



REVISIONES

Diseases associated with loneliness in the elderly: a social challenge

Enfermedades asociadas a la soledad en la persona mayor: un reto social

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ABSTRACT:

Objective: Identify pathologies in the elderly associated with loneliness.

Methodology: Secondary research, integrative review type, structured according to Crossetti's consensus.

Results: After applying descriptors and search strategies, a total of 4,011 articles were identified, after applying filters, inclusion, and exclusion criteria, 27 articles were selected; from these articles 17 corresponded to WoS, 9 to BVS and 1 to PubMed.

Conclusions: The association between loneliness and cognitive impairment, decreased physical fitness, Alzheimer's disease and cardiovascular events is highlighted. It is necessary to establish public policies to prepare people for their future aging process.

Keywords: Disease; loneliness; aging; aging for those 80 and over.

RESUMEN:

Objetivo: Identificar las patologías en la persona mayor asociadas a la soledad.

Metodología: Investigación secundaria, de tipo revisión integrativa, estructurada según consenso de Crossetti.

Resultados: Se identificaron tras la aplicación de descriptores y estrategias de búsqueda un total de 4.011 artículos, posterior a la aplicación de filtros, criterios de inclusión y criterios de exclusión quedaron seleccionados 27 artículos, de los cuales 17 corresponden a WOS, 9 a BVS y 1 a PUBMED.

Conclusiones: Se destaca la asociación entre soledad y el deterioro cognitivo, disminución del estado físico, enfermedad de Alzheimer y eventos cardiovasculares. Se hace necesario establecer políticas públicas de preparación a las personas para su futuro proceso de envejecimiento.

Palabras clave: Enfermedad; Soledad; Envejecimiento; Envejecimiento de 80 y más.

INTRODUCTION

According to the World Health Organization (WHO), currently the number of people aged 60 years or more exceeds that of children under five years of age; additionally, between 2020 and 2030, the percentage of older people will increase by 34 %, following this pattern, by 2050 the number of older people will exceed that of adolescents and young people between 15 and 24 years of age ⁽¹⁾, this phenomenon is known as population ageing.

The above is especially relevant when problems associated with aging, such as loneliness, have been reported ⁽²⁾, which has a negative relationship with the health of older people, with poorer cognitive function, worsening of memory and verbal fluency⁽³⁾. Moreover, this impact on cognitive functioning can exacerbate loneliness, generating a vicious circle that generates an even worse outcome in such population⁽⁴⁾.

Based on the above, considering that physiologically the body loses functions over the years, which make older people more vulnerable, there are risk factors that can aggravate loneliness, as in the case of the current COVID-19 pandemic, which has been associated with an increase in loneliness ⁽⁵⁾, and this, in turn, has been strongly related to the presence of anxiety and depression. Therefore, given the demographic change that the world is experiencing, added to the increase in loneliness in the elderly and its association with health problems, it is important to know what has been described in this regard.

OBJECTIVE

Under the above premise, the following question arises: What diseases are associated with loneliness in the elderly? In order to answer this question, an integrative review was considered to know the state of the art, responding to the objective of identifying the pathologies associated with loneliness in the elderly.

METHODS

Secondary research, of the integrative review type, structured, according to Crossetti⁽⁶⁾, which is comprised by five stages: 1. Problem formulation, 2. Data collection or definitions on literature search, 3. Data evaluation, 4. Data analysis, and finally 5. Presentation of results and interpretation.

To comply with the first stage, the following question was formulated: What diseases are associated with loneliness in the elderly? In the second stage, the different searches were organized in Spanish, English and Portuguese, using the descriptors validated in the DeCS thesaurus and Booleans described in Table No. 1.

Table No. 1. Descriptors and Booleans used in search process

Descriptor in: Spanish English Portuguese	Boolean	Descriptor in: Spanish English Portuguese	Boolean	Descriptor in: Spanish English Portuguese
Anciano Elderly Idoso	AND	Soledad Loneliness Solidão	AND	Enfermedad Disease Doença
Anciano de 80 Años o más Elderly, 80 and over Idoso de 80 Anos ou mais	AND	Soledad Loneliness Solidão	AND	Enfermedad Disease Doença

Source: Self-development, 2022.

The databases used were WoS (Web of Science), PubMed (United States National Library of Medicine), SciELO (Scientific Electronic Library Online) and BVS (Biblioteca Virtual de Salud). Table N°2 shows the search strategies and filters used in each database.

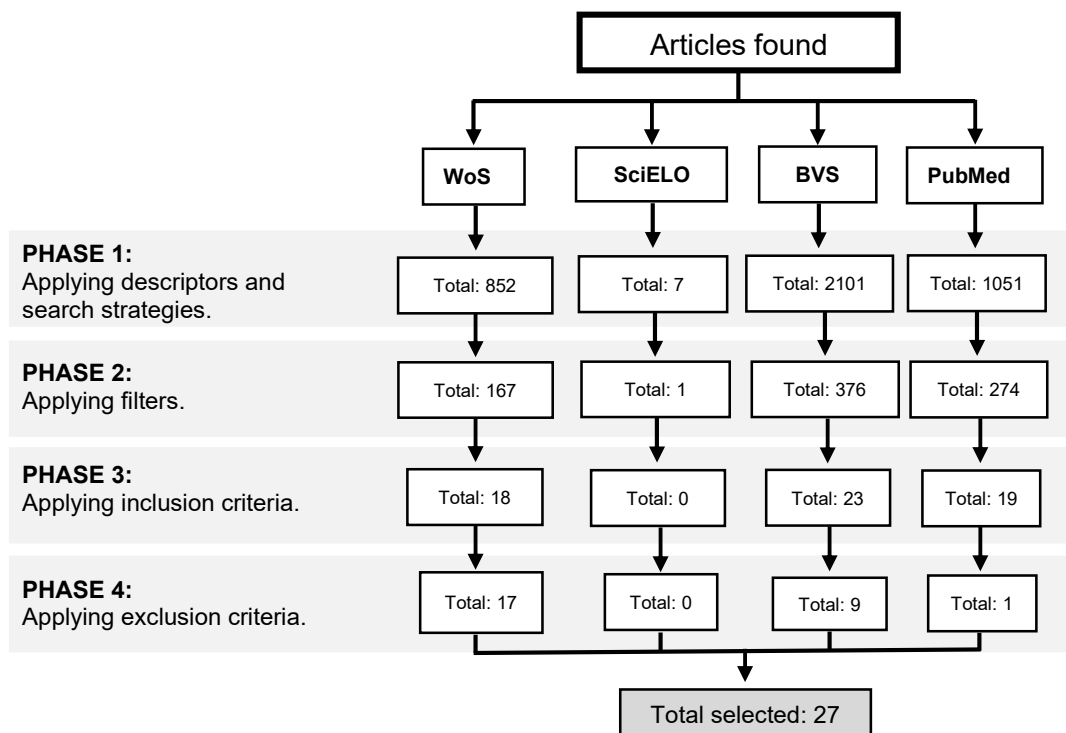
Table No. 2. Search strategies and filters applied

Database	Search mode	Filters applied
WoS	All fields	-Years of publication: 2016-2021 -Web of Science categories: Geriatrics gerontology, Gerontology Multidisciplinary sciences
PubMed	All fields	-Availability: Free full text -Publication date: 5 years -Species: Humans -Language: Spanish, English and Portuguese
BVS	Title, abstract, subject	-Availability: Free full text -Language: Spanish, English and Portuguese -Years: 2016-2021 -Main subject: Loneliness
SciELO	All indexes	-Years of publication: 2016-2021 - Subject areas: Geriatrics; Gerontología (Gerontology); Health

Source: Self-development, 2022.

The inclusion criteria used was composed by articles in the three languages mentioned, published in the period ranging from 2016 to 2021 (until June), and that related loneliness as an independent variable and pathologies in the elderly as dependent variables; the exclusion criteria corresponded to articles that do not have free access, duplicates and letters to the editor. Figure N°1 shows the review flowchart.

Figure No. 1. State of the art review flowchart



Source: Self-development, 2022.

After applying descriptors and search strategies, a total of 4,011 articles were identified, 852 located in the WoS database, 7 in SciELO, 2,101 in BVS and 1,051 in PubMed; after applying the filters, 818 articles remained, of which 167 corresponded to WoS, 1 to SciELO, 376 to BVS and 274 to PubMed. Then, after applying the inclusion criteria, 60 articles remained, 18 corresponding to WoS, 23 to BVS and 1 to PubMed, and finally, after applying the exclusion criteria, 27 articles were selected (2-4,7-30), of which 17 corresponded to WoS (2,4,7-21), 9 to BVS (3,22-29) and 1 to PubMed (30), thus fulfilling stage 3 and 4 of Crossetti.

RESULTS

In compliance with Crossetti's stage 5 "results presentation and interpretation" the most relevant results of the integrative review are summarized in Table N°3 according to article name, authors, country, year, objective and main results.

Table No. 3. Main results of relationship between loneliness in the elderly and associated pathologies in selected articles

Article Name	Authors	Country and Year	Objective	Main Results
Is loneliness a predictor of the modern geriatric giants? Analysis from the health, ageing, and retirement survey in	Giné-Garriga M, Jerez-Roig J, Coll-Planas L, Skelton D, Inzitari M, Booth J et al.	Multi-country (Europe) 2021	Analyze loneliness as a predictor of modern geriatric giants in European older adults, using a longitudinal design of nationally representative data.	Loneliness is a risk factor independent for fatigue, physical inactivity, and cognitive decline in older adults.

Europe ⁽²¹⁾					
Frailty Combined with Loneliness or Social Isolation: An Elevated Risk for Mortality in Later Life ⁽¹⁷⁾	Hoogendijk E, Smit A, Dam C, Schuster N, Breij S, Holwerda T et al.	Netherlands 2020	Frailty, loneliness, and social isolation are associated with adverse outcomes in older adults, but little is known about their combined impact on mortality.	The highest risk of mortality was seen in people with a combined presence of frailty and loneliness or social isolation.	
The effects of loneliness and social isolation on all-cause, injury, cancer, and CVD mortality in a cohort of middle-aged Finnish men ⁽¹⁸⁾	Kraav S, Awoyemi O, Junttila N, Vornanen R, Kauhanen J, Toikko T et al.	Finland 2020	Investigate whether both loneliness and social isolation increase all-cause mortality.	Both loneliness and social isolation increase the risk of mortality from all causes, loneliness and depressive symptoms may mediate the effect of social isolation on increased mortality.	
Loneliness Relates to Functional Mobility in Older Adults with Type 2 Diabetes: The Look AHEAD Study ⁽¹⁹⁾	McCaffery J, Anderson A, Coday M, Espeland M, Gorin A, Johnson K et al.	USA 2020	Examine the relationship of loneliness to disability, objective physical function, and other health outcomes in older people with type 2 diabetes and who are overweight or obese.	Loneliness scores were significantly associated with greater symptoms of disability and slower 4-meter walking speed, in older people with type 2 diabetes, overweight, and obesity.	
Social Isolation and Loneliness as Risk Factors for Grip Strength Decline Among Older Women and Men in China ⁽²⁰⁾	Yu B, Steptoe A, Niu K, Jia X.	China 2020	Examine the relationships of social isolation and loneliness, both individually and simultaneously, on changes in grip strength among Chinese older adults and whether these relationships vary by gender.	A higher level of loneliness was associated with lower grip strength for women.	
Loneliness, social isolation and risk of cardiovascular disease in the English Longitudinal Study of Ageing ⁽²⁶⁾	Valtorta N, Kanaan M, Gilbody S, Hanratty B.	England 2020	There is no objective.	Loneliness is associated with an increased risk of developing coronary heart disease and stroke, independent of traditional risk factors for cardiovascular disease.	
Relationship between loneliness and blood glucose control in diabetes ⁽²⁸⁾	Kobos E, Szewczyk A, Świątkowska T, Kryczka T, Sienkiewicz Z.	USA 2020	1. Determine the relationships between loneliness in old age and metabolic biomarkers and vascular diseases. 2. Evaluate the relationship between loneliness and health	Less than one-fifth (16%) of the patients included in the study had a higher loneliness index, and this loneliness index (total score) significantly correlated with higher blood pressure. No	

			problems.	significant correlations were demonstrated between loneliness and the other 9 indicators of blood glucose control.
Social isolation, loneliness and physical performance in older-adults: fixed effects analyses of a cohort study ⁽²⁹⁾	Philip K, Polkey M, Hopkinson N, Steptoe A, Fancourt D.	England 2020	Assess the relationship between loneliness, different aspects of social isolation, and physical performance over time.	Loneliness and aspects of isolation are associated with poorer physical performance in old age, the findings suggesting that the extent of this association falls below the minimal clinically important difference.
Cardiovascular and all-cause mortality attributable to loneliness in older Swedish men and women ⁽³⁰⁾	Novak M, Waern M, Johansson L, Zettergren A, Ryden L, Wetterberg H et al.	Sweden 2020	Examine whether loneliness predicts cardiovascular and all-cause mortality in older men and women.	Loneliness was shown to be an independent predictor of cardiovascular mortality in women.
Are loneliness and social isolation associated with cognitive decline? ⁽¹⁴⁾	Lara E, Caballero F, Rico-Urbe L, Olaya B, Haro J, Ayuso-Mateo S J et al.	Spain 2019	Examine the association of loneliness and social isolation on cognition over a 3-year follow-up period in middle-aged and older adults.	Loneliness is associated with decreased cognitive function during a 3-year follow-up period.
Loneliness Increases the Risk of All-Cause Dementia and Alzheimer's Disease ⁽¹⁶⁾	Sundström A, Adolfsson A, Nordin M, Adolfsson R.	Sweden 2019	Examine the effect of perceived loneliness on the development of dementia (any cause), Alzheimer's disease (AD) and vascular dementia (VD).	Participants who reported feeling lonely often had a higher risk of developing all-cause dementia and Alzheimer's disease. Adjusting for sociodemographic and health factors, including baseline depressive symptoms, did not alter this association.
Exploring the bidirectional associations between loneliness and cognitive functioning over 10 years: the English longitudinal study of ageing ⁽³⁾	Yin J, Lassale C, Steptoe A, Cadar D.	England 2019	Examine whether there is a bidirectional relationship between loneliness and cognitive function in English older adults (aged 50 years and over) over a 10-year follow-up.	Greater loneliness is associated with poorer cognitive function at baseline and contributes to memory and verbal fluency worsening over a decade. Baseline memory and its rate of decline also contribute to an increase in loneliness over time.

Loneliness, Depressive Symptoms, and Cognitive Functioning Among U.S. Chinese Older Adults ⁽¹³⁾	Kong D, Davitt J, Dong X.	USA 2018	Closing the knowledge gap in US Chinese older adults about whether loneliness is strongly associated with depressive symptoms.	The study findings indicate that loneliness and depressive symptoms act together to influence cognitive functioning.
Does loneliness 'get under the skin'? Associations of loneliness with subsequent change in inflammatory and metabolic markers ⁽¹⁵⁾	Shiovitz-Ezra S, Parag O.	USA 2018	Expand existing knowledge on the associations of loneliness in old age with subsequent change in inflammation as well as metabolic deregulation, using nationally representative longitudinal data.	Loneliness was associated with a change for the worse in most metabolic biomarkers, in lonely older adults they had between 39% and 71% more probability to develop prospective risk levels in three biomarkers: HbA1c, BMI, and metabolic burden. Notable differences were found by race. While loneliness was not significantly associated with risk levels of HbA1c and BMI among whites.
Loneliness 5 years ante-mortem is associated with disease-related differential gene expression in postmortem dorsolateral prefrontal cortex ⁽²²⁾	Canli T, Yu L, Yu X, Zhao H, Fleischman D, Wilson R et al.	USA 2018	There is no objective.	It was informed about 337 positively regulated genes and 43 negatively regulated genes are reported, among which the most important ones were associated with Alzheimer's disease, psychiatric diseases, immune dysfunction and cancer.
Loneliness and Telomere Length: Immune and Parasympathetic Function in Associations With Accelerated Aging ⁽²⁷⁾	Wilson S, Woody A, Padin A, Lin J, Malarkey W, Kiecolt-Glaser J.	USA 2018	Examine associations between loneliness, herpes virus reactivation, and telomere length, with parasympathetic activity as a moderator, in healthy middle-aged and elderly adults.	Loneliness was linked to herpes virus reactivation with cellular aging through shorter telomeres, an important predictor of risk of age-related disease and death.
The relation between living alone and depressive symptoms in older Korean Americans:	Park N, Jang Y, Lee B, Chiriboga D.	USA 2017	Conceptualize the fact of living alone as an objective and structural indicator of social isolation and loneliness as a subjective	Subjective perceptions of loneliness may explain the mechanism through which objective social isolation presents risks

do feelings of loneliness mediate? ⁽⁷⁾				perception of social isolation.	of depressive symptoms.
Loneliness in Older Black Adults with Human Immunodeficiency Virus Is Associated with Poorer Cognition ⁽⁸⁾	Han S, Adeyemi O, Wilson R, Leurgans S, Jimenez A, Oullet L et al.	USA 2017		Test the hypotheses that: 1. Older black adults with HIV would show greater loneliness than older white adults with HIV, and 2. Greater loneliness among older black adults with HIV would be associated with poorer cognitive function.	An inverse association between loneliness and cognitive function is described in older black adults with HIV than in older white adults with HIV.
Loneliness and Cognitive Function in Older Adults: Findings From the Chinese Longitudinal Healthy Longevity Survey ⁽⁴⁾	Zhong B, Chen S, Tu X, Conwell Y.	China 2017		Examine the relationship between loneliness and cognitive function and explore the mediating role of physical health in the loneliness-cognition relationship in Chinese older adults.	Loneliness has an adverse impact on cognitive functioning, and it also indicates that cognitive dysfunction can exacerbate loneliness by creating a "vicious cycle."
Loneliness is adversely associated with physical and mental health and lifestyle factors: Results from a Swiss national survey ⁽¹⁰⁾	Richard A, Rohrmann S, Vandeleur C, Schmid M, Barth J, Eichholzer M.	Switzerland 2017		Examine the prevalence of loneliness among adults in Switzerland and assess the associations of loneliness with various physical and mental health and behavioral factors, as well as assess the modifying effect of sex and age.	Loneliness was associated with poorer physical and mental health, and unhealthy behavior.
All-cause mortality and multimorbidity in older adults: The role of social support and loneliness ⁽¹¹⁾	Olaya B, Domènech-Abella J, Moneta M, Lara E, Caballero F, Rico-Urbe L et al	Spain 2017		Determine whether the effect of multimorbidity on time to mortality is modified by the level of social support and loneliness in a representative sample of 2113 60-year old participants.	Loneliness is not related to an increased risk of mortality in a representative sample of the Spanish elderly population.
Social isolation and loneliness as risk factors for the progression of frailty: the English Longitudinal Study of Ageing ⁽²⁵⁾	Gale C, Westbury L, Cooper C.	England 2017		Investigate whether social isolation and loneliness are independent risk factors for change in frailty status.	Older people who experience high levels of loneliness are at higher risk of becoming physically frail.
Loneliness and cardiovascular disease and the role of late-life depression ⁽¹²⁾	Hegeman A, Schutter N, Comijs H, Holwerda T, Dekker J,	Netherlands 2017		Examine whether loneliness is associated with the presence of cardiovascular diseases, taking into	Only women showed an association between loneliness and cardiovascular disease; however, this

	Stek M et al.		account the role of depression in old age.	association was explained by depression, indicating that loneliness in its own right does not appear to be related to cardiovascular disease.
Loneliness and All-Cause, Cardiovascular, and Non-cardiovascular Mortality in Older Men: The Zutphen Elderly Study ⁽²⁾	Julsing J, Kromhout D, Geleijnse J, Giltay E.	Netherlands, 2016	Determine whether loneliness is independently associated with increased all-cause, cardiovascular, and non-cardiovascular mortality in older men.	Loneliness is common in older men and increases with aging; however, no independent associations were found between loneliness and the risks of death from cardiovascular or non-cardiovascular cause.
Loneliness, depression and cognitive function in older U.S. adults ⁽⁹⁾	Donovan N, Wu Q, Rentz D, Sperling R, Marshall G, Glymour M.	USA, 2016	Examine the reciprocal relationships of loneliness and cognitive function in older adults.	Loneliness and depressive symptoms appear to be risk factors related to cognitive impairment, but low cognitive function does not lead to worsening loneliness over time.
Perceived loneliness among older adults with mild cognitive impairment ⁽²³⁾	Yu J, Lam C, Lee T.	China, 2016	Establish the prevalence of MCI in a community sample in Hong Kong and to determine whether participants with MCI feel significantly lonelier, even after depression has been taken into account.	Loneliness is implicated in Mild Cognitive Impairment (MCI). The relationship between loneliness and mild cognitive impairment is at least partially independent of depression.
Association of Higher Cortical Amyloid Burden With Loneliness in Cognitively Normal Older Adults ⁽²³⁾	Donovan NJ, Okereke OI, Vannini P y col.	USA, 2016	To determine whether cortical amyloid burden is associated with increased loneliness in cognitively normal older adults.	Loneliness is a relevant neuropsychiatric symptom for preclinical Alzheimer's Disease (AD).

Source: Self-development, 2022.

DISCUSSION

Currently there is a large amount of research on the subject ^(2-4,7-30), recognizing that it is a subject that is being highly researched, demonstrating the efforts to clarify the associations between loneliness and morbidities in the elderly.

The majority of results found a relationship between loneliness and pathologies in the elderly (24 of 27 studies). Associations found between loneliness and death were very

diverse, on the one hand, some authors stated that loneliness increases the risk of death ^(18,27), while others report that there is no such relationship ^(2,11), likewise, others describe a relationship when there is loneliness concomitantly with frailty ⁽¹⁷⁾.

Loneliness as a cause of cognitive impairment was present in all the studies that analyzed it ^(3,4,9,13,14,21,23), both independently ^(3,4,14,21,23), as with association with depressive symptoms ^(9,13); an important aspect is the description of a “vicious circle”, product of the exacerbation of loneliness due to cognitive dysfunction ⁽⁴⁾.

Another association identified with loneliness was the physical state of the older adult; in some studies they identified poorer physical health ⁽¹⁰⁾, risk of becoming physically frailer ⁽²⁵⁾, poorer physical performance ⁽²⁹⁾, or risk of fatigue and physical inactivity ⁽²¹⁾.

An interesting aspect to highlight is that in the selected studies that described a relationship associated with one gender, all were linked to women, for example: one article associated loneliness with lower grip strength only in women ⁽²⁰⁾, other authors demonstrated that loneliness is a predictor of cardiovascular mortality in women ⁽³⁰⁾, and another article described a relationship between loneliness and cardiovascular diseases only in women ⁽¹²⁾; however, in this last study the authors reported that said relationship can be explained by depression, which indicated that loneliness in its own right does not seem to be related to cardiovascular disease, although this is subject to discussion, since in another research loneliness was associated with an increased risk of developing depressive symptoms ⁽⁷⁾.

Loneliness was also associated with the risk of developing dementia, one study pointed out its relationship with all-cause dementia and Alzheimer's disease ⁽¹⁶⁾, another with preclinical Alzheimer's disease ⁽²⁴⁾, and finally, an article associated it with multi-morbidities such as Alzheimer's disease, psychiatric diseases, immune dysfunction and cancer ⁽²²⁾.

Regarding the relationship between loneliness and cardiovascular events, one study showed a significant correlation with higher blood pressure ⁽²⁸⁾; additionally, another study related it to a higher risk of developing coronary heart disease and stroke ⁽³⁰⁾. However, another article reported no relationship between loneliness and death from cardiovascular causes ⁽²⁾.

Regarding loneliness and its relationship with race, one study described a significant association between loneliness and risk levels of HbA1c and BMI only in older black adults ⁽¹⁵⁾, consistent with another study that compared relationship between loneliness and cognitive function in older adults with HIV, with a greater association in older black adults ⁽⁸⁾.

Finally, other relationships have been described: such as loneliness with greater symptoms of disability and a slower walking speed of 4 meters in older people with type 2 diabetes, overweight and obesity ⁽¹⁹⁾; others associated loneliness with memory and verbal fluency ⁽³⁾, as well as with the reactivation of the herpes virus ⁽²⁷⁾, and it was also associated with poorer mental health and unhealthy behavior ⁽¹⁰⁾.

CONCLUSION

The present review fulfilled the objective which was to identify the pathologies associated to loneliness in the elderly. There are multiple studies that show the relationship between loneliness and its consequences, with two trends in some pathologies. On the one hand, studies that affirmed their relationship, while others ruled it out. However, there are clear aspects in the selected studies, for example: the obvious effect of loneliness on cognitive decline, decreased physical fitness, Alzheimer's disease and cardiovascular events. On the other hand, contradictions were seen in the relationship between loneliness and the risk of death, as well as with depression. In this context, it is undeniable that further research is required in this regard, in order to clarify these relationships.

The phenomenon of "population aging" is a challenge for society, since it has to adapt to improve the health and functional capacity of older people as much as possible, as well as their social participation and safety. It is necessary to establish public policies to prepare people for their future aging process, in addition to being able to implement various strategies to prevent and/or reduce loneliness in older people.

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