

**Article** 

Not peer-reviewed version

# One-Year Changes in Depressive Symptoms and Cognitive Function Among Brazilian Older Adults Attending Primary Care

Fernanda Maria Silva Rivoli , <u>Antonio Pedro Gabriel Monteiro Galhardo</u> , <u>Giancarlo Lucchetti</u> , Lízia Abreu Ésper , Yan Lyncon Ribeiro , <u>Gerson Santos</u> , <u>Helena José</u> , <u>Luís Sousa</u> \* , <u>Gail Low</u> , <u>Luciano Magalhães Vitorino</u> \*

Posted Date: 5 March 2025

doi: 10.20944/preprints202503.0309.v1

Keywords: aging; depression; cognitive dysfunction; geriatric psychiatry; longitudinal studies



Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Article

# One-Year Changes in Depressive Symptoms and Cognitive Function Among Brazilian Older Adults Attending Primary Care

Fernanda Maria Silva Rivoli <sup>1</sup>, Antonio Pedro Gabriel Monteiro Galhardo <sup>1</sup>, Giancarlo Lucchetti <sup>1</sup>, Lízia Abreu Ésper <sup>1</sup>, Yan Lyncon Ribeiro <sup>1</sup>, Gerson de Souza Santos <sup>2</sup>, Helena José <sup>3,4</sup>, Luís Sousa <sup>3,5</sup>, Gail Low, <sup>6</sup> and Luciano Magalhães Vitorino <sup>1,\*</sup>

- <sup>1</sup> Faculty of Medicine of Itajubá, Itajubá 37502-138, MG, Brazil.
- <sup>2</sup> Department of Medicine, Centro Universitário Ages, Paripiranga 48430-000, BA, Brazil
- <sup>3</sup> Atlântica School of Health, 2730-036 Barcarena, Portugal
- <sup>4</sup> Health Sciences Research Unit: Nursing (UICISA: E), Nursing School of Coimbra, 3004-011 Coimbra, Portugal
- <sup>5</sup> Comprehensive Health Research Centre, University of Évora, 7000-801 Évora, Portugal
- <sup>6</sup> Faculty of Nursing, MacEwan University, Edmonton, Alberta, Canada
- \* Correspondence: lucianoenf@yahoo.com.br; Tel.: +55 (35) 988008269

Abstract: Background: Aging is a global phenomenon closely associated to changes in cognitive function and mental health. These conditions substantially burden public health systems and adversely affect the quality of life of older adults. This study aimed to examine changes in depressive symptoms and cognitive function over a 12-month follow-up period in a cohort of Brazilian older adults attending primary care. Methods: This observational, longitudinal study included a randomized sample of individuals aged ≥60 years residing in São Paulo, Brazil, and registered at a Primary Healthcare Unit (PHU). Data collection involved administering a sociodemographic and health questionnaire along with two validated instruments: the Geriatric Depression Scale-15 (GDS-15) and the Mini-Mental State Examination (MMSE). Linear regression models were used for the analyses. Results: A total of 368 older adults were included, being 63% men and with a mean age of 74.65 years. After one year, depressive symptoms showed a notable increase, with the mean GDS-15 score rising from 5.97 to 7.48 (Cohen-d = 0.542). Likewise, there was a decrease in the mean MMSE score ranging from 19.11 to 18.88 (Cohen-d=0.216). Adjusted regression analyses revealed that depressive symptoms at baseline (B = 0.696; p = 0.048; R<sup>2</sup> = 0.19) and cognitive function at baseline (B = 0.444; p < 0.001; R<sup>2</sup> = 0.26) were predictive of their respective deteriorations over the follow-up period. Conclusion: Depressive symptoms and cognitive decline place a significant burden on public health systems in aging societies. These findings underscore the importance of continuous monitoring and early intervention strategies to mitigate their impact and enhance the quality of life for older adults.

Keywords: aging; depression; cognitive dysfunction; geriatric psychiatry; longitudinal studies

# 1. Introduction

Population aging is a global phenomenon with profound implications for public health. In Brazil, the older population is projected to reach 64 million by 2050, presenting significant challenges for healthcare systems, particularly in the management of chronic diseases, physical frailty, depressive symptoms, and cognitive decline [1,2]. These conditions directly impair the quality of life and functionality of older adults, while simultaneously escalating healthcare costs and demand for targeted interventions [3,4].



Depression is among the most prevalent mental health conditions affecting older adults, with a global prevalence of 28.4%. Its frequency varies across regions, influenced by cultural and socioeconomic factors that shape the onset and progression of symptoms [5,6]. In the same direction, cognitive decline is another critical concern, impacting 21.2% of older adults in long-term care facilities globally [6].

Evidence suggests both conditions frequently co-occur, reinforcing each other in a cycle that exacerbates both mental and cognitive health. Studies conducted in high-income countries indicate that depressive symptoms and cognitive decline become markedly more prevalent after the age of 75 [7,8]. Depressive disorders rank among the leading causes of disability worldwide, particularly among women [9,10].

In Brazil, depressive symptoms and cognitive decline present growing public health challenges, with national data indicating a rising prevalence, particularly among low-income and underserved populations [9,10]. Depressive disorders have become significant contributors to disability-adjusted life years (DALYs) in the country, with rates steadily increasing since 1990 [10].

Despite this, there remains a notable scarcity of longitudinal studies examining the trajectory of depressive symptoms and cognitive function in Brazil. Existing research is predominantly cross-sectional and often overlooks cultural and socioeconomic factors. Additionally, studies focusing on older adults utilizing primary healthcare services—an integral component of Brazil's healthcare system—are limited.

The scarcity of longitudinal studies hinders a comprehensive understanding of the relationship between depressive symptoms and cognitive decline in older adults. Without longitudinal evidence, it is challenging to track the progression of these conditions or determine how clinical and demographic factors influence their development. This kind of evidence would facilitate the design of community-based screening tools, interventions, and policies. [11]

Addressing these gaps is vital for improving both clinical practice and healthcare delivery. Depressive symptoms and cognitive decline significantly impair older adults' functionality and increase their reliance on healthcare services.[12] These conditions are often underdiagnosed in primary care, resulting in delayed treatment and missed opportunities for prevention. [13]

To address these issues, this study aims to examine changes in depressive symptoms *and* cognitive function over a 12-month follow-up period in a cohort of Brazilian older adults attending primary care. Understanding their natural history will enable healthcare professionals to better identify and intervene alongside at-risk older people earlier on.[13]

# 2. Materials and Methods

# 2.1. Study Design

This was an observational, longitudinal study (12-month follow-up), conducted among older adults (≥60 years) residing in São Paulo, BrazilThe study was conducted between 2018 and 2019 and was approved by the Research Ethics Committee of the São Paulo Municipal Health Department (approval number 2.961.352). All participants provided written informed consent before data collection at both baseline and follow-up. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

#### 2.2. Participants and Eligibility Criteria

Participants were older persons registered at the Marcus Wolosker Belenzinho Primary Healthcare Unit (PHU), located in São Paulo, Brazil. This PHU is part of the Unified Health System (Sistema Único de Saúde, SUS), which serves as the primary point of entry for healthcare services. The PHU is situated within an area that, in 2019, was home to some 40,000 persons, among whom 11% were aged 60 years or older. The SUS aims to ensure that primary healthcare facilities like this one address around 80% of the healthcare needs of older persons nationwide, as per the guidelines of Brazil's Ministry of Health.

#### 2.3. Sample Size

Sample size calculations were performed using  $G^*Power 3.1$  software to ensure sufficient power for multivariate regression analyses. Assuming a small effect size ( $f^2 = 0.10$ ),  $\alpha = 0.05$ , power (1- $\beta$ ) = 0.99, and 7 predictors, a minimum sample size of 300 participants was required. To account for potential losses during follow-up, the sample size was increased by 25%, resulting in the recruitment of 400 participants. This final sample size is sufficient to perform robust statistical analyses should there be attrition.

#### 2.4. Procedures at Baseline and Follow-Up

At baseline (Time 0). participants were randomly selected from PHU registries using patient identification numbers. Data collection was conducted during scheduled nursing consultations by a trained nurse with over 10 years of primary healthcare experience. The interviews lasted approximately 40 minutes and were conducted in private settings to ensure confidentiality.

At follow-up (Time 1), assessments were conducted between February and August 2019 using the same protocol. Participants were contacted via phone and scheduled for interviews at the PHU. The follow-up was completed with 368 participants, and all data were collected by the same experienced nurse to maintain consistency.

#### 2.5. Measures

# 2.5.1. Independent Variables

Sociodemographic and health data, including age (years) and gender (male or female), were collected. So too were health-related variables: daily medication use (yes or no), daily number of medications, and the presence of chronic diseases (Do you have any chronic conditions or diseases?" Yes or No). Chronic conditions were defined as those lasting three months or longer, with examples provided, such as hypertension, diabetes, depression, heart disease, arthritis, and cancer. Additional variables included polypharmacy (use of five or more medications daily, yes or no) and a history of falls in the last 12 months (yes or no).

# 2.5.2. Dependent Variables

Depressive symptoms were assessed using the Geriatric Depression Scale-15 (GDS-15), a 15-item instrument validated in Brazilian Portuguese [14]. Scores range from 0 to 15, with higher scores indicating more severe depressive symptoms. The scale includes items such as "Do you feel that your life is empty?" with response options of Yes (1 point) or No (0 points), and "Do you feel happy most of the time?" with responses of Yes (0 points) or No (1 point). A total score of 6 or more suggests the presence of depressive symptoms.

The Mini-Mental State Examination (MMSE), a widely used tool for cognitive function screening in older adults, validated in Brazilian Portuguese [15]. Scores range from 0 to 30, with higher scores indicating better cognitive function. Items include "What is today's date?" under the domain of orientation to time, with responses scored as Correct (1 point) or Incorrect (0 points), and "Spell the word 'WORLD' backward," under attention and calculation, with scoring based on full correctness (1 point) or any errors (0 points). The MMSE assesses various domains, including memory, language, and visuospatial skills, with adjustments for educational differences in Brazilian populations [16,17].

#### 2.6. Statistical Analysis

Data were analyzed using SPSS 26 (SPSS Inc.). Descriptive statistics were performed for continuous and categorical variables. Paired t-tests were used for within-group comparisons of continuous variables, and McNemar's test was applied for categorical variables. Effect sizes were calculated using Cohen's d, with thresholds for small ( $d \le 0.2$ ), medium ( $d \approx 0.5$ ), and large ( $d \ge 0.8$ ) effects [17]. To examine the associations between depressive symptoms (GDS-15) and cognitive

function (MMSE) at baseline and follow-up, simple linear regression models were used. Multivariate linear regression models adjusted for clinically relevant covariates (p < 0.05) included number of medications, self-rated health, polypharmacy, and history of falls. All analyses were performed with a significance level of p < 0.05 and a 95% confidence interval (CI).

# 3. Results

At baseline (Time 0), 400 older adults registered at the Marcus Belenzinho Primary Healthcare Unit (PHU) were recruited. At the 12-month follow-up (Time 1), 368 participants completed the assessments, resulting in a 92% response rate. Reasons for loss to follow-up included relocation (n = 14), death (n = 12), and severe health conditions preventing participation (n = 6). At baseline, participants had a mean age of 74.65 years (SD = 7.99) and 63% were men. The mean number of medications increased significantly from 3.83 (SD = 2.02) to 4.68 (SD = 1.65) (p < 0.001). Self-perceived health worsened, with proportions rating their health as "poor" significantly increasing from 21.21% to 32.03% (p = 0.001). The proportion of participants with taking  $\geq$ 5 medications per day rose from 36.95% to 67.12% (p < 0.001) and nearly everyone had a history of falls at follow-up (68.20% at Time 0 to 99.80% at Time 1; p < 0.001).

Table 1. Sociodemographic and Health Profile of Participants at Baseline (T0) and 12-Month Follow-Up (T1)a.

	1	1 \ /	
Variables	2018 (n=368)	2019 (n=368)	p-Value
Age (M; SD)	74.65 (7.99)	75.36 (7.79)	0.058
Number of Medications	3.83 (2.02)	4.68(1.65)	< 0.001
	n (%)	n (%)	
Gender			
Male	232 (63.0)	233 (63.3)	>0.999
Female	136 (37.0)	135 (36.7)	
Self-Perceived Health			
Excellent	28 (7.60)	16 (4.35)	
Good	114 (30.97)	97 (26.38)	0.001
Fair	148 (40.22)	137 (37.23)	
Poor	78 (21.21)	118 (32.03)	
Chronic disease			
Yes	338 (91,84)	367 (99,72)	< 0.001
No	30 (8,15)	01 (0,27)	
Polypharmacy (≥5 medications)			
Yes	136 (36.95)	247 (67.12)	< 0.001
No	232 (63.05)	121 (32.88)	
History of Falls <sup>b</sup>			
Yes	251 (68.20)	367 (99.80)	< 0.001
No	148 (31.80)	1 (0.20)	

<sup>a</sup>Older adults (n=32) who participated at the baseline, not follow-up, were excluded from this analysis. <sup>b</sup> in the lst 12 months. SD: Standard Deviation.

Table 2 shows that scores on the Geriatric Depression Scale (GDS-15) increased significantly from 5.97 (SD = 2.91) to 7.48 (SD = 2.65) (p < 0.001), yielding a moderate effect size (d = 0.542). Concurrently, there was a slight (d = 0.216) but significant decline in Mini-Mental State Examination (MMSE) scores, from 19.88 (SD = 2.92) to 19.11 (SD = 2.97) (p < 0.001). Cognitive decline, while modest, was statistically significant.

Table 2. Comparison of Depressive Symptoms and Cognitive Function of Participants (n=368).

Variables	T0 (n=368)	T1 (n=368)	p-Value	Effect Size
Depressive Symptoms	Média (SD)	Média (SD)		
GDS-15	5.97 (2.91)	7.48 (2.65)	< 0.001	0.542
Cognitive Function				
MMSE	19.88 (2.92)	19.11 (2.97)	< 0.001	0.216

SD: Standard Deviation; GDS-15: Geriatric Depression Scale-15; MMSE: Mini-Mental State Examination.

The adjusted linear regression analysis revealed that higher levels of depressive symptoms at baseline were significantly associated with higher depressive symptom levels at 12 months (B = 0.696; p = 0.048). Similarly, lower cognitive function at baseline (Time 0) predicted greater cognitive decline one year later, at Time 1 (B = 0.444; p < 0.001).

**Table 3.** Adjusted Linear Regression Analyses of Depressive Symptoms and Cognitive Function at Baseline (Time 0) and 12-Month Follow-Up (Time 1).

Variables	B (SE)	Beta	p-value	Adjusted R <sup>2</sup>
GDS-15*	0.123 (0.047)	0.135	< 0.001	0.13
GDS-15**(Sociodemographic and Clinical)	0.696 (0.386)	0.110	0.048	0.19
$MMSE^a$	0.465 (0.047)	0.457	< 0.001	0.29
MMSE** (Sociodemographic and Clinical)	0.444 (0.049)	0.437	<0.001	0.26

<sup>\*</sup>GDS-15 and MMSE without adjustment; \*\*GDS-15 and MMSE adjusted for clinical variables (number of medications, self-perceived health, polypharmacy, history of falls). SE: Standard Error.

#### 4. Discussion

This longitudinal study provides important insights into the progression of depressive symptoms and cognitive decline among older adults utilizing primary healthcare services in Brazil. Over a 12-month period, we observed a significant worsening of depressive symptoms, alongside a modest but statistically significant decline in cognitive function.

The observed increase in depressive symptoms, as measured by the GDS-15, aligns with prior studies highlighting a growing burden of emotional distress among older adults over time [18–20]. However, in our studied sample, we observed a much higher or moderate statistically significant increase in mean GDS-15 scores after one year.

We also found substantial increases in polypharmacy (from 36.95% to 67.12%), a factor known to exacerbate depressive symptoms [21,22]. Polypharmacy is usually defined as the concomitant use of  $\geq$ 5 drugs and the use of  $\geq$ 10 excessive [23] and can persist [24]. Polypharmacy in older adults has been associated with a significantly higher risk of depression, largely due to adverse drug interactions, side effects, and the cognitive burden of complex medication regimens [21].

Polypharmacy can be associated with multiple adversities, including dementia, enhanced symptoms of depression, and even death [25]. A recent meta-analysis showed that managing these regimens may dampen one's social motivation and even conjure anxiety, particularly at the cusp of older age [26]. One in 4 older people live more isolated lives than before COVID-19 [27], and perhaps also feel fairly/very lonely [28]. We examined data over one year of time. Longer-term observations are warranted to further uncouple links between medication regimens and depressive symptoms.

Cognitive decline, assessed through the MMSE, was modest but statistically significant, corroborating findings from other longitudinal studies involving community-dwelling older adults [29,30]. Despite a small effect size, the steady decline in MMSE scores highlights the vulnerability of cognitive function in aging populations, especially in individuals with multimorbidity and polypharmacy [23,35–37].

Notably, the rise in polypharmacy and a history of falls likely further exacerbated cognitive decline [31,32]. Cognitive impairment is a known to increase falls risks over time [34,38]. Polypharmacy is a double-edged sword with many ugly sides. Other pernicious companions include slower gait [39], frequent hospital admissions, and non-beneficial medication prescribing [34]. Slower gait has enhanced some community-dwelling older persons' risk for falling for up to one year [40]. A lesser capacity to get out and about on one's own volitions, albeit from falls or other traumas, and shrinking social circles can aggravate emotional distress in later life [27,28]. Some older people experiencing physically traumatic events report taking 10 or more medications a day [37]. Persistent complex regimens have put others at a significantly higher risk for falls-related injuries in both hospital and outpatient settings [24].

All such corroborative findings ought to make healthcare practitioners feel ill at ease and engage in continuous monitoring for timely, and ideally preventative, action [34,41]. Regular medication regimen reviews of expected and actual therapeutic effects and ultimately, medication necessity, are key. Culprits otherwise known as 'Medications That Increase the Risk of Falls (FRIDs)', including narcotics, diuretics, betablockers, and antipsychotics [35], require hyper-vigilance. Careful screening would permit deprescribing wherever possible and therapeutic reconciliation [24,35,38,42]. Cognitive impairment obfuscates clinical presentations, particularly among persons living with dementia [33].

Best practices for reducing opioids, benzodiazepines, and other FRIDs should include fall and depression related risk education and a transparent co-designed follow-up plans for patients and their families. Patients without family would benefit from a PHU advocate such as a Nurse Practitioner. Good deprescribing duly considers older person's overall health, and comfort [35,43].

Ultimately, older persons are the ones who have to live with the psychological impacts of medication regimens, day in and day out. Older persons residing in 20 different countries have told us that quality living is about being one's own health steward, both with clarity of mind and with health care practitioners knowing what they value and expect, and their immediate living environment [44]. This cannot be over-emphasized. In this study, as others point out [45], depressive symptoms and cognitive decline can and do co-exist in later life. Depression may impair cognitive processes, such as memory, attention, and executive function, while cognitive decline can exacerbate depressive symptoms by reducing independence and quality of life [46]. We implore health care practitioners to keep this vicious circle in mind early, at the forefront of co-decision-making and codesign of follow-up planning.

Another best practice is establishing a community of care wherein patients and practitioners need to steer clinical decision-making rudders [47]. Shared decision-making and clarity of mind are ideal steadfast companions. Practitioner-devised complex drug regimens and lived cognitive impairment are not. Older people have long argued that having a stake in decision making is important [48]. This can entail exploring, early on, older persons' preferences for numbers of medications, and their perceived impacts and capacity to manage them.

These are critical implications for clinical practice. The strong association between baseline depressive symptoms and their progression over 12 months highlights the importance of early identification and treatment of depression.

Routine depression screening in primary care settings, using validated tools like the GDS-15, should be a priority, and early on to enhance diagnostic accuracy [49]. Early interventions, including both pharmacological and non-pharmacological approaches such as cognitive-behavioral therapy and social engagement programs are also recommended to keep depressive symptoms in tow. Primary care providers should incorporate tools like the MMSE or Mini-Cog into routine evaluations, particularly for patients with known risk factors such as polypharmacy and a history of falls [50,51].

Finally, the study highlights the urgent need for a multidisciplinary approach in primary care. Given the interconnected nature of depressive symptoms and cognitive decline, collaboration among geriatricians, psychologists, and primary care providers is essential. Comprehensive care models addressing both mental and physical health could improve outcomes for older adults while reducing

long-term healthcare burdens [50]. Other essential practitioners helping older persons to co-design follow-up plans include pharmacists, nurse practitioners, and occupation therapists.

Despite its strengths, this study has several limitations. The sample was drawn from a single PHU in São Paulo, which may limit the generalizability of what we found. Additionally, while validated instruments (GDS-15 and MMSE) were used, reliance on self-reported data for variables such as medication use and fall history may introduce recall bias. Future research should consider integrating objective measures and exploring the role of social determinants—such as own living environment and access to adjunct therapies and programs—in shaping the progression of depressive symptoms and cognitive decline. Expanding longitudinal studies to diverse settings would also enhance our understanding of these conditions and their broader implications.

# 5. Conclusions

This study demonstrates that depressive symptoms and cognitive decline are significant and interrelated challenges for older adults in primary care settings. The observed worsening of depressive symptoms and modest cognitive decline over 12 months underscores the importance of early detection and intervention.

Our findings advocate for routine screening, the adoption of early comprehensive and codesigned interventions to mitigate the impact of these conditions. Future research should focus on elucidating the mechanisms linking depressive symptoms and cognitive decline and evaluating the effectiveness of co-designated early intervention and follow-up plans. We can best uncouple these links within multi-disciplinary teams with older people helping to steer clinical decision making rudders.

**Author Contributions**: Conceptualization, L.M.V. and G.S.S.; methodology, L.M.V and G.S.S.; software, L.MV.; validation, L.M.V, and G.L.; formal analysis, L.M.V.; investigation, L.M.V and G.S.S; data curation, L.M.V, and G.L.X.; writing—original draft preparation, F.M.S.R., A.P.G.M.G., L.A.E., Y.L.R.; writing—review and editing, L.M.V., L.S., G.Low, and H.J. and G.L.; visualization, L.M.V., H.J., L. S. and G.L.; supervision, L.M.V; project administration, All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of the São Paulo Municipal Health Department (approval number 2.961.352).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study. **Data Availability Statement:** Data will be available upon request (lucianoenf@yahoo.com.br).

Conflicts of Interest: The authors declare no conflicts of interest.

# References

- Dall, T. M.; Gallo, P. D.; Chakrabarti, R.; West, T.; Semilla, A. P.; Storm, M. V. An Aging Population and Growing Disease Burden Will Require a Large and Specialized Health Care Workforce by 2025. *Health Affairs* 2013, 32 (11), 2013–2020. https://doi.org/10.1377/hlthaff.2013.0714.
- 2. Tramujas Vasconcellos Neumann, L.; Albert, S. M. Aging in Brazil. *Gerontologist* **2018**, *58* (4), 611–617. https://doi.org/10.1093/geront/gny019.
- 3. Prince, M. J.; Wu, F.; Guo, Y.; Gutierrez Robledo, L. M.; O'Donnell, M.; Sullivan, R.; Yusuf, S. The Burden of Disease in Older People and Implications for Health Policy and Practice. *Lancet* **2015**, *385* (9967), 549–562. https://doi.org/10.1016/s0140-6736(14)61347-7.
- 4. GBD 2019 Dementia Forecasting Collaborators. Estimation of the Global Prevalence of Dementia in 2019 and Forecasted Prevalence in 2050: An Analysis for the Global Burden of Disease Study 2019. *Lancet Public Health* 2022, 7 (2), e105-e25. https://doi.org/10.1016/s2468-2667(21)00249-8.

- 5. Hu, T.; Zhao, X.; Wu, M.; Li, Z.; Luo, L.; Yang, C.; Yang, F. Prevalence of Depression in Older Adults: A Systematic Review and Meta-Analysis. *Psychiatry Research* **2022**, 311 (0165-1781), 114511. https://doi.org/10.1016/j.psychres.2022.114511.
- Chen, P.; Cai, H.; Bai, W.; Zhang, Q.; Su, Z.; Tang, Y.-L.; Ungvari, G. S.; Ng, C. H.; Xiang, Y.-T. Global Prevalence of Mild Cognitive Impairment among Older Adults Living in Nursing Homes: A Meta-Analysis and Systematic Review of Epidemiological Surveys. *Transl Psychiatry* 2023, 13, 88. https://doi.org/10.1038/s41398-023-02361-1
- 7. Weyerer, S.; Eifflaender-Gorfer, S.; Wiese, B.; Luppa, M.; Pentzek, M.; Bickel, H.; Bachmann, C.; Scherer, M.; Maier, W.; Riedel-Heller, S. G. Incidence and Predictors of Depression in Non-Demented Primary Care Attenders Aged 75 Years and Older: Results from a 3-Year Follow-up Study. *Age and Ageing* **2013**, *42* (2), 173–180. https://doi.org/10.1093/ageing/afs184.
- 8. Borelli, W. V.; Zimmer, E. R.; Bieger, A.; Coelho, B.; Pascoal, T. A.; Chaves, M. L. F.; Amariglio, R.; Castilhos, R. M. Subjective Cognitive Decline in Brazil: Prevalence and Association with Dementia Modifiable Risk Factors in a Population-Based Study. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* 2022, 14 (1). https://doi.org/10.1002/dad2.12368.
- 9. Zenebe, Y.; Akele, B.; W/Selassie, M.; Necho, M. Prevalence and Determinants of Depression among Old Age: A Systematic Review and Meta-Analysis. *Ann Gen Psychiatry* **2021**, 20 (1), 55. https://doi.org/10.1186/s12991-021-00375-x.
- 10. Bonadiman, C. S. C.; Malta, D. C.; de Azeredo Passos, V. M.; Naghavi, M.; Melo, A. P. S. Depressive Disorders in Brazil: Results from the Global Burden of Disease Study 2017. *Popul Health Metr* **2020**, *18* (S1),6. https://doi.org/10.1186/s12963-020-00204-5.
- 11. Nóbrega, I. R. A. P. da; Leal, M. C. C.; Marques, A. P. de O.; Vieira, J. de C. M. Fatores Associados à Depressão Em Idosos Institucionalizados: Revisão Integrativa. *Saúde em Debate* **2015**, 39 (105), 536–550. https://doi.org/10.1590/0103-110420151050002020.
- 12. García-Peña, C.; Espinel-Bermúdez, C.; Tella-Vega, P.; Pérez-Zepeda, M. U.; Gutiérrez-Robledo, L. M. Longitudinal Studies and Older Adults Cohorts. In *Aging Research Methodological Issues*. García-Peña, C., Gutiérrez-Robledo, L.M., Pérez-Zepeda, M.U., editors. Springer International Publishing: Cham, Swisse, 2018; pp. 95–113. https://doi.org/10.1007/978-3-319-95387-8 8.
- 13. Pereira, M.E.A.; Santos, G.d.S.; Almeida, C.R.d.; Nunes, K.C.S.; Silva, M.C.M.d.; José, H.; Sousa, L.; Vitorino, L.M. Association between Falls, Fear of Falling and Depressive Symptoms in Community-Dwelling Older Adults. *Healthcare* **2024**, *12*, 1638. https://doi.org/10.3390/healthcare12161638
- 14. Paradela, E. M. P.; Lourenço, R. A.; Veras, R. P. Validação Da Escala de Depressão Geriátrica Em Um Ambulatório Geral. *Revista de Saúde Pública* **2005**, *39* (6), 918–923. https://doi.org/10.1590/s0034-89102005000600008.
- 15. Folstein, M. F.; Folstein, S. E.; McHugh, P. R. "Mini-Mental State". A Practical Method for Grading the Cognitive State of Patients for the Clinician. *J Psychiatr Res* **1975**, 12 (3), 189–198. https://doi.org/10.1016/0022-3956(75)90026-6.
- 16. Laks, J.; Baptista, E. M. R.; Contino, A. L. B.; Paula, E. O. de; Engelhardt, E. Mini-Mental State Examination Norms in a Community-Dwelling Sample of Elderly with Low Schooling in Brazil. *Cadernos de Saúde Pública* **2007**, 23 (2), 315–319. https://doi.org/10.1590/s0102-311x2007000200007.
- 17. Bertolucci, P.H.; Brucki, S.M.; Campacci, S.R; Juliano, Y. The Mini-Mental State Examination in a General Population: Impact of Educational Status. *Arg Neuropsiquiatr* **1994**, *52* (1), 1–7.
- 18. Schaakxs, R.; Comijs, H. C.; Lamers, F.; Beekman, A. T. F.; Penninx, B. W. J. H. Age-Related Variability in the Presentation of Symptoms of Major Depressive Disorder. *Psychol Med* **2017**, 47 (3), 543–552. https://doi.org/10.1017/s0033291716002579.
- 19. Wilder, M. E.; Kulie, P.; Jensen, C.; Levett, P.; Blanchard, J.; Dominguez, L. W.; Portela, M.; Srivastava, A.; Li, Y.; McCarthy, M. L. The Impact of Social Determinants of Health on Medication Adherence: A Systematic Review and Meta-Analysis. *Journal of General Internal Medicine* **2021**, *36* (5). https://doi.org/10.1007/s11606-020-06447-0.
- 20. Comijs, H. C.; Nieuwesteeg, J.; Kok, R.; van Marwijk, H. W.; van der Mast, R. C.; Naarding, P.; Voshaar, R. C. O.; Verhaak, P.; de Waal, M. W.; Stek, M. L. The Two-Year Course of Late-Life Depression; Results from

- the Netherlands Study of Depression in Older Persons. *BMC Psychiatry* **2015**, *15* (1). https://doi.org/10.1186/s12888-015-0401-5.
- 21. Vitorino, L.M.; Lopes, J.; Souza Santos, G.; Oliveira, C.; Helena, J.; Sousa, L.; Prevalence of Polypharmacy of Older People in a Large Brazilian Urban Center and its Associated Factors. *International Journal of Environmental Research and Public Health*. **2023**, 20 (01).
- 22. Livingston, G.; Huntley, J.; Liu, K. Y.; Costafreda, S. G.; Geir Selbæk; Suvarna Alladi; Ames, D.; Banerjee, S.; Burns, A.; Brayne, C.; Fox, N. C.; Ferri, C. P.; Gitlin, L. N.; Howard, R.; Kales, H. C.; Kivimäki, M.; Larson, E. B.; Noeline Nakasujja; Rockwood, K.; Samus, Q. Dementia Prevention, Intervention, and Care: 2024 Report of the Lancet Standing Commission. *Lancet* 2024, 404 (10452). https://doi.org/10.1016/s0140-6736(24)01296-0.
- 23. Yu, X.; Qian, Y.; Zhang, Y.; Chen, Y.; Wang, M. Association between Polypharmacy and Cognitive Impairment in Older Adults: A Systematic Review and Meta-Analysis. *Geriatric Nurs* **2024**, *59*, 330–337. https://doi.org/10.1016/j.gerinurse.2024.07.005.
- 24. Xue, L.; Boudreau, R. M.; Donohue, J. M.; Zgibor, J. C.; Marcum, Z. A.; Costacou, T.; Newman, A. B.; Waters, T. M.; Strotmeyer, E. S. Persistent Polypharmacy and Fall Injury Risk: The Health, Aging and Body Composition Study. *BMC Geriatrics* **2021**, 21 (1). https://doi.org/10.1186/s12877-021-02695-9.
- 25. Palapinyo, S.; Methaneethorn, J.; Leelakanok, N. Association between Polypharmacy and Depression: A Systematic Review and Meta-Analysis. *J. Pharm. Pract. Res.* **2021**. https://doi.org/10.1002/jppr.1749.
- Wiersema, C.; Oude Voshaar, R. C.; van den Brink, R. H. S.; Wouters, H.; Verhaak, P.; Comijs, H. C.; Jeuring, H. W. Determinants and Consequences of Polypharmacy in Patients with a Depressive Disorder in Later Life. *Acta Psychiatr. Scand.*2022, 146 (1), 85–97. https://doi.org/10.1111/acps.13435.
- 27. World Health Organization. *WHO launches commission to foster social connection*. World Health Organization. 2023 Available online: https://www.who.int/news/item/15-11-2023-who-launches-commission-to-foster-social-connection. (accessed on 3 March 2025).
- 28. Maese, E. *Almost a Quarter of the World Feels Lonely*, 2023. Available online: Gallup.com. https://news.gallup.com/opinion/gallup/512618/almost-quarter-world-feels-lonely.aspx. (accessed on 3 March 2025).
- 29. Beekman, A. T. F.; Geerlings, S. W.; Deeg, D. J. H.; Smit, J. H.; Schoevers, R. S.; de Beurs, E.; Braam, A. W.; Penninx, B. W. J. H.; van Tilburg, W. The Natural History of Late-Life Depression: a 6-year prospective study in the community. *Arch Gen Psychiatry* **2002**, *59* (7), 605. https://doi.org/10.1001/archpsyc.59.7.605.
- 30. Chui, H.; Gerstorf, D.; Hoppmann, C. A.; Luszcz, M. A. Trajectories of Depressive Symptoms in Old Age: Integrating Age-, Pathology-, and Mortality-Related Changes. *Psychol Aging g* **2015**, 30 (4), 940–951. https://doi.org/10.1037/pag0000054.
- 31. Lovett, R. M.; Bonham, M.; Julia Yoshino Benavente; Zahra Hosseinian; Greg Joseph Byrne; Maria Varela Diaz; Bass, M.; Yao, L.; A. Adin-Cristian; Batio, S.; Kim, M.; van; Moran, M.; Buchanan, D.; Hunt, J.; Young, S.; Gershon, R.; Nowinski, C. J.; Wolf, M. S. Primary Care Detection of Cognitive Impairment Leveraging Health and Consumer Technologies in Underserved US Communities: Protocol for a Pragmatic Randomised Controlled Trial of the MyCog Paradigm. *BMJ Open* **2023**, *13* (10), e080101. https://doi.org/10.1136/bmjopen-2023-080101.
- 32. Pettigrew, C.; Soldan, A. Defining Cognitive Reserve and Implications for Cognitive Aging. *Curr Neurol Neurosci Rep* **2019**, *19* (1). https://doi.org/10.1007/s11910-019-0917-z.
- 33. Zhao, M.; Chen, Z.; Xu, T.; Ping, F.; Tian, F. Global Prevalence of Polypharmacy and Potentially Inappropriate Medication in Older Patients with Dementia: A Systematic Review and Meta-Analysis. *Front. Pharmacol.* **2023**, 14. https://doi.org/10.3389/fphar.2023.1221069.
- 34. Scheel, J.; Luttenberger, K.; Graessel, E.; Kratzer, A.; Donath, C. Predictors of Falls and Hospital Admissions in People with Cognitive Impairment in Day-Care: Role of Multimorbidity, Polypharmacy, and Potentially Inappropriate Medication. *BMC Geriatrics* **2022**, 22 (1). https://doi.org/10.1186/s12877-022-03346-3.
- 35. Ie, K.; Chou, E.; Boyce, R. D.; Albert, S. M. Fall Risk-Increasing Drugs, Polypharmacy, and Falls among Low-Income Community-Dwelling Older Adults. *Innovation in Aging* **2021**, 5 (1). https://doi.org/10.1093/geroni/igab001.

- 36. Leelakanok, N.; D'Cunha, R. R. Association between Polypharmacy and Dementia a Systematic Review and Metaanalysis. *Aging & Mental Health* **2018**, 23 (8), 932–941. https://doi.org/10.1080/13607863.2018.1468411.
- 37. Molino, C.G.R. C; Rübel, L.; Mantegazza, N.; Bischoff-Ferrari, H. A.; Freystaetter, G. Association of Polypharmacy with Cognitive Impairment in Older Trauma Patients: A Cross-Sectional Study. *European Journal of Hospital Pharmacy* 2023, ejhpharm-2022-003645. https://doi.org/10.1136/ejhpharm-2022-003645.
- 38. Zhang, X.; Jiao, J.; Guo, N.; Bo, H.; Xu, T.; Wu, X. Association of Polypharmacy with Falls among Older Chinese Inpatients: A Nationwide Cohort Study. *Geriatrics & Gerontology International* **2021**, 21 (9), 810–817. https://doi.org/10.1111/ggi.14245.
- 39. Watanabe, K.; Umegaki, H.; Sugimoto, T.; Fujisawa, C.; Komiya, H.; Nagae, M.; Yamada, Y.; Kuzuya, M.; Sakurai, T. Associations between Polypharmacy and Gait Speed according to Cognitive Impairment Status: Cross-Sectional Study in a Japanese Memory Clinic. *Journal of Alzheimer's Disease* **2021**, *82* (3), 1115–1122. https://doi.org/10.3233/jad-201601.
- Adam, C. E.; Fitzpatrick, A. L.; Leary, C. S.; Anjum Hajat; Ilango, S. D.; Park, C.; Phelan, E. A.; Semmens, E. O. Change in Gait Speed and Fall Risk among Community-Dwelling Older Adults with and without Mild Cognitive Impairment: A Retrospective Cohort Analysis. *BMC Geriatrics* 2023, 23 (1). https://doi.org/10.1186/s12877-023-03890-6.
- 41. Hoel, R. W.; Giddings Connolly, R. M.; Takahashi, P. Y. Polypharmacy Management in Older Patients. *Mayo Clinic Proceedings* **2021**, *96* (1), 242–256. https://doi.org/10.1016/j.mayocp.2020.06.012.
- 42. Sousa, L.; Tomás, J.; Severino, S.; Valido, S.; Santos, MJ; José, H. Prevention of Falls in the Elderly: A Challenge in Patient Safety. *Salud, Science and Technology* **2024**, *4*, 1000. https://doi.org/10.56294/saludcyt20241000.
- 43. Bai, W.; Chen, P.; Cai, H.; Zhang, Q.; Su, Z.; Cheung, T.; Jackson, T.; Sha, S.; Xiang, Y.-T. Worldwide Prevalence of Mild Cognitive Impairment among Community Dwellers Aged 50 Years and Older: A Meta-Analysis and Systematic Review of Epidemiology Studies. *Age and Ageing* **2022**, *51* (8), afac173. https://doi.org/10.1093/ageing/afac173.
- 44. World Health Organization. WHOQOL: *Measuring quality of life*. World Health Organization. 2025 Available online: https://www.who.int/tools/whoqol (accessed on 3 March 2025).
- 45. Steffens, D. C.; Manning, K. J.; Wu, R.; Grady, J. J. Effects of Longitudinal Changes in Neuroticism and Stress on Cognitive Decline. *The American Journal of Geriatric Psychiatry* **2023**, 31 (3), 171–179. https://doi.org/10.1016/j.jagp.2022.10.005.
- 46. Zhu, Y.; Li, C.; Xie, W.; Zhong, B.; Wu, Y.; Blumenthal, J. A. Trajectories of Depressive Symptoms and Subsequent Cognitive Decline in Older Adults: A Pooled Analysis of Two Longitudinal Cohorts. *Age and Ageing* **2021**. https://doi.org/10.1093/ageing/afab191.
- 47. Power, M.; Quinn, K.; Schmidt, S. Development of the WHOQOL-Old Module. Quality of Life Research 2005, 14, 2197–2214. https://doi.org/10.1007/s11136-005-7380-9.
- 48. World Health Organization. World mental health report: Transforming mental health for all. World Health Organization. 2022 Available online: https://www.who.int/publications/i/item/9789240049338. (accessed on 3 March 2025).
- 49. Park, S.-H.; Kwak, M.-J. Performance of the Geriatric Depression Scale-15 with Older Adults Aged over 65 Years: An Updated Review 2000-2019. *Clinical Gerontologist* 2020, 44 (2), 1–14. https://doi.org/10.1080/07317115.2020.1839992.
- 50. Abrantes, G. G. de; Souza, G. G.; Cunha, N. M.; Rocha, H. N. B. da; Silva, A. O.; Vasconcelos, S. C. Depressive Symptoms in Older Adults in Basic Health Care. *Revista Brasileira de Geriatria e Gerontologia* **2019**, 22 (4). https://doi.org/10.1590/1981-22562019022.190023.
- 51. Uomoto, K. E. Increasing Identification and Follow-up of Older Adult Depression in Primary Care. *J Prim Care Community Health* **2023**, *14*, 215013192311527. https://doi.org/10.1177/21501319231152758.

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.