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## ORIGINAL ARTICLE

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### **Cognitive impairment and depressive symptoms: effects on functional disability, falls, hospitalization, and polypharmacy in a longitudinal follow-up**

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## ABSTRACT

**Introduction:** The ageing process is associated with a higher prevalence of depression and cognitive impairment, negatively affecting health. **Objective:** Analyse the effects of cognitive impairment and depressive symptoms on the risk of functional disability, falls, hospitalisation, and polypharmacy in a two-year follow-up. **Methods:** Longitudinal study, developed with 200 participants over 45 years old from primary healthcare centres in Três Lagoas, Mato Grosso do Sul, Brazil. The participants were initially evaluated using cognitive and depressive symptoms screening instruments. After two years, functional disability (instrumental activities of daily living), falls, hospitalisation, and polypharmacy were evaluated. Multinomial regression models were performed to assess the effects of cognitive impairment and depressive symptoms on outcomes. **Results:** 38.5% of the participants had a cognitive impairment, and 55.0% had depressive symptoms. Cognitive impairment at baseline was associated with an increased risk of disability to shopping (OR=2.946), performing housework (OR=2.196), and managing finances (OR=3.488). Depressive symptoms were related to a higher risk of dependence on traveling (OR=1.614), administering medications (OR=5.745), managing finances (OR=2.876), falls (OR=1.960), and polypharmacy (OR=2.464). Participants with the two associated conditions were at higher risk of dependence on using the telephone (OR=2.701), travelling (OR=2.177), shopping (OR=2.890), administering medications (OR=4.773), and managing finances (OR=3.799). **Conclusion:** Cognitive impairment was associated with dependence in three activities after two years. Depressive symptoms were related to a greater risk of dependence in three activities, falls, and polypharmacy. The cumulative effect of cognitive impairment and depressive symptoms negatively influenced the performance in five instrumental activities of daily living.

**Keywords:** aged; cognitive dysfunction; depression; longitudinal studies; middle aged.

## INTRODUCTION

Brazil has been going through a process of demographic and epidemiological transition, which culminates in an increase in life expectancy and in the prevalence of chronic non-communicable diseases, which can accelerate the frailty process and increase the risks of mortality, falls, and hospitalisation<sup>1</sup>. Some psychiatric and neurological clinical conditions can be highlighted, such as cognitive impairment and depression. They hurt the individual's daily life, interfering with their activities of daily living and interpersonal relationships, and having a relevant impact on the public health expenditures<sup>2</sup>. Activities of daily living are activities that we perform in our daily lives. They can be basic, like those we perform with our own body, and which are fundamental to our survival, or more complex, called Instrumental Activities of Daily Living (IADLs), which support daily life at home<sup>3</sup>.

Cognitive impairment is a clinical condition that negatively affects health and may be related to the diagnosis of mild cognitive impairment, as well as to several dementia conditions<sup>4</sup>. Unlike developed countries, which have a decreasing prevalence of cognitive impairment in older adults, in Brazil, there was a significant increase in this rate between 2000 and 2015<sup>5</sup>.

Attention should be paid to the serious consequences of cognitive impairment, which is usually accompanied by functional disability, decreased performance of daily activities, and social relationships<sup>6</sup>. Patients with some degree of cognitive decline have higher rates of hospital admissions, which are accompanied by a higher risk of developing delirium, dehydration, and the occurrence of falls<sup>7</sup>. A study conducted with older individuals with cognitive impairment showed that 41.7% had already suffered falls, with visual impairment, body imbalance, and polypharmacy<sup>8</sup> (use of five or more medications)<sup>9</sup> as risk factors for this event.

Depression is one of the most common mental disorders among the population, and major depression mainly affects individuals over 55 years of age, which represents 1.8% of the general population<sup>10</sup>. A meta-analysis also identified that 17.1% of individuals over 75 years of age present some type of depressive symptoms, while the same occurs in 19.5% of individuals over 50 years of age<sup>11</sup>. There are some risk factors for this psychological condition, such as female sex, cognitive decline, health impairment, and the use of tobacco and alcohol<sup>12</sup>.

Depression can have different clinical presentations in older individuals, making diagnosis difficult<sup>13</sup>. It also has consequences, such as increased risk of morbidity and functional dependence, decreased physical and cognitive health, and increased mental health. self-neglect<sup>14</sup>. In addition to raising health costs, depressive conditions increase the sensation of pain and intensify the risks of malnutrition, infections, hip fractures, and functional disability<sup>15</sup>.

In line with these findings, it is known that, in general, depression and cognitive impairment can occur together in older individuals, which consequently causes an even more intense variety of physical and emotional problems, which negatively compromise the quality of life<sup>15</sup>.

Considering the negative impact that these two clinical conditions, cognitive impairment and depression, can have on the quality of life of the older population, it is necessary to analyse their consequences in depth. There is a lack of data in the current literature about some variables that can be influenced by these clinical aspects, especially when identified concomitantly in individuals.

Thus, this research aimed to analyze the effects of cognitive impairment and depressive symptoms on the risk of functional disability, falls, hospitalization, and polypharmacy in a two-year follow-up. We hypothesize that: 1) Cognitive impairment is associated to functional disability in a two-year follow-up; 2) Depressive symptoms is associated to functional disability and

polypharmacy in a two-year follow-up; 3) The combined effects of cognitive impairment and depressive symptoms are more severe, and are associated to functional disability, falls, hospitalisation, and polypharmacy in a two-year follow-up.

## **METHODS**

This is a longitudinal study with a two-year follow-up, conducted with individuals over 45 years of age registered in primary healthcare centres in the city of Três Lagoas in Mato Grosso do Sul, Brazil. The present study is part of a larger research conducted by the Research Group “Assistance, research, teaching and management in Public Health”.

The inclusion criteria were being 45 years of age or older, being registered in one of the nine primary healthcare centres in the municipality, and having the ability to answer the questionnaire (assessed by the interviewer's perception).

The baseline was carried out between November 2018 and June 2019. The sample size was calculated using the formula for estimating proportion in a finite population, using a significance level of 5% ( $\alpha=0.05$ ) and a sampling error of 6% ( $e=0.06$ ), and the conservative estimate of 50% ( $p=0.50$ ), whose value provides the largest sample size. Considering a finite population of  $n=26,331$  (total of individuals over 45 years of age in the municipality), the minimum sample was 265 individuals, to which 10% was added to mitigate possible losses, resulting in 292 participants. A minimum of 30 participants were randomly selected from a list of all individuals over 45 years of age provided by each of the nine health teams. During the data collection, the convenience sample was composed of 300 individuals (final sample error of 5.6%).

Follow-up was conducted between February and December 2021, on average, 2.4 years after the baseline assessment. All baseline participants were sought to participate in the follow-up.

The evaluations were carried out by trained evaluators at the participants' homes or the primary healthcare centres and lasted around 40 minutes each.

The data collected at baseline were: a) Sociodemographic characterisation: sex (male, female), age (in years - continuous and categorized into adults - 45–59 years and older adults - 60 years or more), marital status (with a partner, without a partner), education (in years - continuous and categorized as illiterate, 1–4 years, 5–8 years, 9 years and over). b) Cognitive impairment: assessed by the Mini-Mental State Examination (MMSE) 30-point version, which is an instrument for tracking the cognitive situation and includes the domains of temporal and spatial orientation, immediate memory, attention and calculation, recall memory, and language. The instrument has a maximum score of 30 points, and the higher the score, the better the cognitive performance<sup>16</sup>. The cut-off scores were adjusted according to the level of education of the participants, being <26 for those with nine or more years of education, < 24 for those with 5–8 years of education, <22 for 1–4 years, and <17 for illiterate<sup>17</sup>. c) Depressive symptoms: evaluated by the Center for Epidemiological Studies, and d) Depression (CES-D). It has been validated in Brazil in populations of adolescents, adults, and older adults. It has 20 items that correspond to the frequency of depressive symptoms experienced in the week before the interview. The final score ranged from 0 to 60. For adults, the cut-off score for the presence of depressive symptoms is  $\geq 16$  points, and for older adults, it is  $\geq 12$  points<sup>18,19</sup>.

The follow-up data were the following (after two years): a) Functional disability: assessed by the Lawton and Brody Scale, which determines the degree of dependence for the performance of IADL: using a telephone, travelling, shopping, preparing meals, performing housework, administering medications, and managing finances. The scores ranged from 7 (totally dependent) to 21 (totally independent). Individuals with a score between 7 and 20 were considered dependent,

and those with a score equal to 21 were considered independent<sup>20</sup>. b) Occurrence of falls: assessed by the question “Have you had any falls in the last two years?”. c) Occurrence of hospitalisation: assessed by the question “Did you need to be hospitalized or use high-complexity services such as urgency/emergency units for at least 24 hours in the last two years?”. d) Occurrence of polypharmacy: the number of medications the participant took per day was questioned, with the use of five or more medications being considered polypharmacy, as it is the most used definition worldwide<sup>9</sup>.

Statistical Package for the Social Sciences (SPSS) version 25.0 was used for data analysis. To characterise participants at baseline (Table 1) and outcomes at follow-up (Table 2), we used absolute and relative frequencies (n and %), mean, standard deviation ( $\pm$ ), and Confidence Interval of the prevalence (95%CI). Participants who were lost in the follow-up assessment were compared using the chi-square test with those re-evaluated regarding sex, age group, marital status, and education. To assess the effects of cognitive impairment and depressive symptoms alone on outcomes, individual multinomial regression models were performed. Cognitive impairment and depressive symptoms were the independent variables. The dependence in each IADL, the occurrence of falls, hospitalisation, and polypharmacy were the dependent variables (Table 3). Finally, the last model (Table 4) evaluated the concomitant occurrence of cognitive impairment and depressive symptoms (independent variable) with the outcomes (dependent variables). All models were controlled for sex (ref: male) and age (ref: adult). Results with a p-value  $\leq 0.05$  were considered significant.

The Federal University of Mato Grosso do Sul ethics committee in research with human beings approved the study (approval numbers 2,596,194 e 4,467,405). All participants read and signed the written Informed Consent Form before the two interviews.

## RESULTS

Of the 300 participants evaluated in the baseline, 14 had died, 20 refused to participate, 24 were not found at home after three attempts at alternate times, 19 addresses were not found due to outdated registration, and 23 had changed addresses during the follow-up period. The final sample consisted of 200 participants (66.7% of the total baseline sample). No significant differences were identified regarding sex ( $p=0,667$ ), age group ( $p=0,086$ ), marital status ( $p>0,999$ ), and education ( $p=0,619$ ) between participants who were lost to follow-up and those re-evaluated, indicating a nondifferential loss.

Table 1 shows the characterisation data of the participants at baseline. Regarding the independent variables, 38.5% of the participants had cognitive impairment, 55.0% had depressive symptoms, and 21.5% had both concomitant conditions. As for the outcomes evaluated, 45.0% were dependent for IADL, with highest prevalence for travelling (26.5%), shopping (23.0%) and managing finances (23.0%); 34.0% of the participants reported falls, 22.0% reported hospitalisations, and the prevalence of polypharmacy was 20.0% (Table 2).

Table 3 shows that cognitive impairment at baseline was associated with dependence on the following IADLs: shopping (OR=2.946), performing housework (OR=2.196), and managing finances (OR=3.488) after two years. Depressive symptoms were related to a greater risk of dependence on traveling (OR=1.614), administering medications (OR=5.745), managing finances (OR=2.876), occurrence of falls (OR=1.960), and polypharmacy (OR=2.464).

Finally, Table 4 shows the results data for the concomitant presence of cognitive impairment and depressive symptoms at baseline. Individuals with the two associated conditions had a higher risk of dependence on using the telephone (OR=2.701), travelling (OR=2.177),

shopping (OR=2.890), administering medication (OR=4.773), and managing finances (OR=3.799). No associations were identified with falls, hospitalisation, and polypharmacy.

## **DISCUSSION**

This study identified the risk of adverse outcomes, after two years, in individuals with cognitive impairment, depressive symptoms, and with the two concomitant conditions. Cognitive impairment was associated with an increased risk of dependence on shopping, performing housework, and managing finances. Depressive symptoms were related to a higher risk of dependence on traveling, administering medication, managing finances, occurrence of falls, and polypharmacy. The concomitant presence of cognitive impairment and depressive symptoms was associated with a higher risk of dependence on using a telephone, traveling, shopping, administering medication, and managing finances after two years.

Cognitive impairment is initially related to the difficulty in performing advanced activities of daily living, progressing with worsening performance in IADLs and, finally, interfering with the individual's basic activities<sup>21</sup>. Cognitive decline mainly affects activities that involve memory or more complex reasoning, such as shopping and money management<sup>22</sup>. The same relationship is evidenced in another study, which indicates that the practice of IADLs needs other domains than memory, such as visuospatial orientation and attention, which are also impaired in cases of cognitive decline<sup>23</sup>. This evidence corroborates with the results found in this study since participants with cognitive impairment showed significant dependence on more complex activities, which often involve memory for their complete execution, such as shopping, organizing finances, and household chores.

In line with these findings, one study looked at individuals with mild cognitive impairment who progressed and who did not progress to dementia after five years. Two groups of IADLs were analysed; the first was related to organisational activities, such as cleaning and cooking, and the second was more complex, covering the use of a telephone, medication, shopping, and handling money. It was observed that in individuals who progressed to dementia, the decline in more complex activities is more pronounced, especially in the two years before diagnosis<sup>24</sup>. It also reinforces the importance of identifying the exact moment that these limitations appear, along with their trajectory and evolution, as they are sensitive markers for the progression of cognitive decline<sup>25</sup>. This becomes extremely relevant in clinical practice, as it allows for early interventions in these individuals.

Additionally, depression is a disabling disorder, especially in older individuals, being related to the increase in comorbidities and sedentary lifestyles, contributing to the occurrence of dependence on more complex daily activities<sup>26</sup>. This helps explain the dependence on activities such as travelling, administering medications, and managing finances in the sample that presented depressive symptoms in this study. In line with these findings, a cross-sectional study also related depression with a greater chance of dependence on IADLs, falls, poorer sleep quality, and multiple comorbidities<sup>27</sup>. Our study did not analyze sleep quality and the presence of multimorbidity but identified a relationship between depressive symptoms and polypharmacy, a condition related to the presence of multiple diseases<sup>28</sup>.

The presence of depression in older individuals attended by primary healthcare was associated with the use of more medications chronically<sup>29</sup>. Another study related the occurrence of mental disorders, especially depression, with the increased use of psychotropic drugs by the older population<sup>30</sup>, which may justify the relationship identified between depressive symptoms and

polypharmacy. Depression can also increase and exacerbate other medical symptoms, resulting in a greater demand for health services (increased hospitalisation) and the use of more medications<sup>31</sup>.

Furthermore, the use of psychotropic drugs directly influences the development of functional disability in individuals and the increase in the number of falls among them<sup>30</sup>. The occurrence of falls is directly associated with the presence of depressive symptoms<sup>32</sup>. First, people with depression become more socially and physically isolated, contributing to muscle weakness and, consequently, a greater occurrence of falls<sup>33</sup>. Furthermore, the use of antidepressants also has side effects such as dizziness and increased risk of osteoporosis, which further contributes to falls and fractures<sup>33</sup>. These data reinforce that in this study, there was a higher risk of falls and polypharmacy among people with depressive symptoms.

Our results also showed a portion of the sample that presented, simultaneously, depressive symptoms and cognitive impairment. This was already expected since part of the older population has this association, having a higher risk of dementia<sup>34</sup>. This interaction between clinical conditions is complex since depression can be both a risk factor and a consequence of cognitive impairment<sup>35</sup>. Patients with worsening depressive symptoms are known to have a more rapid decline in cognitive function<sup>36</sup>.

A study indicated that depressive symptoms and the individual's cognitive impairment are related to the decrease in functional capacity, which may be a cause or a symptom since the social interaction of these people is compromised<sup>37</sup>. This is also reflected in this study, which identified significant dependence for performing some IADLs, such as using the telephone, travelling, shopping, administering medication, and managing finances. Another investigation also showed that individuals with subjective cognitive decline and depressive symptoms are more likely to have objective memory impairment<sup>38</sup>. This becomes a possible explanation for the difficulty in

performing more complex activities, which require the use of memory, such as using the telephone and shopping.

In this study, the association of the two conditions did not present a significant relationship with falls, hospitalisations, and polypharmacy. A possible justification for this is that the study was conducted during the COVID-19 pandemic. At that time, as a way of minimising the viral spread, social distancing measures were implemented, such as closing shops, quarantining and banning agglomerations<sup>39</sup>. Consequently, the population spent more time at home, avoiding going to hospitals and medical appointments, which may also have reflected in their lower use of medication. Additionally, the isolation condition is also related to physical inactivity<sup>40</sup>. However, other explanations may be related to this result and can be investigated in future research.

Our study has limitations, such as the sample loss between the two data collections, the impossibility of generalizing the data, the lack of medical diagnosis of depression and cognitive impairment; and, that the follow-up happened when the COVID-19 pandemic still had high incidence and mortality rates in Brazil, which may have interfered with the participants' responses. Despite the limitations, the strengths are that the sample is composed of individuals over 45 years of age, evaluating individuals in the ageing process and before reaching old age to promote early interventions, and the longitudinal design.

## **Conclusion**

Cognitive impairment and depressive symptoms negatively influenced the outcomes after two years. Cognitive impairment was related to a higher risk of dependence in IADLs; depressive symptoms with greater risk of dependence on IADLs, occurrence of falls and polypharmacy; and the concomitant presence of cognitive impairment and depressive symptoms was associated with

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a higher risk of dependence in IADLs using the telephone, travelling, shopping, administering medication and managing finances. Early assessment and monitoring of the health of the ageing population are important to avoid harm to the most vulnerable individuals.

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**Table 1:** Characterisation of participants at baseline (n=200). Brazil, 2018–2019.

Variable	n (%) or mean ( $\pm$ standard deviation)
<b>Sex</b>	
Male	67 (33.5)
Female	133 (66.5)
<b>Age</b>	
Adults (45–59 years)	61.7 ( $\pm$ 11.0)
Older adults (60y+)	91 (45.5)
109 (54.5)	
<b>Marital status</b>	
With partner	112 (56.0)
Without partner	88 (44.0)
<b>Education</b>	
Illiterate	5.8 ( $\pm$ 4.4)
1–4 years	28 (14.0)
5–8 years	60 (30.0)
9 years and over	61 (30.5)
	51 (25.5)
<b>MMSE</b>	
Cognitive impairment (bellow the cut-off)	23.0 ( $\pm$ 4.1)
	77 (38.5)
<b>CES-D</b>	
Depressive symptoms	17.6 ( $\pm$ 12.9)
	110 (55.0)
<b>Concomitant cognitive impairment and depressive symptoms</b>	
	43 (21.5)

MMSE: Mini-Mental State Examination. CES-D: Center for Epidemiological Studies – Depression.

**Table 2:** Prevalence of outcomes in participants (n = 200) after two years. Brazil, 2021.

<b>Variable</b>	<b>n (%) or means (<math>\pm</math> standard deviation)</b>	<b>CI95% (prevalence)</b>
<b>IADL dependence</b>		
Using the telephone	24 (12.0)	8.2 – 17.2
Traveling	53 (26.5)	20.9 – 33.0
Shopping	46 (23.0)	17.7 – 29.3
Preparing meals	28 (14.0)	9.8 – 19.5
Performing housework	42 (21.0)	15.9 – 27.2
Administering medications	15 (7.5)	4.6 – 12.0
Managing finances	46 (23.0)	17.7 – 29.3
<b>Falls</b>	68 (34.0)	27.8 – 40.8
The number of falls	2.7 ( $\pm$ 3.1)	
<b>Hospitalisation</b>	44 (22.0)	16.8 – 28.2
Number of hospitalisations	1,5 ( $\pm$ 1.0)	
<b>Polypharmacy</b>	40 (20.0)	15.1 – 26.1
Number of medications/days	3.5 ( $\pm$ 2.5)	

CI: confidence interval. IADL: instrumental activities of daily living.

**Table 3:** Cognitive impairment and depressive symptoms as factors associated with the dependence on instrumental activities of daily living, falls, hospitalisation, and polypharmacy after two years. Brazil, 2021.

<b>Variable</b>	<b>OR</b>	<b>CI95%</b>	<b>p-value</b>
<b>Cognitive impairment</b>			
Using the telephone	2.448	0.939-6.382	0.067
Traveling	1.647	0.821-3.303	0.160
Shopping	2.946	1.348-6.438	<b>0.007</b>
Preparing meals	1.947	0.794-4.777	0.145
Performing housework	2.196	1.028-4.692	<b>0.042</b>
Administering medications	3.091	0.897-10.657	0.074
Managing finances	3.488	1.614-7.542	<b>0.001</b>
Falls	0.664	0.355-1.241	0.200
Hospitalisation	0.796	0.397-1.595	0.520
Polypharmacy	1.284	0.608-2.710	0.512
<b>Depressive symptoms</b>			
Using the telephone	1.697	0.674-4.272	0.261
Traveling	1.614	1.171-4.803	<b>0.016</b>
Shopping	1.880	0.887-3.985	0.100
Preparing meals	1.603	0.457-0.597	0.887
Performing housework	1.642	0.791-3.408	0.183
Administering medications	5.745	1.239-26.638	<b>0.025</b>
Managing finances	2.876	1.349-6.129	<b>0.006</b>
Falls	1.960	1.052-3.654	<b>0.034</b>
Hospitalisation	0.837	0.425-1.647	0.606
Polypharmacy	2.464	1.124-5.404	<b>0.024</b>

\* Adjusted for sex and age. OR: Odds Ratio. CI: confidence interval

**Table 4:** Cumulative effects of cognitive impairment and depressive symptoms as factors associated with the dependence on instrumental activities of daily living, falls, hospitalisation, and polypharmacy after two years. Brazil, 2021.

<b>Cognitive impairment + depressive symptoms</b>	<b>OR</b>	<b>CI</b>	<b>p-value</b>
Using the telephone	2.701	1.055-6.916	<b>0.038</b>
Traveling	2.177	1.041-4.552	<b>0.039</b>
Shopping	2.890	1.308-6.385	<b>0.009</b>
Preparing meals	1.519	0.576-4.005	0.398
Performing housework	2.017	0.927-4.389	0.077
Administering medications	4.773	1.496-15.235	<b>0.008</b>
Managing finances	3.799	1.772-8.145	<b>0.001</b>
Falls	0.950	0.484-1.862	0.880
Hospitalisation	0.589	0.265-1.311	0.195
Polypharmacy	1.764	0.814-3.822	0.150

\* Adjusted for sex and age. OR: Odds Ratio. CI: confidence interval