; Webber, Porter, & Menec, 2010). The IADL included the following activities: preparing meals; money management; shopping; housekeeping; and use of public transportation (Lawton & Brody, 1969). Finally, the BADL included: getting up from a chair without arms; getting in or out of bed; eating, bathing, dressing; and being able to go to the toilet in time (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963).

All domains of disability were categorized into no difficulty, some difficulty, great difficulty and not able to perform the activity. Further, the responses were classified into two groups: no difficulty/some difficulty and great difficulty/not able. Therefore, disability was defined as a report of great difficulty or not able to perform one and two or more items considered in each domain of disability. No difficulty or some difficulty was considered as a reference category.

2.4 Covariates

Covariates comprised baseline socio-demographic characteristics (age, gender, education and marital status), health behaviours (current smoking, alcohol consumption and physical activity) and health indicators (systolic blood pressure, fasting glucose, total cholesterol, *Trypanosoma cruzi* infection, cognitive functioning, body mass index, heart attack, stroke, angina and arthritis). These potential covariates were selected based on the previous study of the association between disability and mortality (Hennessy et al., 2015; Majer, Nusselder, Mackenbach, Klijs, & van Baal, 2011; Tiainen, Luukkaala, Hervonen, & Jylhä, 2013; Lima-Costa, Peixoto, Matos, Firmo, & Uchôa, 2011; Murtagh & Hubert, 2004; Nybo et al., 2003).

Current smokers were participants who had smoked at least 100 cigarettes during their lifetime and continue smoking at the time of interview. The use of alcohol was evaluated by consumption, in any amount, in the twelve months preceding the interview. Information on participation in physical activity was obtained at baseline cohort questionnaire consisting of questions about physical activities in the preceding 90 days. The level of physical activity was calculated based on the oxygen consumption for each reported activity, which allowed quantify energy expenditure in METs (metabolic equivalente

task), according to the compendium of physical activity (Ainsworth et al., 2011). Thus, it was considered physically inactivite the older adults with energy expenditure less than 450 MET-minutes/week. Further details on the assessment of physical activity in Bambuí Cohort members were reported in a previous publication (Ramalho, Lima-Costa, Firmo, & Peixoto, 2011).

The BMI was calculated from the ratio between the weight (kg) and height squared (m^2) and was used as a continuous variable. The anthropometric assessment was performed using standard techniques and equipments. Cognitive function was assessed using the Portuguese version of the Mini-Mental State Examination (MMSE) and was used as a continuous variable. The *T. cruzi* infection was assessed by three assay simultaneously - a hemaglutination assay (Biolab Mérieux, Rio de Janeiro, Brazil) and two ELISA (Enzyme-Linked Immunonoabsorbent Assay) (Abbott Laboratories, USA and Wiener Laboratories, Argentina); Infection was defined as positive serology in all three tests and the absence of infection when all the results were negative. A medical history of stroke (No authors listed, 1994) and angina (Rose, 1962) were assessed by a standardized questionnaire, while the medical diagnostic of heart attack and arthritis were assessed by a self-reported question. Systolic blood pressure was defined as the average of the last two measurements, among the three collected using a standardized protocol. Fasting blood glucose and total cholesterol was determined in the laboratory with standard enzymatic methods.

The interviews were conducted in the participants' homes and the physical examination and collection of blood samples were performed at the project's health clinic, except if the participant could not leave their home. Blood samples were collected after a recommended 12 hours of fasting and all procedures were conducted by interviewers and technicians previously trained. Further details can be seen elsewhere (Lima-Costa, Firmo, & Uchoa, 2011).

2.5 Statistical Analysis

The distribution of all variables considered in this study was performed for the whole population and also by gender. The association of these variables with gender was based on Pearson's chi-square test to compare frequencies, Student's t test to compare means and Mann-Whitney test to compare medians. The crude mortality rates were estimated using person-years at risk (pyrs) as the denominator for each disability measured and gender.

The adjusted analysis of the association among the three disability measurements and mortality were based on estimates of the Hazard Ratio (HR) and their 95% confidence interval, using the Cox proportional hazards models, confirming the proportionality of risk over time, based on Schoenfeld residuals. For each disability measure, three models with progressive adjustments and an interaction term between disability and gender were constructed. Therefore, the results were presented for the total population (without the interaction term) and for each gender (considering the interaction term). For models with interaction term the HR and confidence intervals were estimated for linear combination. In the first model, estimates were adjusted for socio-demographic variables (age, marital status and education level). The second model included the variables of the first model plus health behavior variables (current smoking, alcohol consumption and physical activity). The third model included the variables of the second model plus health conditions indicators (systolic blood pressure, fasting glucose, total cholesterol, *T. cruzi* infection, cognitive function, body mass index, stroke, heart attack, angina and arthritis).

We also performed a sensitivity analysis to verify the possible influence of disability in BADL, the most severe group according to hierarchical approach (Ramos et al., 2013) on estimates of the Hazard Ratio (HR) for disability in IADL and in mobility tasks. The IADL group was not excluded from the mobility model, because the hierarch between these two domains of disability may not be linear, considering that mobility is broadly defined as the ability to move both indoor and outdoor and, therefore has a strong relation with the IADL (Barberger-Gateau, Rainville, Letenneur, & Dartigues, 2000; Webber, Porter, & Menec, 2012).

Statistical analyses were performed using version 13.0 Stata statistical software (StataCorp, College Station, TX USA).

3. Results

Of the 1,606 participants at baseline, 1,333 (83.0%) had complete information on all variables included in this analysis. During the mean follow-up time of 10.9 years, 50.4% (672) of the population died and 8.2% (110) of participants were lost (their vital status could not be assessed), leading to 14,573 person-years of observation.

Table 1 shows the baseline characteristics according to sociodemographic variables, health behavior and health indicators by sex. 61.0% were women and the average age was 68.9 years (SD = 7.0). Among men, there was a higher proportion of married, smokers and drinkers, but this group showed lower mean/median values of BMI, total cholesterol and MMSE, and lower prevalence of physical inactivity, *T. cruzi* infection, angina and arthritis, as well as mobility, IADL and BADL disabilities.

The overall mortality rate was 46.1 per 1,000 pyrs, and it was higher among men (54.5 per 1,000 pyrs), compared to women (41.2 per 1,000 pyrs). For both sexes, the mortality rate was higher among those who reported one or two or more disabilities in mobility tasks, IADL and BADL, as compared with the group whitout disability in these activities (Table 2).

Adjusted hazard ratios and 95% confidence intervals for 15-year all-cause mortality, in each disability domain and by sex, are shown in Table 3. Considering all participants, the fully adjusted model showed an increased risk of death among participants who reported disabilities in two or more activities in mobility, IADL and BADL (HR: 1.82, 95%CI: 1.50-2.22; HR: 1.68, 95%CI: 1.36-2.07; HR: 1.51, 95%CI: 1.17-1.94, respectively). Among men, the three disability domains showed significant risk of death in all levels of disability in the first model (adjusted by socio-demographic characteristics), but after full adjustment, the disability in one BADL lost their statistical significance. Among women, the risk of death was less consistent compared to men, and significant associations were observed only for groups who reported two or more disabilities in all domains (mobility: HR = 1.75, 95%CI: 1.38-2.21; IADL: HR = 1.43, 95%CI: 1.11-1.84 and BADL: HR = 1.43, 95%CI: 1.05-1.95, considering the fully adjusted model).

The sensitivity analysis showed that the limitations in performing BADL, the most severity domain, had small impact on the association between mobility tasks or IADL and mortality. It was observed a reduction of the HR values, both among men (HR: 1.74; 95%CI: 1.17-2.57 and HR: 1.58; 95%CI: 1.03-2.41) and among women (HR: 1.52; 95%CI: 1.13-2.04 and HR: 1.36; 95%CI: 0.99-1.88), for two or more limitations in mobility tasks and IADL, respectively.

4. Discussion

This study investigated the prognostic value of three domains of disability by gender, in a Brazilian socioeconomically disadvantaged and multiracial older adult population. The results showed

that: (1) disability is an important prognostic factor for all-cause mortality in this population and the potential confounders had small impact in this association; (2) there was no evidence for an important difference in the prognostic value of disability on mortality between these domains and by gender, although this association was slightly stronger among men; (3) the influence of BADL on the association between mobility or IADL and mortality was not significant and it could not explain the significant associations found.

The association between BADL and IADL disability and mortality observed in Bambuí is consistent with some studies conducted in developed countries, such as United States (Fried et al., 1998; Hennessy et al., 2015; Stineman et al., 2012), Canada (St Johon, Tyas, Menec, & Tate, 2014), Japan (Takata et al., 2013; Tsuji, et al., 1995) and Europe (Pudaric, Sundquist, & Johansson, 2003; Tiainen, Luukkaala, Hervonen, & Jylhä, 2013; van Houwelingen et al., 2014). On the other hand, this evidence was not observed among elderly over 80 years old, living in Italy (Cesari et al., 2008) for both domains, and among elderly from Netherlands (van Houwelingen et al., 2014) for the IADL disability. In Brazil, only two previous studies have investigated this association and showed an increased risk of death among older adults with worse performance in BADL and IADL (Ramos, Simões, & Albert, 2001) and among those with great difficult or inability to perform four or more BADL (Lima-Costa, Peixoto, Matos, Firmo, & Uchôa, 2011). Our results add to the literature by showing a similarity of the risk of BADL and IADL limitations on all-cause mortality in both sexes, considering the overlap of confidence intervals observed in the analysis.

There is little evidence about the effect of limitations in mobility tasks on all-cause mortality, and a significant association was found only among older adults living in United States (Hardy, Kang, Studenski, & Degenholtz, 2011), Canada (St Johon, Tyas, Menec, & Tate, 2014) and Europe (Tiainen, Luukkaala, Hervonen, & Jylhä, 2013). The significant association between walking speed and survival reinforces our findings (Studenski et al., 2011). This fact can be explained by the ideia that when walking the body requires energy, movement control, support and needs the functioning of various organs, including the heart, lungs and systems (circulatory, nervous and musculoskeletal) (Studenski et al., 2011). This evidence could explain the association observed for both sexes among older adults from

Bambuí, even after adjustment for potential confounders. It could also highlight the potential predictive value of these limitations as a good indicator of survival among older adults.

The difference of the magnitude of the association between each domain of disability and mortality in the same population has been poorly explored in the literature. Some studies considered diferent domains in a single scale of disability and showed an important gradient between severity of physical limitation and mortality risk (Barberger-Gateau, Rainville, Letenneur, & Dartigues, 2000; Ramos, Simões, & Albert, 2001; St Johon, Tyas, Menec, & Tate, 2014). This gradient could also be found when two domains were analysed separarately, but with the same magnitude for each domain, (Hennessy et al., 2015; Majer, Nusselder, Mackenbach, Klijs, & van Baal, 2011; Tiainen, Luukkaala, Hervonen, & Jylhä, 2013) as observed in Bambuí. Therefore, our results suggest that the severity of physical limitation (number of activities with great difficulty/not able to perform in this study) is more important to predict all-cause mortality over 15-year of follow-up than considering different domains or the combinations of these domains in a single scale, as observed in some studies. This point was reinforced by our sensitivity analysis, which showed that the exclusion of the group with BADL disability had a small impact on the predictive value of physical limitation in mobility tasks and IADL limitations on mortality risk. This result demonstrate that the risk of death associated with IADL limitations and mobility tasks could not be explained by the presence of BADL disability in this group, which are considered of greater severity.

The possible differences between sexes in the association between disability in all domains and mortality risk were poorly investigated in previous studies. In Bambuí, when gender was considered as a potential effect modifier, only in the first model the interaction term was significant ($p<0.05$) for the three domains, with the strongest association observed among men, but this interaction was not significant after adjustment for confounders, and the association was just slightly stronger among men in the final models. Similarly, a nine year follow-up study with participants over 90 years of age living in Finland showed that dependency in mobility and BADL was more strongly associated with mortality among men than women (Tiainen, Luukkaala, Hervonen, & Jylhä, 2013). On the other hand, similar effect in both sexes was observed for BADL and mobility among elderly from Netherlands (Majer,

Nusselder, Mackenbach, Klijs, & van Baal, 2011) and in the elderly's cohort older than 90 years old living in Denmark, for disability in BADL (Nybo et al., 2003).

Usually women experience higher rates of disability, despite living longer than men (Camargos, Perpetuo, & Machado, 2005; Drumond Andrade, Guevara, Lebrão, de Oliveira Duarte, & Santos, 2011; Dunlop, Hughes, & Manheim, 1997; Hardy, Allore, Guo, & Gill, 2008; van Houwelingen et al., 2014). This high frequency of disability among older women can be due to the high incidence and long duration of the limitation in performance BADL, resulting in low rates of recovery and mortality, compared to men (Dunlop, Hughes, & Manheim, 1997; Hardy, Allore, Guo, & Gill, 2008). A recent analysis using data from the English Longitudinal Study of Ageing (ELSA) suggests that higher disability proportion among women can be a function of longer survivorship with disability rather than higher incidence and these differences between sexes could not be explained by gender-specific health conditions, body structure or by definition of disability itself (Pongiglione, De Stavola, Kuper, & Ploubidis, 2016). This pattern may have been reproduced in Bambuí, when we observed a more consistent association between disability and mortality among men, and suggest that other mechanisms may explain the pathway between disability and mortality in each sex (Pongiglione, De Stavola, Kuper, & Ploubidis, 2016). Therefore, it is important to explore this fact further.

This study has some limitations. As in all cohort studies, selective survival before entering into the cohort must be considered. In addition, changes over time in exposure status and health status were not investigated. This limitation, however, do not preclude our conclusion that, despite eventual unmeasured changes over time, baseline disability is an independent predictor for mortality in this population. Another important point to highlight is that there is no single method for assessing functional capacity and this makes it difficult to compare the results due to the diversity of instruments and cutoff points. On the other hand, the Bambui Cohort Study of Aging is a long-term population-based cohort study, with a high response rate at the baseline and minimal losses during follow-up (8.3%). Data were obtained by trained professionals and by standard techniques. Deaths during the 15-year follow-up period were confirmed through the information system on mortality and all potential confounding factors that could influence disability and mortality were considered. It should be noted that most of the literature on disability has been produced in developed countries. Therefore, our findings can contribute

to a better understanding of this process among poor socioeconomic circunstances providing new insights for the international literature. However, further studies are needed to verify whether the pattern found in the Bambui Cohort Study can be generalized to other communities.

To our knowledge, this is the first study conducted in a Latin-american country, which investigated the burden of three different domains of disability on mortality, considering a wide range of covariates and possible gender differences. The results indicated similar risk of death for mobility, IADL and BADL in both sexes, suggesting that any of these domains can be used appropriately to identify risk of all-cause mortality among older adults, irrespective of sex and hierarchical structure of these domains. The number of activities with limitations was an important factor. Thus, vulnerable groups of older adults i.e. with functioning limitations should be monitored by the health system, aiming at reducing the risk of death.

Conflict of interest

The authors declare that they have no competing interests

Author's Contributions

CMN, JAOF, MFL-C, SVP substantially contributed to the concept and design of the study, acquisition, analysis and interpretation of data; drafting and revising the manuscript critically. CDO substantially contributed to the drafting and critically revised the manuscript for important intellectual content. . All the authors reviewed and approved the submitted version of the manuscript.

Ethics

The Bambuí Project was approved by the Ethics Research Committee of the Oswaldo Cruz Foundation. Written informed consent was obtained from all participants at baseline and at all follow-up interviews.

References

[No authors listed]. (1994). Plan and operation of the Third National Health and Nutrition Examination Survey, 1988-94. Series1: programs and collection procedures. *Vital and Health Statistics. Ser 1. Programs and collection procedures*, 32, 1-407.

Ainsworth, B. E., Haskell, W. L., Herrmann, S. D., Meckes, N., Bassett, D. R. Jr., Tudor-Locke, C., et al. (2011). Compendium of physical activities: a second update of codes and MET values. *Medicine and Science in Sports and Exercise*, 43, 1575–1581.

Barberger-Gateau, P., Rainville, C., Letenneur, L., & Dartigues, J.F. (2000). A hierarchical model of domains of disablement in the elderly: a longitudinal approach. *Disability and Rehabilitation*, 22, 308-317.

Camargos, M. C., Perpetuo, I. H., & Machado, C. J. (2005). Life expectancy with functional disability in elderly persons in São Paulo, Brazil. *Revista Panamericana de Salud Public*, 17, 379–86.

Cesari, M., Onder, G., Zamboni, V., Manini, T., Shorr, R. I., Russo, A., et al. (2008). Physical Function and self-rated health status as predictors of mortality: results from longitudinal analysis in the ilSIRENTE study. *BMC Geriatr*ics, 8. doi: 10.1186/1471-2318-8-34.

Chen, H. Y., Wang, C. Y., Lee, M. Y., Tang, P. F., Chu, Y. H., & Suen, M. W. (2010). A hierarchical categorisation of tasks in mobility disability. *Disability and Rehabilitation*, 32, 1586-1593.

de Oliveira, C., Marmot, M. G., Demakakos, P., Mambrini, J. V. M., Peixoto, S. V., & Lima-Costa. (2016). Mortality risk attributable to smoking, hypertension and diabetes among English and Brazilian older adults (The ELSA and Bambui cohort ageing studies). *European Journal of Public Health*, 26, 831-835.

Doblhammer, G., & Hoffmann, R. (2009). Gender differences in trajectories of health limitations and subsequent mortality. A study based on the German socioeconomic panel 1995-2001 with mortality

follow-up 2002-2005. The *Journals of Gerontology. Series B, Psychological Science and Society Sci*ence, 64, 482-491.

Drumond Andrade, F. C., Guevara, P. E., Lebrão, M. L., de Oliveira Duarte, Y. A., & Santos, J. L. (2011). Gender Differences in Life Expectancy Among Older Adults in São Paulo, Brazil. *Women's Health Issues*, 21, 64-70.

Dunlop, D. D., Hughes, S. L., & Manheim, L. M. (1997). Disability in activities of daily living: patterns of change and a hierarchy of disability. *American Journal of Public Health*, 87, 378-383.

Ferreira, T. C. B. R., Coimbra, A. M. V., Falsarella, G. R., Costallat, L. T. L., & Coimbra, I. B. (2016). Mortality in Brazilian community-dwelling older adults: 7 years of follow up in primary care. *Geriatrics & Gerontology International*, 16, 804-809.

Fried, L. P., Kronamal, R. A., Newman, A. B., Bild, D. E., Mittelmark, M. B., Polak, J. F., et al. (1998). Risk factors for 5-year mortality in older adults: the Cardiovascular Health Study. *JAMA*, 279, 585-592.

Gill, T. M., Gahbauer, E. A., Murphy, T. E., Han, L., & Allore, H. G. (2012). Risk factors and precipitants of long-term disability in community mobility: A cohort study of older persons. *Annals of Internal Medicine,* 156, 131-140.

Hardy, S.E., Allore, H.G., Guo, Z., & Gill, T.M. (2008). Explaining the effect of gender on functional transitions in older persons. *Gerontology*, 54, 79-86.

Hardy, S.E., Kang, Y., Studenski, S.A., & Degenholtz, H.B. (2011). Ability to walk 1/4 mile predicts subsequent disability, mortality and health care costs. *Journal of General Internal Medicine*, 26, 130-135.

Harris, T., Kovar, M. G., Suzman, R., Kleinman, J. C., Feldman, J. J. (1989). Longitudinal study of physical ability in the oldest-old. *American Journal and Public Health,* 79, 698-702.

Hennessy, S., Kurichi, J. E., Pan, Q., Streim, J. E., Bogner, H. R., Xie, D., & Stineman, M. G. (2015). Disability stage is an independent risk factor for mortality in Medicare Beneficiaries aged 65 years and older. *PM & R: The Journal of Injury, Function and Rehabilitation*, 7, 1215-25.

IBGE Censo de 2010 [2010 census]. Rio de Janeiro, Brazil: Instituto Brasileiro de Geografia e Estatística, 2011.

Katz, S., Ford, A. B., Moskowitz, R. W., Jackson, B. A., Jaffe, M. W. (1963). Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *JAMA*, 185, 914-919.

Kinsella, K. & He, W. (2009). An aging world: 2008. U.S. Census Bureau, International Population Reports, P95/09-1. U.S. Government Printing Office, Washington DC. Retrieved November 14, 2016, from http//:www.census.gov/prod/2009/pubs/p95-09-1.pdf.

Lawton, M.P. & Brody, E.M. (1969). Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist*, 9, 179-186.

Lima-Costa, M. F., De Oliveira, C., Macinko, J., & Marmot, M. (2012). Socioeconomic inequalities in health in older adults in Brazil and England. *American Journal of Public Health*, 102, 1535-41.

Lima-Costa, M.F., Firmo, J.O., & Uchoa, E. (2011). Cohort profile: the Bambuí (Brazil) cohort study of ageing. *International Journal of Epidemiol*ogy, 40, 862–867.

Lima-Costa, M. F., Peixoto, S. V., Matos, D. L., Firmo, J. O., & Uchôa, E. (2011). Predictors of 10-year mortality in a population of community-dwelling Brazilian elderly: the Bambuí Cohort Study of Aging. *Cadernos de Saúde Pública,* 27, 360-369.

Majer, I. M., Nusselder, W. J., Mackenbach, J. P., Klijs, B., van Baal, P. H. (2011). Mortality risk associated with disability: A population-based record linkage study. *American Journal of Public Health*, 101, 9-15.

Murtagh, K.N., & Hubert, H.B. (2004). Gender differences in physical disability among na elderly cohort. *American Journal of Public Health,* 94, 1406-1411.

Nagi, S. Z. (1976). An epidemiology of disability among adults in the United States. *The Milbank Memorial Fund Quartely. Health and Society,* 54, 439-467.

Nybo, H., Petersen, H. C., Gaist, D., Jeune, B., Andersen, K., McGue, M., et al. (2003). Predictors of mortality in 2,249 nonangenarians – The Danish 1905-cohort study. *Journal of the American Geriatrics Society*, 51, 1365-1373.

Oksuzyan, A., Juel, K., Vaupel, J.W., & Christensen, K. (2008). Men: good health and high mortality. Sex diferences in health and aging. *Aging Clinical and Experimental Research*, 20, 91-102.

Pongiglione, B., De Stavola, B.L., Kuper, H., & Ploubidis, G.B. (2016). Disability and all-cause mortality in the older population: evidence from the english longitudinal study of ageing. *European Journal of Epidemiology*, 31, 735-746.

Pudaric, S., Sundquist, J., & Johansson, S. E. (2003). Country of birth, instrumental activities of daily living, self-rated health and mortality: a Swedish population-based survey of people aged 55–74. *Social Science & Medicine* , 56, 2493-2503.

Ramalho, J. R., Lima-Costa, M. F., Firmo, J. O., & Peixoto, S. V. (2011). Energy expenditure through physical activity in a population of community-dwelling Brazilian elderly: cross-sectional evidences from the Bambuí cohort study of aging. *Cadernos de Saude Publica*, 27, 399–408.

Ramos, L. R., Andreoni, S., Coelho-Filho, J. M., Lima-Costa, M. F., Matos, D. L., Rebouças, M., & Veras, R. (2013). Perguntas mínimas para rastrear dependência em atividades de vida diária em idosos. *Revista de Saúde Publica*, 47, 506-513.

Ramos, L.R., Simões, E.J., & Albert, M.S. (2001). Dependence in activities of daily living and cognitive impairment strongly predicted mortality in older urban residents in Brazil: a 2-year follow-up. *Journal of the American Geriatrics Society,* 49, 1168-75.

Rose G. (1962). The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bulletin of the World Health Organization*, 27, 645–658.

St Johon, P. D., Tyas, S. L., Menec, V., & Tate, R. (2014). Multimorbidity, disability and mortality in community-dwelling older adults. *Canadian Family Physician*, 60, e272-280.

Stineman, M. G., Xie, D., Pan, Q., Kurichi, J. E., Zhang, Z., Saliba, D., et al. (2012). All-Cause 1-,5-, and 10-year mortality among elderly people according to activities of daily living stage. *Journal of the American Geriatrics Society*, 60, 485-492.

Stuck, A. E., Walthert, J. M., Nikolaus T., Büla C. J., Hohmann C., & Beck J. C. (1999). Risk factors for functional status decline in community-living elderly people: a systematic literature review. *Social Science & Medicine,* 48, 445-469.

Studenski, S., Perera, S., Patel, K., Rosano, C., Faulkner, K., Inzitari, M., et al. (2011). Gait speed and survival in Older Adults**.** *JAMA*, 305, 50-58.

Takata, Y., Ansai, T., Soh, I., Awano, S., Nakamichi, I., Akifusa, S., et al. (2013). High-level activities of daily living and disease specific mortality during a 12 year follow-up of an octogenarian population. *Clinical Interventions in Aging*, 8, 721-728.

Tiainen, K., Luukkaala, T., Hervonen, A., & Jylhä, M. (2013). Predictors of mortality in men and women aged 90 and older: a nine-year follow-up study in the vitality 90+ study. *Age and Ageing*, 42, 468-475.

Tsuji, I., Minami, Y., Li, J. H., Fukao, A., Hisamichi, S., Asano, H., et al. (1995). Dementia and physical disability as competing risks for mortality in a community-based sample of the elderly Japanese. The *Tohoku Journal of Experimental Medicine*, 176, 99-107.

van Houwelingen, A. H., Cameron, I. D., Gussekloo, J., Putter, H., Kurrle, S., de Craen, A. J., et al. (2014). Disability transitions in the oldest old in the general population. The Leiden 85-plus study. *Age*, 36, 483-493.

Webber, S.C., Porter, M.M., & Menec, V.H. (2010). Mobility in older adults: a comprehensive framework. *The Gerontologist*, 50, 443-450.

Table 1. Selected baseline characteristics of study participants by sex. The Bambuí Cohort Study of Aging, 1997.

Characteristics	Total (N=1,333)	Males (n=520)	Females (n=813)	p-value[1]
Age in years, mean (SD)	68.9 (7.0)	68.6 (7.1)	69.0 (6.9)	0.379
Schooling less than 4 years, n (%)	849 (63.7)	316 (60.8)	533 (65.6)	0.076
Married/live together, n (%)	666 (49.6)	394 (75.8)	272 (33.5)	<0.001
Current smokers, n (%)	233 (17.5)	150 (28.9)	83 (10.2)	<0.001
Alcohol consumption in the last year, n (%)	286 (21.5)	228 (43.9)	58 (7.1)	< 0.001
Physical Inactivity, n (%)	364 (27.3)	118 (22.7)	246 (30.3)	0.002
Body mass index in kg/m2, mean (SD)	25.1 (5.0)	24.0 (10.5)	25.9 (5.3)	<0.001
Total cholesterol in mg/dL, mean (SD)	233.9 (49.1)	220.8 (46.0)	242.2 (49.1)	<0.001
Fasting glucose in mg/dL, median	99 (91-111)	99 (91-111)	100 (90-112)	0.588
Systolic blood pressure in mmHg, mean (SD)	137.2(22.6)	137.6 (22.7)	137.0 (22.6)	0.670
Mini-Mental State Examination score, median (IQR)	26 (23-28)	25 (21-27)	26 (24-28)	<0.001
Trypanossoma cruzi infection, n (%)	501 (37.6)	161 (31.0)	340 (41.8)	<0.001
Angina, n (%)	123 (9.2)	33 (6.4)	90 (11.1)	0.004
Stroke, n (%)	46 (3.5)	15 (2.9)	31 (3.8)	0.365
Heart attack, n (%)	62 (4.6)	27 (5.2)	35 (4.3)	0.453
Arthritis, n (%)	422 (31.7)	142 (27.3)	280 (34.4)	0.006
Number of mobility disability, n (%)				
0	765 (57.4)	332 (63.8)	433 (53.3)	<0.001
1	220 (16.5)	79 (15.2)	141 (17.3)	
2 or more	348 (26.1)	109 (21.0)	239 (29.4)	
Number of IADL disability, n (%)				
0	746 (56.0)	362 (69.6)	384 (47.2)	<0.001
1	292 (21.9)	74 (14.2)	218 (26.8)	
2 or more	295 (22.1)	84 (16.2)	211 (26.0)	
Number of BADL disability, n (%)				
0	1060 (79.5)	434 (83.5)	626 (77.0)	0.006
1	152 (11.4)	42 (8.1)	110 (13.5)	
2 or more	121 (9.1)	44 (8.5)	77 (9.5)	

SD: Standard deviation. IQR: interquartile range. BADL: Basic activities of daily living. IADL: Instrumental Activities of daily living.[1] p-value: Pearson's chi-square test for comparison between proportion, Student's t test for differences between means and Mann Whitney test for differences between medians.

1   Table 2. Number of deaths and mortality rates over 15-year follow-up by baseline disability domains and sex. The Bambuí Cohort Study of Aging, 1997-2011.

Disability domains	Total		Men		Women	
	Number of deaths	Mortality rate per 1,000 pyrs	Number of deaths	Mortality rate per 1,000 pyrs	Number of deaths	Mortality rate per 1,000 pyrs
Number of mobility disability						
0	316	35.3	157	41.7	159	30.6
1	113	46.5	50	68.3	63	37.2
2 or more	243	76.2	85	98.5	158	67.9
Number of IADL disability						
0	314	36.2	167	41.0	147	31.9
1	142	43.8	51	75.7	91	35.4
2 or more	216	81.2	74	120.4	142	69.5
Number of BADL disability						
0	494	41.4	225	48.4	269	36.9
1	88	55.8	32	87.3	56	46.3
2 or more	90	84.7	35	102.1	55	76.5
Total	672	46.1	292	54.5	380	41.2

2   BADL: Basic activities of daily living. IADL: Instrumental Activities of daily living. pyrs: person-years at risk.

3

4

5

6

7

8 Table 3: Hazard ratios for 15-year mortality by baseline disability domains and sex. The Bambuí Cohort Study of Aging, 1997-2011.

Disability domains	Total			Males*			Women*		
	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95%CI)
Number of physical mobility disability (vs none)									
1	1.26 (1.02-1.57)	1.25 (1.01-1.55)	1.28 (1.03-1.60)	1.44 (1.04-1.98)	1.41 (1.02-1.94)	1.51 (1.09-2.09)	1.13 (0.84-1.51)	1.13 (0.84-1.51)	1.13 (0.84-1.52)
2 or more	2.20 (1.85-2.63)	1.94 (1.61-2.33)	1.82 (1.50-2.22)	2.58 (1.97-3.37)	2.07 (1.56-2.75)	1.92 (1.43-2.58)	1.97 (1.57-2.46)	1.84 (1.47-2.32)	1.75 (1.38-2.21)
Number of IADL disability (vs none)									
1	1.29 (1.05-1.59)	1.17 (0.95-1.44)	1.15 (0.93-1.42)	1.89 (1.38-2.59)	1.62 (1.17-2.23)	1.54 (1.12-2.13)	0.98 (0.76-1.28)	0.94 (0.72-1.22)	0.94 (0.72-1.22)
2 or more	2.05 (1.70-2.48)	1.79 (1.47-2.19)	1.68 (1.36-2.07)	2.63 (1.98-3.48)	2.17 (1.62-2.91)	2.07 (1.53-2.79)	1.66 (1.31-2.11)	1.53 (1.19-1.96)	1.43 (1.11-1.84)
Number of BADL disability (vs none)									
1	1.26 (0.99-1.59)	1.20 (0.95-1.51)	1.16 (0.92-1.47)	1.58 (1.09-2.29)	1.52 (1.05-2.20)	1.43 (0.97-2.09)	1.10 (0.83-1.47)	1.05 (0.78-1.40)	1.04 (0.78-1.40)
2 or more	1.92 (1.52-2.41)	1.70 (1.34-2.16)	1.51 (1.17-1.94)	2.42 (1.69-3.47)	2.04 (1.41-2.94)	1.65 (1.11-2.45)	1.65 (1.23-2.22)	1.52 (1.12-2.05)	1.43 (1.05-1.95)

9 HR: Hazard Ratio (95% confidence interval). BADL: Basic activities of daily living. IADL: Instrumental Activities of daily living.
10 Model 1: adjusted by ager, gender, schooling and marital status. Model 2: Adjusted by variables in model 1 plus current smoking, alcohol consumption and physical activity. Model 3: adjusted
11 by variables in model 2 plus body mass index, systolic blood pressure, fasting glucose, total cholesterol, Mini-Mental State Examination, *T. cruzi* infection, stroke, angina, heart attack and
12 arthritis.
13 * Models including the interaction term between sex and disability domain.