Depressive symptoms and physical frailty in the older adults: an integrative review

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Abstract

Objective: to identify the relationship between depressive symptoms and physical frailty in the older adults through an integrative literature review. *Method:* searches were performed in portals and databases: Virtual Health Library, SciELO, Web of Science and PUBMED. The inclusion criteria were having been published in the period from 2012 to 2020, to appear in full, to be directly related to the theme and registered in Portuguese and/or English. To categorize the articles included in the study, the following information was extracted: author(s) and year, type of study and sample, objective(s) and main results. To illustrate selection of articles, the flowchart of the Preferred Reporting Items for Systematic Reviews and Meta-analyses were used, the Oxford Centre for Evidence-Based Medicine to classify the level of evidence and the EndNote Web for managing the bibliography. *Results:* of the 486 articles found, 126 were excluded due to duplication, 339 did not meet the pre-established criteria, and 21 articles that made up the review corpus. There was an association between depressive symptoms and physical frailty in the older adults, with the ability to be predictors of each other, being related to negative outcomes for the health of the older adults, among them: cognitive impairment, limited activities, increased mortality, among others. *Conclusion:* depressive symptoms and physical frailty are present among the older adults, with a reciprocal association, negatively influencing their clinical condition. The results help to clarify these conditions and provide knowledge for the prevention and development of interventions in the gerontological area, benefiting the health of the older adults.

Keywords: Depression. Frailty. Frail Elderly. Health of the Elderly. Geriatrics.

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INTRODUCTION

Frailty among older people is considered a priority in public health, as its presence predicts the occurrence of adverse events that threaten the long-term sustainability of health actions and systems[1]. In addition, it has a negative influence on the quality of life of the older person[2].

Physical frailty is defined as "a clinical condition in which there is an increase in an individual's vulnerability to the development of dependence and/or increased mortality when exposed to a stressor"[3]. It can be assessed from the frailty phenotype[4], which is composed of five biological markers: unintentional weight loss, self-reported fatigue/exhaustion, decreased handgrip strength, decreased physical activity level, and reduced gait speed. The older person with three or more of these markers is classified as frail, one or two pre-frail and no marker, not frail[4].

The condition of physical frailty is prevalent in older people[4,5] and has been a frequent topic of research due to its impacting effects on the vulnerability of older people, which lead to a cascade of negative health outcomes. The reduction in quality of life, reduction in basic activities of daily living (BADL), physical limitations, social isolation, hospitalization, increased morbidity and mortality are highlighted[6].

The presence of physical frailty in older people generates a state of alert for health professionals, due to the older person's predisposition to vulnerability and, consequently, physical and functional decline. It is associated with the presence of other geriatric conditions, such as depressive symptoms[7]. Special attention should be directed to frail older people for the onset of depressive symptoms[8,9].

Although it is widely recognized, so far there is no established definition for depressive symptoms, depressive symptomatology subtly manifests itself with dysphoria and somatic symptoms, being often associated with traces of depression[10].

Depressive symptoms predict the same adverse outcomes of physical frailty in older people and share somatic symptoms and risk factors such as sedentary lifestyle, weight loss, fatigue and low level of physical activity[11].

A cross-sectional descriptive study conducted by the Frailty Network for Older Brazilians (FIBRA), with 2,402 older people residents of seven Brazilian cities, identified a significant association between the prevalence of depression and physical frailty markers. Among them, unintentional weight loss, reduced gait speed and fatigue/exhaustion stand out[12].

However, contrasting the findings of the *op.cit.* study, an observational research carried out in India with 165 older people (≥60 years old), it identified that although a third of the participants, 54 (32.7%) had depression and 64 (38.8%) physical frailty, there was no significant association between them[13].

It is observed that the relationship between depressive symptoms and physical frailty in older people is still not fully clarified, configuring a scientific gap. Considering the current and relevant theme, the integrative literature review can clarify and present scientific knowledge to understand the factors that contribute to the etiology and prognosis of these syndromes, as well as contribute to the improvement of gerontological care actions.

Given the above, this study aims to identify the relationship between depressive symptoms and physical frailty in older people through an integrative literature review.

METHOD

It is an integrative literature review, which generates new knowledge on a given topic, reviewing, criticizing and synthesizing representative literature, in an integrated manner, so that new structures and perspectives are generated[14].

The review followed six steps[15]: 1-Theme identification and selection of the research question; 2-Establishment of inclusion/exclusion criteria, search and selection of literature; 3-Characterization of studies; 4-Assessment of studies included in the integrative review; 5-Interpretation of results; 6-Synthesis of knowledge or presentation of the review.

In the first stage, the relationship between depressive symptoms and physical frailty in older people was identified as a problem. To construct

the research question, the PICO strategy was used, so that the letter P corresponds to the population (older people), I for interest (depressive symptoms and physical frailty), C for comparison (any comparison) and O for outcomes (relationship). Given the above, the following question was structured: *What is the relationship between depressive symptoms and physical frailty in older people?*

In the second stage, the following inclusion criteria were established for the articles: having been published from January 2012 (the year when the term physical frailty was created) to May 2020; appearing as articles available in full and directly related to the topic; being in Portuguese and/or English.

The following were defined as exclusion criteria for articles: appearing as an editorial, review, experience report, theoretical reflection, dissertation, thesis, monograph, letter, summary of proceedings and events; review articles and those that did not answer the research question.

Searches were performed in portals and electronic databases covering studies/research in the health area: *National Library of Medicine* and *National Institutes of Health* (NCBI/PUBMED), *Web of Science, Virtual Health Library* (VHL) and *Scientific Electronic Library Online* (SciELO).

Search strategies were used in Portuguese and English, which were developed from the application of "*Descriptors in Health Sciences*" (DeCS), "*Medical Subject Headings*" (MeSH) and keywords. To obtain the largest number of articles, combinations between the descriptors were used, with the help of the Boolean operators "OR" and "AND" with the following terms: "*Frail Elderly*" AND ("*Depression*" OR "*Depressive Symptoms*").

Searches for studies, selection, extraction and analysis of data were carried out by two researchers independently. Aiming to reduce possible errors in the search, evaluation, analysis and interpretation of the studies in view of the doubts that arose from the review process, a third researcher was consulted to resolve them.

The management of the bibliography found for the selection of articles included in the corpus of the integrative review was carried out through the computer program *EndNote*®, which helped in the exclusion of duplicate studies, keeping only the first version found. To illustrate the selection of articles in the integrative review corpus, the flowchart of *Preferred Reporting Items for Systematic Reviews and Metaanalyses* (PRISMA)[16] (Figure 1) was used in the results.

In the third stage, the information extracted from the articles included in the study was categorized according to: author(s)/year of publication, type of study/sample, objective, and main results (Table 1).

In the fourth stage, the articles included in the study were analyzed in detail in the search for explanations and results, through recurrent reading. Subsequently, the studies were classified according to the level of evidence (Table 1) based on the classification proposed by the *Oxford Center for Evidence-Based Medicine* (2009)[17], consisting of five hierarchical levels of evidence by type of study, which can be visualized in Chart 1.

The fifth stage was designed with the interpretation of results, thus helping to discuss the relevant data from the studies. The sixth stage was completed with the presentation of the review/synthesis of knowledge. These steps were interpreted and presented in a narrative way.

This integrative review ensured the ethical aspects, ensuring respect for copyright, for citation we used the Vancouver standards and authors' references.

RESULTS

The initial search in the databases resulted in 486 articles. Of these, 126 duplicate studies were excluded, and 360 studies were selected for the general evaluation, of which 303 were excluded after reading the title and/or abstract because they were not related to the topic. Thus, 57 complete articles were evaluated for eligibility criteria, 36 of which were excluded after reading in full for not answering the research question, leaving 21 articles that presented the eligibility characteristics for inclusion in this review. Figure 1 shows a flowchart of the selection of articles from identification to inclusion in the corpus of the integrative review.

Chart 1. Levels of Evidence by Study Type. Curitiba, PR, 2020.

Levels of Evidence	Types of studies
1 a	Systematic review (with homogeneity) of randomized controlled clinical trials (ECCR).
1 b	ECCR with a narrow confidence interval (CI).
1 c	Therapeutic results of the "all or nothing" type.
2 a	Systematic review (with homogeneity) of cohort studies.
2 b	Individual cohort study (including lower quality ECCR, eg, follow-up below 80%).
2 c	Research results (observation of therapeutic results or clinical evolution); Ecological studies.
3 a	Systematic review (with homogeneity) of case-control studies.
3 b	Individual case-control study.
4	Case reports (including lower quality cohort or case-control).
5	Expert opinion without explicit critical appraisal, physiology studies, bench research and "*first principles*".

Source: Translated and adapted from the classification of the *Oxford Centre Evidence-Based Medicine* (2009)[17]

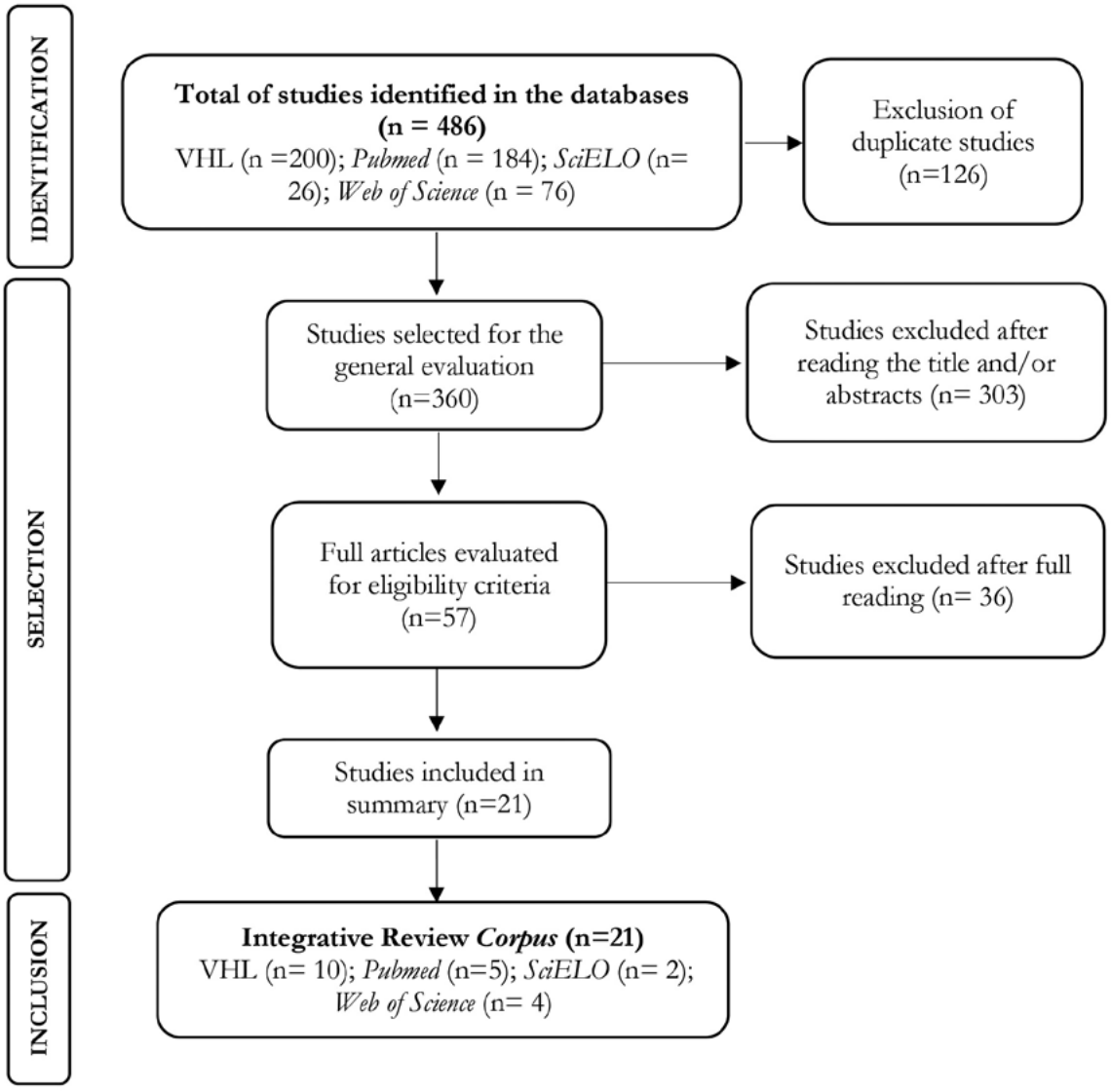

Figure 1. Flowchart of the selection of articles from the integrative review corpus. Curitiba, PR, 2020.

The majority of publications were published in 2017 (n=7; 33.3%) and 2015 (n=3; 14.3%), followed by 2019 (n=3; 14.3%), 2018 (n=2; 9.5%), 2016 (n=2; 9.5%), 2014 (n=2; 9.5%), 2020 (n=1; 4.8%) and 2012 (n=1; 4.8%).

The main language of dissemination of the studies was English (n=19; 90.5%), followed by Portuguese (n=2; 9.5%). Regarding the countries of origin of the publications, Brazil (n=4; 19.0%) and the United States (n=4; 19.0%) stood out.

Regarding the methodological design, cross-sectional (n=8; 38.1%) and longitudinal (n=8; 38.1%) studies predominated, followed by prospective cohort studies (n=4; 19.0%), and randomized controlled clinical trial (ECCR) (n=1; 4.8%). In the sample size, there was a quantitative variation from 246 older people in a controlled and randomized clinical trial to 27,652 older people in a prospective cohort study.

As for the level of evidence of the analyzed studies, level 2b (n=11; 52.4%) predominated, followed by level 2c (n=9; 42.8%) and 1a (n=1; 4.8%). For better visualization and analysis of the articles selected in the review, Table 1 was built, with categorization of the studies included in the review.

Table 1. Categorization of studies that made up the *corpus* of the integrative review. Curitiba, PR, 2020.

Author(s) /Year	Type of study/ Sample	Objective(s)	Main results/ Level of Evidence
Guedes et al., 2020[18]	Cross section/ n= 5,501	To categorize non-frail, pre-frail and frail older people in terms of fast and slow gait speed.	The presence of depressive symptoms gradually increased with the onset of frailty and there was a significant association between the conditions (p<0.01) /2c.
Silva et al., 2019[19]-	Cross section/ n= 360	To estimate the prevalence of depressive symptoms and associated factors in older patients treated at a referral center.	There was an association between depressive symptoms and physical frailty [*Odds ratio* (OR) =1.94, 95% CI 1.41-2.66] /2c.
Chang et al., 2019[20]	Longitudinal/ n= 3,352	To examine the co-occurrence of frailty and depressive symptoms at the end of life, the possibility of reversal of symptoms, their reciprocal relationship and the effects on mortality.	The coexistence of frailty and depression symptoms was associated with higher mortality (p<0.05) /2b.
Park and Lee, 2019[21]	Longitudinal/ n= 486	To analyze the factors associated with frailty among young older adults (<75 years old) and old older adults (>75 years old).	Depression was associated with worsening frailty over a three-year period (p<0.001) /2c.
Herr et al., 2018[22]	Cross section/ n= 1,253	To estimate the prevalence of frailty among centenarians included in a multinational study and investigate associated factors.	The overall prevalence of frailty (3 criteria or more) was 64.7%. Among the factors associated with frailty was the presence of depression (p<0.05) /2c.
Lee, Won and Son, 2018[23]	Cross section/ n= 289	To identify the influence of combined depression and physical frailty on cognitive impairment in heart failure.	The combined influence of depression and physical frailty increased the risk of cognitive impairment in unadjusted models (OR 4,360) and adjusted models (OR 3,545) /2c.
Albala et al., 2017[24]	Longitudinal/ n= 2,098	To study the frequency of the frailty phenotype and its association with mental health and survival in Chilean older people.	There was an association between physical frailty and depression (p<0.001) /2b.

to be continued

Continuation of Table 1

Author(s) /Year	Type of study/ Sample	Objective(s)	Main results/ Level of Evidence
Ding, Kuha and Murphy, 2017a[25]	Longitudinal/ n= 4,638	To investigate physical, psychological and social predictors of physical frailty.	Depressive symptoms predict high levels of future physical frailty (p<0.05) /2b.
Ding, Kuha and Murphy, 2017b[26]	Longitudinal/ n= 4,638	To identify moderators and mediators of the effect of physical frailty in changing activity limitation in older people.	Physical frailty produces significant indirect effects through depressive symptoms and cognitive impairment in changing activity limitation in older people (p<0.05) /2b.
Lohman, Mezuk and Dumenci, 2017[27]	Longitudinal/ n= 13,495	To estimate the independent and joint associations between frailty and depression trajectories and the probability of admission and falls in nursing homes resulting in injury.	Faster increases in frailty and depression symptoms were associated with greater chances of home hospitalization and severe falls over time (Frailty: OR Nursing home =1.33, 95% CI: 1.09-1.66; OR Fall =1.52, 95% CI: 1.12 to 2.08; Depression: OR Nursing home =3.63, 95% CI: 1.29 to 9.97; OR Fall =1.16, 95% CI: 1.01 to 1.34)/2b.
Ng et al., 2017[28]-	Randomized controlled clinical trial/ n= 246	To investigate the effects of multi-domain lifestyle interventions in reducing depressive symptoms among frail and pre-frail older adults living in the community.	Interventions in multiple lifestyle domains that reverse frailty among older people also reduce depressive symptoms (p<0.05) /1b.
Tavares et al., 2017[29]	Cross section/ n= 1,609	To investigate the association of frailty syndrome with socioeconomic and health variables in older people.	Factors associated with pre-frailty and frailty were: functional incapacity for basic and instrumental activities of daily living and indicative depression (p<0.001) /2c.
Veronese et al., 2017[30]	Longitudinal/ n= 4,077	To investigate whether frailty and pre-frailty are associated with an increased risk of depression in a prospective cohort of community older people.	Frailty and pre-frailty did not predict the onset of depression during 2 years of follow-up. However, slow gait speed was a significant independent predictor of future depression (p=0.05) / 2b.
Lohman et al., 2016[31]	Cross section/ n= 3,453	To estimate the correlation between depression and concurrent frailty models.	It was observed that the three frailty definition models presented a significant correlation with depression (p<0.01) /2c.
Nascimento, Batistoni and Neri, 2016[12]	Cross section/ n= 2,402	To identify the relationships of the presence of depression, with frailty and pre-frailty in older people in the community.	An association was found between depression and frailty profiles (p<0.001) /2c.
Almeida et al., 2015[32]	Prospective cohort/ n= 2,565	To determine the relative mortality associated with past and current depression, taking into account the frailty effect.	The crude mortality risk was 4.26 for men with depression at baseline compared to men who were never depressed, and 1.79 after adjusting for frailty /2b.
Makizako et al., 2015[33]	Prospective cohort/ n= 3,025	To determine whether frailty is an important and independent predictor of incident depressive symptoms in older adults without depressive symptoms at baseline.	Frailty (adjusted OR 1.86, 95%CI 1.05–3.28, p = 0.03) was an independent predictor of incident depressive symptoms / 2b.
Ramos et al., 2015[34]	Cross section/ n= 639	To assess the prevalence and factors associated with depressive symptoms in non-institutionalized older people.	The prevalence of depressive symptoms was 27.5% and it was associated with physical frailty (p<0.001) /2c.

to be continued

Continuation of Table 1

Author(s) /Year	Type of study/ Sample	Objective(s)	Main results/ Level of Evidence
Brown et al., 2014[35]	Longitudinal/ n= 1,027	To identify striking characteristics of frailty that increase the risk of death in depressed older people.	The confluence of specific frailty characteristics [fatigue (RR=1.94, 95% CI=1.11-3.40) and slow gait speed (RR=1.84, 95% CI=1.05-3.21)] and depressive illness (p = 0.03) is associated with an increased risk of death in older people /2b.
Feng et al., 2014[36]	Prospective cohort/ n= 1,827	To examine the cross-sectional and longitudinal relationships between physical frailty at baseline and depressive symptoms at baseline and at follow-up.	The cross-sectional analysis showed an association between physical frailty and a higher prevalence of depressive symptoms (p<0.001). The longitudinal analysis revealed that pre-frail and frail individuals were more likely to present new and persistent depressive symptoms /2b.
Lakey et al., 2012[37]	Prospective cohort/ n= 27,652	To examine associations of depressive symptoms, antidepressant use, and duration of use with incident frailty.	After 3 years, 14.9% (n=4,125) of women became frail and those with high scores of depressive symptoms had the highest risk of incident frailty (OR =2.19, 95% CI =1.86-2.59) /2b.

*LE: Level of Evidence; Note: (n=21 studies). Source: The authors (2020).

DISCUSSION

Depressive symptoms and physical frailty are clinical conditions that have a high prevalence in older people, with a significant association between them[12,18,19,21,24,25,29,31,34,38]. The association between the variables was verified mainly among oldest people, according to a study carried out with 1,253 centenarians[22].

Findings from three studies highlight that physical frailty was a predisposing factor for the onset and persistence of depressive symptoms [33,36,39], being evidenced that the presence of depressive symptoms increased gradually, according to the onset of frailty[18].

Frail individuals may be more likely to develop depressive symptoms due to impaired functional abilities, physical inactivity, functional disability, and social isolation. In addition, multisystem physiological dysregulation in frailty is an important biological factor that predisposes, precipitates and perpetuates depression in old age[28,36]. Once frailty develops, clinically significant depression is more likely[39].

Frailty as a predictor of depressive symptoms is an important finding pointed out by studies[28,33,36] with a high level of evidence 1b and 2b. Thus, the identification of the physical frailty syndrome may be relevant in screening older people at risk of mental health deterioration[39]. The presence of physical frailty markers, including slow gait speed[30], fatigue and exhaustion, weakness and low physical activity were also presented as predictors of future depression[33,36].

There is a bidirectional relationship between the study variables, and physical frailty can incite depressive symptoms, as well as research showing depressive symptoms are predictors of physical frailty[21,25,27,37,40]. Findings from the literature included in this study revealed that older people with depressive symptoms are at greater risk of developing physical frailty. The presence of depressive symptoms can cause changes in behavior and social involvement, reflecting the worsening of functional status and physical frailty[12].

It is noteworthy that the depression-frailty relationship can be influenced by the use of antidepressants. In the United States of America (USA), a prospective cohort study[37] carried out with 27,652 non-frail older women (≥65 years old) examined associations of depressive symptoms, use

of antidepressants and duration of use with incident frailty. In the study, users who had depressive symptoms were 3.63 times more likely to develop frailty than non-users and non-depressed users (95% CI =2.37-5.55). A possible effect of antidepressants in increasing the risk of falls and fractures was pointed out, which in turn are associated with the development of frailty[37].

From the studies *op.cit.* it is possible to verify that both depressive symptoms and physical frailty can be predictors of each other. Results of a systematic review and meta-analysis confirm this bidirectional relationship, which identified a reciprocal interaction between depression and frailty in older people. Each condition is associated with an increased prevalence and incidence of the other, and can be risk factors for reciprocal development[38].

On the other hand, the overlapping of symptoms makes it difficult to explain how the bidirectional relationship occurs, suggesting that psychological vulnerability, reflected by depression, can be an important component of frailty[31].

Considering the relationship between depressive symptoms and physical frailty, some studies have reported negative health outcomes in older people as a result of these conditions when they act in association. Among the outcomes, the following stand out: cognitive impairment[18,23,24], activity limitation[26], worse self-rated health[19,21], functional disability for BADL and instrumental activities of daily living (IADL)[19,29], falls and hospitalizations[18,19,27].

It is noticed that the relationship between depressive symptoms and physical frailty ranges from cognitive impairment to functional incapacity, causing limitations in the activities of older people, especially IADL. These activities require greater physical and cognitive integrity, as they are related to the subject's social participation, such as shopping and using means of transport. The loss of autonomy and limitations in daily life can generate imbalance in the emotions, well-being and social image of older people[19].

The outcomes observed in the studies described in this review showed that the relationship between depressive symptoms and physical frailty contribute to increased mortality in older people[20,32,35]. In view of these outcomes arising from the relationship between depressive symptoms and physical frailty, interventions that help to reduce these conditions are necessary to prevent morbidity and mortality.

In Singapore, a randomized controlled study conducted with a sample of 246 older people, for a period of 12 months, investigated the effects of lifestyle interventions in various domains (nutritional, physical, cognitive) among older people with physical frailty in reducing depressive symptoms. In the study, the interventions proved to be effective in reversing physical frailty and had psychological benefits in reducing depressive symptoms, noticing changes in the parameters of physical frailty significantly associated with changes in the Geriatric Depression Scale (GDS) score[28].

Interventions that help reverse frailty can mediate the observed improvement in mood functioning. When depressive symptoms and physical frailty are present together, clinical and multimodal lifestyle interventions targeting common psychosocial and biological factors can prevent the onset of symptoms and reduce the severity of syndrome symptoms and adverse health outcomes[28,36].

It was observed that the studies that discussed the theme were mostly longitudinal with 2b level of evidence, which allows establishing cause and effect relationships between the research variables. However, there is a need for further studies with strong scientific evidence.

As probable limitations of this integrative review, the lack of standardization of the instruments for evaluating the variables investigated in the studies of the corpus of analysis is highlighted, which can influence the interpretation of the results. Language restrictions in the search for publications may have limited the results. As the study's strengths, clarity and methodological rigor stand out, as well as a relevant thematic approach that contributes to the practice of evidence-based care.

CONCLUSION

The integrative review showed an association between depressive symptoms and physical frailty in

older people, and it was found that these syndromes have the ability to be predictors of each other, contributing to the reciprocal onset and increase.

The association between depressive symptoms and physical frailty was related to negative health outcomes for older people, such as: cognitive impairment, activity limitation, worse self-rated health, functional disability for BADL and IADL, falls, hospitalizations, and increase in mortality.

Knowledge of these outcomes alerts to the importance of investing in preventive interventions for these syndromes, as well as the adoption of effective approaches to their treatment. Studies have shown that interventions help to reverse physical frailty and can influence the improvement of depressive symptoms.

The results produced in this study help to clarify the relationship between depressive symptoms and physical frailty in older people, while providing knowledge for the development of interventions in the gerontological area. Further research is suggested to contribute to the enrichment and deepening of this theme.

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