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Heric Carvalho Vieira, Daniela Zanini, Brenno Bianchoni Loureiro, Felipe José Nascimento Barreto

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The impact of loneliness on the development of alzheimer's disease in women: a systematic review

Short Title: Loneliness and Alzheimer's Disease in women

Heric Carvalho Vieira[1], Daniela Zanini[1], Brenno Bianchoni Loureiro[2], Felipe José Nascimento Barreto[1]

[1]Curso de Medicina, Universidade Federal da Fronteira Sul (UFFS), Chapecó, SC, Brazil.
[2]Escola de Medicina, Universidade Federal de Ouro Preto (UFOP), Ouro Preto, MG. Brazil.

Correspondence:
Felipe José Nascimento Barreto
Universidade Federal da Fronteira Sul, Campus Chapecó
Rodovia SC 484, Km 02, s/n, bairro Fronteira Sul, (saída para Guatambu), Chapecó - SC
Postal code: 89815-899
Email: felipe.barreto@uffs.edu.br
Phone Number:+55 (54) 981055617

ABSTRACT

INTRODUCTION: Alzheimer's disease (AD) is the leading cause of dementia in the elderly and involves pathophysiological events which results in progressive cognitive impairment and functional disabilities. Loneliness is a unique condition in which an individual perceives themselves as socially isolated, even when they are among other people. It is also a worldwide public health challenge associated with higher mortality, and risk of cardiovascular and psychiatric diseases. The aim of this study is to investigate the impacts of loneliness on the development of AD in women.

METHODS: Systematic Review registered in PROSPERO (CDCRD42024521068) and adherent to PRISMA and Cochrane guidelines. In November 2025, systematic searches conducted by independent reviewers were carried out in international databases. The methodological quality of the included studies was assessed using the Newcastle-Ottawa Scale and the Downs and Black Checklist.

RESULTS: A significant association is suggested between loneliness and the development of AD. Possible causal mechanisms were identified, namely chronic stress associated with loneliness, lack of social and emotional support, and reduced cognitive and social activity. The organization of studies allows for an analysis of the incidence of AD, the progression of cognitive decline, and the relationship with neurobiological changes associated with loneliness.

CONCLUSION: Despite being a complex and barely understood relationship, Loneliness may play a relevant role in the development of AD among women. Psychosocial factors must be considered in the context of aging and women's mental health, emphasizing its role in increasing the risk and progression of the disease.

Keywords: Alzheimer's disease, loneliness, women.

1. INTRODUCTION

Alzheimer's Disease (AD) is a progressive neurodegenerative condition that represents the leading cause of dementia in the elderly.[1] With an incidence higher in women, its number of cases is expected to triple by 2050, potentially reaching 150 million affected individuals.[2,3] Understanding AD risk factors is essential to implementing preventive strategies, as modifying certain aspects of lifestyle can prevent up to 40% of cases.[4]

The pathophysiology of AD has not yet been completely elucidated. Still, the predominant hypothesis involves changes in the amyloid precursor protein and the production of beta-amyloid, leading to the formation of amyloid plaques and neurofibrillary tangles.[5,6] These changes start asymptomatic but eventually cause cognitive impairment over the years, especially episodic memory, as well as functional disabilities.[7] The diagnosis of AD is based on clinical presentation and complementary tests, such as neuroimaging and, in large centers, biomarkers in plasma and cerebrospinal fluid. The disease current treatment is symptomatic and requires multidisciplinary approach; however, none of current treatment options modify its inexorable progression.[8,9] Given the complexity of AD etiopathogenesis, it is crucial to identify early intervention strategies to mitigate the risk of disease progression.[3]

Loneliness is best predicted characterized by a discrepancy between an individual's preferred social relationships and those experienced.[10] This discrepancy leads to negative experiences, such as feeling isolated and experiencing dysphoria associated with the perception of social isolation, even in the presence of other people. Loneliness definition

highlights a unique condition in which an intrinsic need of social species is not limited to the presence of others but also to the presence of significant individuals whom one can trust, who provide a life purpose, and with whom one can interact and collaborate. Subjectivity and the perception of the social environment as welcoming or hostile emerge as distinctive elements of the experience of loneliness. [10,11] It is noteworthy that loneliness differs from social isolation, which is defined as an objective construct measured through indicators such as living alone, infrequent social contacts, low levels of social activity, or an objective scarcity of social partners and interactions with others.[12]

Worldwide, feelings of loneliness are of greater concern among elderly, and have a global prevalence of 28% in this age group.[13,14] Several factors are associated with increased risk of loneliness in older adults: cognitive impairment, poor health, female gender, depression, being widow or single, living in rural residency or long-term care institutions.[14] Also, loneliness is strongly associated with adverse health outcomes, such as mental illness, cardiovascular disease and early death.[11,14] Individuals who feel lonely have a greater risk of developing heart and psychiatric diseases, as well as their outcomes.[11]

Substantial empirical evidence indicates loneliness as a modifiable risk factor for the development of AD and other related dementias.[15,16] In mice models of AD, social isolation has been associated with Alzheimer's disease-like pathophysiology such as increased amyloid plaque deposition, neurofibrillary tangles and neuroinflammation.[17] According to a Swedish prospective population-based 20-years follow-up study, perceived loneliness increases risk for all-cause dementia and especially for AD, even after adjusting for potential confounders.[18]

However, there is still a significant gap in knowledge regarding the neurobiological and psychological conditions that establish a clear and evident connection between loneliness and cognitive decline in humans. Especially among women, who have twice as likely to develop AD as men, and current research aimed at identifying AD risk and protective factors in this gender has focused mainly on biological mechanisms, and less on social and cultural factors.[19] The aim of this study is to investigate the impacts of loneliness on the development of AD in women.

2. METHODS

This work is a Systematic Review (SR) registered in the International Prospective Register of Systematic Reviews (PROSPERO) database, code CDCRD42024521068. The

qualitative results are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The SR protocol structure follows current suggestions of the Cochrane Library.[20]

2. 1 RESEARCH STRATEGY

During November 2025, electronic searches were conducted in databases by two independent investigators. The databases used were PubMed, Medical Literature Analysis and Retrieval System Online (Medline), Chinese Academy of Medical Sciences & Peking Union Medical College (CAMS/PUMC), and Latin American and Caribbean Health Sciences Literature (LILACS).

The search strategy was defined through the development of a question based on the PECO strategy, which represents an acronym for “Patient, Exposure, Context, and Outcomes”, cardinal components for constructing research question and for bibliographic search for evidence.[21] From this strategy, the following question was generated: What are the impacts of loneliness on women in the development of Alzheimer's disease?

To answer the research question, descriptors were used following DeCS/MeSH (Health Sciences Descriptors/Medical Subject Headings), combined with the boolean operators "AND" and "OR". The descriptors and operators that were used are: (*Alzheimer disease OR Alzheimer’s disease OR Alzheimer's Dementia OR Alzheimer's Syndrome OR Acute Confusional Senile Dementia OR Alzheimer's Type Dementia OR Alzheimer Type Senile Dementia OR Primary Senile Degenerative Dementia) AND (loneliness OR Social isolation) AND (women OR woman).* Studies published from March 2014 to October 2025 were included in the research.

2.2 INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria were outlined considering three main dimensions: type of study, type of participants, and type of exposure. Regarding the type of study, observational studies were considered eligible, including both case-control designs and cohort and cross-sectional studies, since they are the main types of studies for risk assessment and prognosis.[22] Regarding the type of participants, the inclusion encompassed, not exclusively, studies involving women. Finally, regarding the type of exposure and outcome, the inclusion criteria did not establish specific restrictions, allowing for a varied range of contexts and results associated with loneliness and the development of AD.

The exclusion criteria were equally strict. According to the type of study, case reports, ecological studies, prevalence and incidence studies, as well as theses and dissertations, grey literature, and literature reviews were excluded. Experimental designs, such as randomized clinical trials, were also excluded. As for the type of participants, studies that were limited to men and caregivers were excluded to preserve the sample homogeneity in relation to the group of interest.

2.3 DATA EXTRACTION

The present review was outlined for exploratory purposes, with no intention of conducting a meta-analysis. The articles were independently evaluated by two authors responsible for data extraction. After reading both title and abstract, articles that clearly did not meet the eligibility criteria were excluded. For eligibility confirmation, these two authors read the entire articles using a standardized eligibility assessment form. An electronic spreadsheet was made on Google Sheets™ software and data was classified among three domains: (i) selected by title (number; original title; authors, year of publication, Digital Object Identifier (DOI), database; (ii) selected by abstract (number, original title, authors, abstract, keywords, year, DOI/link and database and; (iii) selected by full text (number; title; objective; methodology; study location, discussion and results). When comparing records of each reviewer, small discrepancies were agreed upon during online reunions on Google Meet™ video conferencing system.

2.4 BIAS EVALUATION

Two instruments recommended by the Cochrane Collaboration were used for the assessment of the studies' methodological quality: the *Newcastle-Ottawa Scale* and the Downs and Black Checklist.[22] The first questionnaire encompassing the assessment of bias risk through participant selection, comparability of groups in the study, methods for outcome assessment, verification of exposure, and adequate follow-up.[23] Each aspect has different evaluation items, where indicative high-quality responses receive stars. The selection dimension has four items, and the exposure/outcome dimension has three, with the potential to receive up to one star each. The comparability dimension has one item, which can receive up to two stars. This scoring system, ranging from zero to nine stars, allows for a semi-quantitative assessment of the study's methodological quality.[22] A cutoff point developed by McPheeters et al. was used, in which a score of seven stars or more can indicate "good" quality.[24] The second instrument, the Downs and Black Checklist

corresponds to 27 questions that assess methodological quality based on reporting, external validity, bias, confounding factors, and chance power.[25] Each item is evaluated with a binary score to produce a total score for each study. Articles that scored above 70% were categorized as having high methodological quality.[26]

3. RESULTS

Figure 1 describes the studies' identification, selection, eligibility, and inclusion process. In total, 80 articles were selected from the database searches: 46 from PubMed/Medline, 14 from CAMS/PUMC, and 20 from LILACS, the latter accessed via Biblioteca Virtual em Saúde (Virtual Health Library). No additional records were identified from SciELO databases.

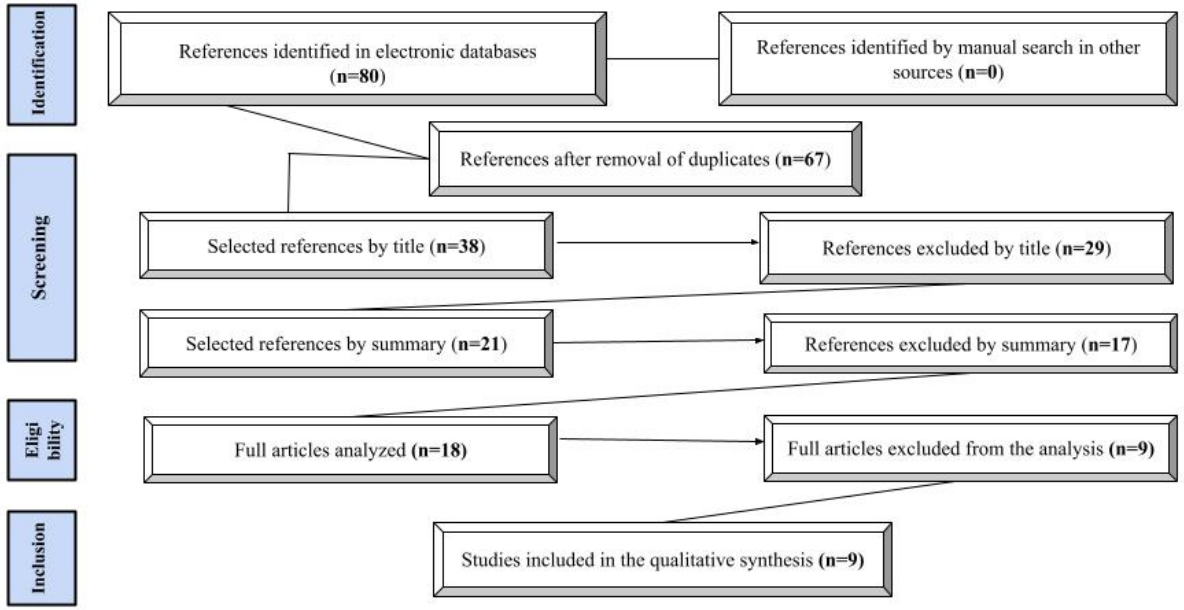

Figure 1— PRISMA flowchart for selecting articles from the Systematic Review. Source: the authors (2025).

After identifying and removing duplicates (n=13), 67 potential articles were forwarded for evaluation based on their titles and abstracts. At the end of this phase, 17 articles remained for evaluation by their full text. Of these, eight articles were excluded for not meeting the eligibility criteria, as detailed in Figure 1. The specific reasons for exclusion were: Five (5) studies focused exclusively on caregivers of patients with AD or dementia, contradicting the exclusion criterion to preserve sample homogeneity in relation to the group of interest (women with loneliness/AD). One (1) article was of an experimental design (e.g., a randomized clinical trial), which was excluded to ensure the analysis focused on observational studies. One (1) article did not address loneliness or social isolation as the main exposure of interest. Finally, one (1) article was excluded for being a prevalence and incidence study without assessing risk or prognosis, which were the central components of the research question. Therefore, nine articles were eligible for data extraction.

Table 1 summarizes the nine articles selected for this study and their main outcomes. The included studies address different aspects of the topic, providing a comprehensive view of the existing literature. In addition, they present a diverse methodological approach, including prospective cohorts and cross-sectional and longitudinal observational studies, which provide significant breadth to the analysis of the impacts of loneliness on the development of AD in elderly women. Such diversity allows for a comprehensive investigation of the factors associated with loneliness and the development of AD, considering different temporal perspectives and variable control. Of the selected studies, 70% were conducted in North America (United States), 20% in European countries (United Kingdom and Sweden), and 10% in Oceania (Australia). In addition, 40% of the studies were of the cross-sectional observational type, 20% of the longitudinal observational type, 20% of the prospective cohort type, and 20% of the longitudinal cohort type, and one study was based on neurobiological analysis.

Table 1 — Summary of selected articles (n=9).

Authors/Year	Local	Study design	n	Female participants	Instruments to assess loneliness	Instruments to assess DA	Main Outcomes
Hendriks et al., 2024.[34]	UK	Prospective cohort	356,052	195,830 (55.3%)	Sociodemographic survey data (presence of social isolation)	ICD-10	The study found 39 risk factors for Young-Onset Dementia (YOD), including social isolation, orthostatic hypotension, vitamin D deficiency, and high levels of CRP. Social isolation stands out as the greatest risk.
Salinas et al., 2022.[27]	USA	Prospective cohort	2,308	1,292 (56%)	CES-D	DSM-IV; Structural MRI	In 10 years of monitoring dementia, loneliness has been linked to a higher risk of this condition, even in adults considered to be at low risk. It suggests a significant role of loneliness in brain health.
Tao et al.,2022.[28]	USA	Longitudinal cohort	2,609	1,400 (54%)	CES-D	CERAD-WL, VST; AD8; MoCA; Structural MRI	The female sex is more prone to experiencing persistent loneliness, which suggests that this may intensify cognitive decline, especially in the presence of APOEε4. Due to the aging population and increased social isolation, loneliness can become a public health concern.
Dabiri; Mwendwa; Campbell, 2024.[16]	USA	Longitudinal cohort	2,248	1,142 (73%)	De Jong-Gierveld Loneliness Scale	Criteria of the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association; structural MRI	The findings indicate the link between loneliness and a higher risk of cognitive decline in older adults, with changes observed in specific brain areas and altered gene expression. Elevated inflammatory cytokines and BDNF expression have been identified as factors linking loneliness to cognitive decline. The difference in the impact of loneliness between genders was also explored.
d'Oleire Uquillas et al., 2018.[29]	USA	Cross-sectional	117	69 (59%)	UCLA-loneliness scale (3 items)	Functional neuroimaging (FTP-PET, PiB-PET); Presence of APOEε4	Greater loneliness is associated with higher tau pathology in the right entorhinal cortex, even when considering the connection to GDP, especially in carriers of the APOEε4 gene. Exploratory maps suggest that loneliness is related to neurobiological characteristics, primarily in the entorhinal cortex, indicating a neurobiological basis for the subjective experience of loneliness.
Joyce et al., 2021.[30]	Australia	Cross-sectional	11,498	6,054 (52%)	CES-D; Lubben Social Network Scale	DSM-IV	Social isolation and other social factors are linked to lower cognitive function among women. Although men report more social isolation, it did not correlate with cognitive function. It is important to consider gender differences when analyzing connection between social health and cognition.
Lapane et al., 2022.[31]	USA	Cross-sectional	721,074	497,542 (69.1%)	Social Connectedness Index	Cognitive Function Scale	The severity of cognitive impairment, care facility type, and residence length were associated with social connections in nursing homes. In contrast, the quality of the facilities showed no relationship. This highlights the importance of social interactions and the caregiving environment for social well-being.

Donavan et al., 2016.[32]	USA	Longitudinal observational	79	43 (54.43%)	UCLA-loneliness scale (3 items)	Functional neuroimaging (PiB-PET)	Possible association between loneliness and cortical amyloid load in cognitively normal elderly individuals and new evidence that loneliness is a relevant neuropsychiatric symptom for preclinical Alzheimer's disease.
Hasselgren et al., 2020.[33]	Sweden	Longitudinal observational	892	672 (75.3%)	Question about chronic loneliness from Database: Gothenburg H70 Birth Cohort Study; The Prospective Populations Study on Women	DSM-III-R	Women reported more experiences of depression, chronic loneliness, and prolonged stress compared to men. They also showed lower self-esteem but were more satisfied with their social situation. A significantly larger number of women developed dementia compared to men. Although the model used to explore general psychological distress did not fit the data, female sex indirectly influenced dementia, mediated by general psychological distress and education.

Source: the authors (2025). UK = United Kingdom. ICD-10 = International Classification of Diseases. USA = United States of America. CES-D = Center for Epidemiologic Studies Depression Scale. DSM-IV = Diagnostic and Statistical Manual of Mental Disorders. VST = Victoria Stroop Test. CERAD = Word List Memory Test. AD8 = Washington University Dementia Screening Test. MoCA = Montreal Cognitive Assessment. PCR = C-Reactive Protein. BDNF = Brain-Derived Neurotrophic Factor. MRI = Magnetic Resonance Imaging. UCLA = University of California Los Angeles. FTP- PET = Flortaucipir Positron Emission Tomography. PiB-PET = Pittsburgh Compound-B Positron Emission Tomography. APOEε4 = Apolipoprotein E ε4.

The organization of studies can be structured according to the main outcomes investigated: the incidence of AD, the progression of cognitive decline, and the relationship between loneliness and neurobiological changes. The analysis of risk factors, such as the presence of comorbidities, the level of social interaction, and the emotional state of elderly women, can be conducted in-depth, considering the contribution of each study to understanding these complex interactions and making a specific thematic cut.

The results of these nine studies provide a comprehensive view of the complex interaction between psychosocial, neurobiological, and demographic factors in dementia. In a retrospective analysis of prospectively collected data, lonely adults had higher 10-year dementia risk, and hazard ratio ranged from 1.54 (95% CI 1.06–2.24) on overall incidence, to 3,03 (95% CI, 1.63–5.62) among lonely participants <80 years of age without APOE ε4 alleles.[27] Tao et al. corroborated these findings, highlighting the association of persistent loneliness with cognitive decline, particularly in women in the presence of APOEε4.[29]

Furthermore, Dabiri, Mwendwa, and Campbell demonstrated that loneliness is associated with a higher risk of cognitive decline in older adults, with changes observed in specific brain areas and altered gene expression.[16] d'Oleire Uquillas et al. found an association between loneliness and cortical amyloid load in cognitively normal older adults, suggesting a role of loneliness as a neuropsychiatric symptom relevant to preclinical AD.[29]

The studies by Joyce et al. and Laplane et al. showed that loneliness is associated with poorer cognitive function, depression, suicidal ideation, and frailty in older adults, especially in long-term care contexts.[30, 31] Donovan et al. highlighted the association between a higher cortical amyloid load and greater loneliness in cognitively normal older adults, especially in carriers of APOEε4.[32] Hasselgren et al. found that general psychological distress may mediate the relationship between female sex, education, and dementia, while Hendriks et al. provided insights on global patterns of early-onset dementia.[33,34] These studies highlight the importance of integrated approaches that consider not only the clinical and biological aspects of dementia but also the underlying social and emotional factors.

Concerning to assess the methodological quality of studies, Table 2 presents the risk of bias for cohort studies using the Newcastle-Ottawa scale. In this context, only one of the nine studies selected, which is the study conducted by Dabiri, Mwendwa, and Campbell, had an inferior methodological quality according to cutoff point established.[16] This finding may be related to the method of biomarkers' neuropathological analysis adopted in the study. Table 3 presents the scores of the Downs and Black Checklist, where

articles that received a score higher than 70% were categorized as having high methodological quality. Therefore, studies with a total score of 18 or higher were considered excellent quality. In this sense, 44.4% of the selected studies obtained these referred values: Hendriks et al., Salinas et al., Dabiri, Mwendwa and Campbell, and d'Oleire Uquillas et al.[16,27,29,34] The score of these scales was not used as a criterion for including or excluding articles but rather as a supplementary indicator of the methodological quality of the studies. These analyses provide a solid foundation for interpreting the results and reinforce the reliability of the conclusions presented about the relationship between loneliness and the development of Alzheimer's disease in elderly women.

Table 2 — Risk of bias for cohort studies using the Newcastle-Ottawa scale.

Reference	Drawing	Selection	Comparability	Outcome	Total Score (maximum: 09)
Hendriks et al., 2024.[24]	Prospective cohort	4	1	3	**8**
Salinas et al., 2022.[27]	Prospective cohort	3	1	3	**7**
Tao et al.,2022.[28]	Longitudinal Cohort	4	1	3	**8**
Dabiri; Mwendwa; Campbell, 2024.[16]	Longitudinal cohort and neuropathological analysis of biomarkers	2	1	3	**6**
d'Oleire Uquillas et al., 2018.[29]	Cross-sectional	4	1	3	**8**
Joyce et al., 2021.[30]	Cross-sectional	4	1	2	**7**
Lapane et al., 2022.[31]	Cross-sectional	3	1	3	**7**
Donavan et al., 2016.[32]	Longitudinal observational	4	1	3	**8**
Hasselgren et al., 2020.[33]	Longitudinal observational	4	1	3	**8**

Source: the authors (2025).

Table 3— Risk of bias for cohort studies using the Downs and Black Checklist.

Reference	Drawing	Report	External Validity	Bias	Confounding variable	Poder	Total Score (maximum: 27)
Hendriks et al., 2024.[24]	Prospective cohort	10	2	2	3	1	**18**
Salinas et al., 2022.[27]	Prospective cohort	8	2	6	4	1	**21**
Tao et al.,2022.[28]	Longitudinal Cohort	7	1	3	4	0	**15**
Dabiri; Mwendwa; Campbell, 2024.[16]	Longitudinal cohort and neuropathological analysis of biomarkers	10	1	3	4	1	**19**
d'Oleire Uquillas et al., 2018.[29]	Cross-sectional	10	0	5	3	1	**19**
Joyce et al., 2021.[30]	Cross-sectional	7	1	3	1	0	**12**
Lapane et al., 2022.[31]	Cross-sectional	8	0	3	0	0	**11**
Donavan et al., 2016.[32]	Longitudinal observational	6	2	2	3	0	**13**
Hasselgren et al., 2020.[33]	Longitudinal observational	4	0	3	0	0	**7**

Source: the authors (2025).

4. DISCUSSION

There is some evidence in the current literature elucidating the complex interactions between loneliness and AD in women, emphasizing the interrelationship between psychosocial and biological aspects of brain health, especially in the context of aging and neurodegeneration. As a complex phenomenon per se, loneliness has been associated with various negative impacts on health, especially in specific populations, such as women, an association that can be understood through biopsychosocial mechanisms.[12] Also, elder age is often linked to the loss of social relationships resulting from adverse life conditions and events common in this age group, such as the death of a spouse, relatives, and friends, as well as physical and mental health.[12] The impacts of social isolation and loneliness on the lives of elderly people after Covid-19 pandemia have gained prominence, and it is noteworthy that a substantial number of studies selected in this study were developed after pandemia had been declared worldwide.

It is important to emphasize that loneliness, although often associated with disorders such as depression, can exist as an independent measure. Even when present in depression scales used in the selected articles from this study, loneliness should not be viewed solely as a depressive disorder symptom, but as a complex subjective experience that can significantly affect mental health on its own. The results support the hypothesis that loneliness may play a relevant role in the development of this syndrome in women, as possible causal mechanisms have been identified, namely chronic stress associated with loneliness, lack of social and emotional support, as well as reduced cognitive and social activity.[28,30,31,33,34]

In this context, it is worth remembering that the impacts of loneliness on the development of AD in women can be broad and influence different aspects of mental health and brain functions. Therefore, it is noteworthy that loneliness can contribute to increased chronic inflammation and oxidative stress, such as the presence of elevated levels of pro-inflammatory cytokines and the expression of brain-derived neurotrophic factor, processes that are strongly implicated in the development and progression of AD.[16] Furthermore, changes were identified in specific brain regions, such as the inferior parietal lobe, the anterior insula, and the superior temporal sulcus, in individuals who reported greater loneliness.[3,16] Relationships were also found between loneliness and gene expression in dorsolateral prefrontal cortex and amygdala.[16] In addition, it was observed that a higher cortical amyloid load was associated with higher scores on the UCLA Loneliness Scale.[16,32]

The lack of intellectual and social stimulation can accelerate cognitive decline and increase the risk of developing dementia, including Alzheimer's disease. Individuals who feel lonely tend to engage less in activities of this kind and social interactions.[31] Furthermore, in the research by Hasselgren *et al.*, it was observed that loneliness could contribute to the development of emotional symptoms, such as depression and anxiety, which in turn are linked to a higher risk of mental impairment and dementia.[33, 35] Understanding these relationships can be fundamental for developing more effective preventive and therapeutic strategies for AD, focusing not only on clinical aspects but also on the social and emotional factors that influence the course of the disease.

Furthermore, it is worth noting that the aging process of the population is a contemporary, irreversible, and diversified phenomenon; that is, it is a plural process, influenced by distinct experiences and marked by historical gender inequalities, especially against women, which intensify in this phase of life.[36] The increase in the population of elderly women is a reality that presents challenges, as at this stage of life, they face a greater propensity for isolation, loneliness, economic difficulties, lack of care, social and material vulnerabilities, abandonment, and various forms of violence, more than elderly men.[36] Therefore, women's longevity should be examined carefully, especially regarding the relationships between women, old age, and loneliness. Although loneliness is not exclusive to old age, it is a condition that, once present, adversely impacts individuals' physical and mental health.[36] In this sense, it can be said that loneliness among elderly people is not determined solely by age but mainly by gender condition.[37] Such a fact suggests that loneliness may play a crucial role in AD development in women through the mechanisms above. These impacts of loneliness can have profound implications for the mental and brain health of elderly women, highlighting the importance of preventive and therapeutic approaches that consider not only biological aspects but also psychosocial and emotional factors in the prevention and treatment of AD in women during aging.

Until now, the present study is the first systematic review on current scientific literature that focuses on the relationship between loneliness and DA in female gender. Its critical and transparent methodology aimed to ensure reliability and relevance of the results presented. However, some significant limitations must be addressed. It is important to consider heterogeneity among selected studies, as well as the lack of resources to explore this drawback. The research period was limited to the last 11 years in order to evaluate more recent articles, thus the review remains current. Also, a meta-analysis was

not conducted due to the insufficient number of primary studies with comparable quantitative data, which would limit the statistical power of the meta-analysis.

5. CONCLUSION

Loneliness and the onset of AD in old age are growing problems related to the greater life expectancy nowadays. The studies selected by this systematic review provided a greater understanding of how loneliness can play a relevant role in the development of AD in women, highlighting the importance and complexity of this theme, considering different temporal and methodological perspectives.

The analysis of the included articles suggested that loneliness may play a significant role in increasing the risk and progression of AD in women. Moreover, the survey of studies conducted in different regions of the world indicates that the phenomenon of loneliness occurs globally, which requires broad health interventions and policies aimed at the prevention and management of loneliness to significantly reduce the incidence of dementia in women.

As a public health issue, loneliness should not be underestimated as a risk factor for the mental and cognitive health of elderly women. Broad interventions to significantly mitigate loneliness throughout life requires a full engagement and support of the entire community. Social and psychological support programs aimed at this vulnerable population can be useful to promote social network, recognize practical implications for developing preventive interventions and minimize negative effects of loneliness on women's cognitive and mental health. Finally, more primary studies are necessary to further elucidate the underlying mechanisms by which loneliness affects brain function and contributes to the progression of AD in elderly women.

Author contributions: CRediT TaxonomyHeric VieiraConceptualization-Lead, Formal analysis-Equal, Investigation-Equal, Methodology-Equal, Writing - original draft-EqualBrenno LoureiroData curation-Equal, Formal analysis-Equal, Investigation-Equal, Methodology-EqualDaniela ZaniniSupervision-Supporting, Validation-Supporting, Visualization-SupportingFelipe BarretoProject administration-Equal, Supervision-Equal, Writing - review & editing-Lead

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