

REVIEW ARTICLE



Frailty and physical activity in centenarians: A systematic review

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ABSTRACT

There is a lack of studies evaluating frailty and physical activity in people aged 100 years or older. This review aimed to synthesize the evidence on frailty and physical activity in centenarians. A systematic review was conducted according to the PRISMA guidelines. We searched the PubMed, CINAHL, SCOPUS, Web of Science, and Lilacs databases for articles published until 18 June 2020. This review was registered with PROSPERO (CRD42020162913). Five studies were included in this review according to the eligibility and exclusion criteria. In summary, the reviewed studies show that centenarians are fragile and that frailty increases with age; however, women are frailer than men. The most common frailty criteria were low physical activity level (78% to 72.5%), muscle weakness (84.2% to 66%), and slow walking speed (77.6% to 48.4%). Most centenarians perform less exercise than younger older adults, have a low physical activity level, live in nursing homes, and exhibit functional disability. Regarding the methodological quality of the studies, one article was classified as regular and the other four as poor. Frailty and a low physical activity level are common in centenarians. Experimental studies with better methodological quality are necessary to better understand the causal relationship between variables.

Keywords: aged, 80 and over; centenarians; physical activity; frailty; systematic review; longevity.

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INTRODUCTION

Recent decades have witnessed an increase in the population of older adults aged 100 years or older, the so-called centenarians¹. This increase in long-lived populations is often accompanied by frailty and physical inactivity². This frailty is characterized by high vulnerability to health risks, including physical deficits and mortality³⁻⁵. Physical inactivity renders the older adult frail and consequently increases the risks of functional disabilities, with the individual becoming dependent on activities of daily living (ADLs)²⁻⁶.

Some systematic reviews on frailty, physical activity (PA), and older adults have been published⁷⁻¹¹. However, most of the studies evaluated the effect of PA on health consequences in frail older adults or on the level/progression of frailty in this population. Furthermore, there is a lack of reviews that specifically analyze centenarians since the published reviews involved older adults of other age groups.

Studies¹²⁻¹⁷ have demonstrated an increase in frailty among older adults, as well as a lack of information about frailty in the oldest-old. A review on frailty syndrome¹⁸ found that the incidence of this outcome increases with age in women, Afro-Americans, and

individuals with low education levels, low income, health problems, chronic diseases, and disabilities. However, the review did not report the age range of the studies. In addition to these characteristics of frail older adults, cross-sectional studies showed that PA is associated with a lower incidence of frailty in adults and older adults^{19,20}. A cohort study demonstrated that high-intensity PA was associated with a lower risk of frailty and pre-frailty in older adults with a mean age of 74 years²¹. However, those studies did not involve centenarians.

Given the aforementioned studies, there is an obvious lack of reviews that investigate the scientific evidence on frailty and PA in centenarians. Such reviews would help us understand how these variables behave in such a long-lived population and consequently support public health interventions designed to postpone new declines associated with aging and mortality. This study will assist health professionals, caregivers of the elderly, managers of geriatric institutions, and relatives. In addition, the results of this review will support interventions involving institutionalized centenarians and those living in nursing homes who generally have greater deficits in PA. Thus, the research question that guides this systematic review is: What is the scientific evidence on frailty and physical activity in centenarians?

Therefore, the objective of the present study is to synthesize scientific evidence provided by studies that assessed frailty and PA in centenarians.

METHODS

Search strategy and databases

For this systematic review, we searched PubMed, CINAHL, SCOPUS, Web of Science, and Lilacs databases and other sources to identify studies including the terms "centenarians", "frailty", and "physical activity/physical exercise". Articles published in English, Portuguese or Spanish, considering the entire publication period of these databases until 18 June 2020, were retrieved. The following search terms listed in the Medical Subject Headings (MeSH) of PubMed were used: Centenarian OR "Aged, 80 and over" OR "Oldest-old" AND "Physical activity" OR Exercise AND "Frail elderly" OR Frailty OR "Frailty syndrome". The inclusion and exclusion criteria were applied considering MeSH terms. Within this context, the term "Aged 80 and over" is necessary as an inclusion criterion since it is the main term that comprises the keyword "centenarian". In addition, the criteria used to broaden the search and thus improve the retrieval of articles.

All procedures from the inclusion of the article after the database search to full-text reading were performed using the Rayyan QCRI® web application²². This systematic review was registered with the International Prospective Register of Ongoing Systematic Reviews (PROSPERO) under CRD42020162913. An independent reviewer (PSF) searched the titles in the databases. The titles of articles that did not mention any relationship with the above-cited terms were excluded. Two independent reviewers (PSF and BSC) then read the full text of the selected articles to identify those for final analysis. Disagreements were resolved by consensus with a third reviewer (FSP).

The checklist proposed by Downs and Black²³ was applied to evaluate the methodological quality of the studies included in this review. This checklist is appropriate to evaluate the quality of randomized and non-randomized studies, including observational studies. The answers were scored as 1 (criterion present) and 0 (criterion absent), except for question #5 which allowed three answers scored from 0 to 2, resulting in a total score of 28. The higher the score, the better the methodological quality of the study²³. The articles were divided into four quality categories²⁴⁻²⁶: excellent (score of 26-28), good (20-25), regular (15-19), and poor (≤14). The methodological quality was assessed by two independent reviewers (PSF and FSP) and disagreements were resolved until a consensus was reached.

Selection and eligibility criteria

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were used for the identification and selection of the articles in the databases (Figure 1). The included articles followed the eligibility criteria based on the PECO acronym, i.e., studies including "centenarians, oldest-old and 80 years or older" as population, "physical activity and exercise" as exposure, and "frailty, frailty syndrome, frail older adult" as an outcome. The comparison item was not included.

The following articles were excluded from this review: studies whose samples/participants did not include individuals aged 100 years or older; studies that did not report the analysis of data specific for centenarians; studies that did not use any frailty criterion or frailty screening instrument or whose instrument was unclear regarding the approach to physical frailty, and studies that did not evaluate PA or other types of PA (for example, physical exercise). Theses, dissertations, letters, and reviews were also excluded (Figure 1). For the synthesis of the results, the following information was extracted from the selected studies: author, year, location, study design, aim, population and sample, instruments, main results, and conclusion. In addition, the methodological quality of the studies was assessed.

RESULTS

A total of 3,542 titles were identified in the following databases: Lilacs (n=98), PubMed (n=1,355), CINAHL (n=659), Web of Science (n=47), and SCOPUS (n=1,383). Of these, 1,420 duplicate titles were excluded, the remaining 2,122 for reading. Next, 2,180 articles were excluded after reading the title and 47 after reading

the abstract. Eleven articles were selected for full-text reading. Six of these articles were excluded three. They did not clearly state the frailty assessment used and three because they did not specifically analyze data of centenarians. Five articles were included in the review (Figure 1).

Regarding the characteristics of the studies, the five articles were observational studies, including three cross-sectional studies²⁷⁻²⁹, one longitudinal study³⁰, and one cohort study³¹. The studies were published the Gu et al.³⁰ and Dupre et al.³¹; Duarte et al.²⁷, Herr et al.²⁸, and Ribeiro et al.²⁹. Regarding the country of origin, two studies were conducted in Portugal²⁷⁻²⁹, two in China^{30,31}, and one involved five countries (Japan, France, Switzerland, Denmark, and Sweden) that are part of the Country Oldest Old Project (5-COOP)²⁸. There was a predominance of females in all studies²⁷⁻³⁰

and the number of participants varied widely. The longitudinal³⁰ and cohort studies³¹, both conducted in China, involved 3,088 centenarians each, while the cross-sectional Portuguese study involved 50 participants²⁷ (Table 1).

Concerning the instruments used for measuring frailty, three studies²⁷⁻²⁹ had the frailty phenotype as a basis, which evaluates five criteria: slow walking speed, muscle weakness, fatigue, weight loss, and low PA levels³.

The studies of Duarte et al.²⁷ and Ribeiro et al.²⁹ used the same assessment instruments since they are part of the same population-based database, the PT100 Oporto Centenarian Study. In the PT100 study, weight loss was evaluated through the question "Have you lost a lot of weight recently without wishing to do so? ("a lot" was defined as 6 kg in the last 6 months or 3 kg in the

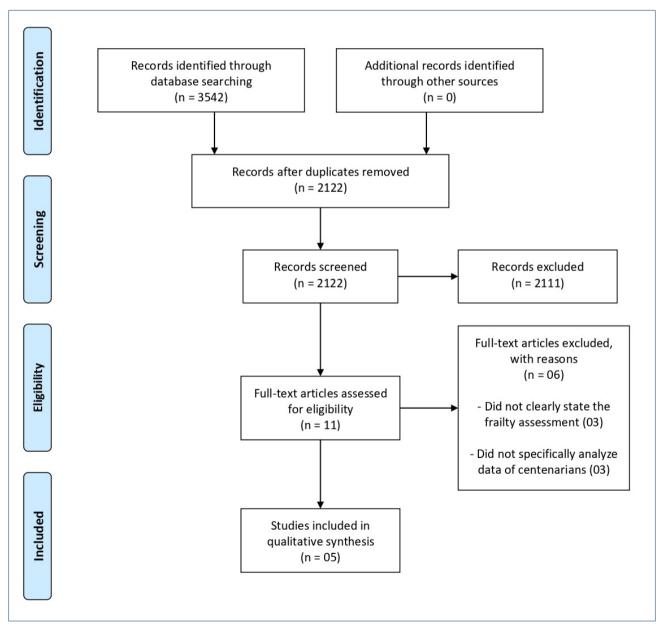


Figure 1: PRISMA flow diagram of articles for inclusion in the systematic review.

Table 1: Description of each included study.

Table 1: Description of a		Population			
Study design	Aim	sample [≥100] and gender	Instruments	Main results	Conclusion
Gu et al., 2009 ³⁰ , China. Longitudinal study	This study investigates the factors associated with frailty and the association of frailty with mortality in a a national sample of adults aged 65 – 109 in China.	N= 15.919 (69 to 109 years) n [3.088] ♂ 655 ♀ 2.433	FI: Evaluation of the items: self-reported health status, cognitive status, disability, hearing and visual capacity, depression, heart rate, and several chronic diseases. PA: Question about regular exercise.	- FI varies according to age and gender: Female (65 years old: 0.10; 80 years old: 0.15; and 100 years old or more: 0.40); Male at 65 years old: 0.8; at age 80: 0.13; and at 100 years old or more: 0.29); - The prevalence of regular exercise varies according to age group, sex and decreases with advancing age (65 to 79 years old - 35.6% women and 44.9% men; 100+ - 13.4% women and 30.2% men); - Regular exercise and FI, showed a strong and negative association when comparing younger elderly people with centenarians, both for women (65 to 79 years old - OR 0.66 p <0.001; 100+ - OR 0.28 p <0.001) and for men (65 to 79 years old - OR 0.70 p <0.001; 100+ - OR 0.23 p <0.001).	Frailty increases with age, for both women and men. Women are frailer than men of all ages. Centenarians with higher FI, practice less physical exercise than younger elderly people, of both genders.
Dupre et al., 2009 ³¹ , China. Longitudinal study	To examine the association between frailty and type of death among the world's largest oldest-old population in China.	N= 15 919 (65 to 109 years) n [3.088] ♂ × ♀ ×	FI: Evaluation of the items: self-reported health status, cognitive status, disability, hearing and visual capacity, depression, heart rate, and several chronic diseases. PA: Question about regular exercise.	- IF (fragility levels in quartiles) varies according to age and sex: Female (65 to 79 years old - least frail 62.8 / frailer 3.7; ≥ 100 years old – least frail 3.6 / frailer 48.2); Male (65 to 79 years old - least frail 63.5 / frailer 8.2; ≥ 100 years old - least frail 1.9 / frailer 22.8); Men practiced more exercises than women, but this practice decreased for both genders, as the IF increased: least frail - ♂ - 51.5 / ♀ - 39.5 and frailer - ♂ - 17.3 / ♀ - 6.7	Frailty increases with age, for both women and men. Men exercise more than women. This practice decreases proportionally with the level of frailty.
Duarte et al., 2014 ²⁷ , Portugal. Cross-sectional study	The purpose of this study is to analyze the prevalence of physical frailty and the sociodemographic, functionality, and health factors associated with this syndrome in a sample of people 100 and more years old.	N= 114 n [50] ♂ 08 ♀ 42	FP: Evaluation of five criteria: Reduction in gait speed, dynapenia, self-reported fatigue, low body mass, and PA level. PA: Question about dancing, walking, rural work, or gardening.	- 96% of centenarians were considered pre-frail and frail;	Frailty is associated with functional status; Most centenarians are pre-frail and frail, live in nursing homes, and have a low level of PA.

Continue...

Table 1: Continuation.

Author/Year/ Location/ Study design	Aim	Population sample [≥100] and gender	Instruments	Main results	Conclusion
Ribeiro et al., 2018 ²⁹ , Portugal. Cross-sectional study	The study aimed to characterize the frailty phenotype in a sample of centenarians and add to the current body of knowledge on the relationship between frailty and depressive symptoms in such an advanced age.	N= 297 n [91] ♂ 13 ♀ 78	FP: Evaluation of five criteria: Reduction in gait speed, dynapenia, self-reported fatigue, low body mass, and PA level. PA: Question about dancing, walking, rural work, or gardening.	- 94.5% were considered pre-frail and frail; - There was a significant difference between frailty and functional status (p <0.001); - Frail centenarians were more likely to have depression when compared to pre-frail ones (OR 3.92 / 95% CI 1.48-10.4 p <0.006) The most frequent frailty criteria in centenarians were: low level of PA (72.5%), dynapenia (69.2%), reduced gait speed (48.4%), fatigue (45.1%), and weight loss (11%).	Most centenarians are pre-frail and frail; The frail are more likely to have depression than the pre-frail; Frailty is associated with functional status; Centenarians have a low level of PA.
Herr et al., 2018 ²⁸ , Japan (JPN), France (FRA), Switzerland (SWI), Denmark (DEN) and Sweden (SWE). Cross-sectional study	This study aimed to estimate the prevalence of frailty and to analyze associated factors among centenarians included in the 5-COOP.	N= 1253 n [1.228]	FP: Evaluation of five criteria: Reduction in gait speed, dynapenia, self-reported fatigue, low body mass, and PA level (all self- reported.). PA: Question about no regular exercise or outdoor activity (self-reported) And/or bedridden or unable to transfer from bed to chair without help.	- 95% of centenarians (1/3 of the sample) are considered pre-frail and/ or frail; - In all countries there is a higher prevalence of frail centenarians, the variation was 51.5% in Sweden to 77.7% in Switzerland; - The most frequent frailty criteria in centenarians were: dynapenia (84.2%), reduced gait speed (77.6%), low level of PA (72.5%), fatigue (43.8%), and weight loss (23.8%); - The low level of PA showed an association with institutionalized centenarians (OR 1.58 / 95% CI 1.12–2.23 p <0.001); - The low level of PA showed an association with functional disability (≥2 ADLs) (OR 2.99 / 95% CI 2.14–4.18 p> 0.001).	Most centenarians are pre-frail and frail; Low PA level is the third most frequent frailty criteria; The low level of PA is higher in institutionalized centenarians and those with functional disabilities.

Legend: ≥100 = One hundred years or more; N = population; [n] = sample; \Diamond = male; Q = female; OR = Odds Ratio; ADLs = Activity Daily Life; FI = Frailty Index; FP = Frailty Phenotype; PA = Physical Activity; × = not included; ≥ = greater than or equal to.

last month). Muscle weakness was evaluated based on hand grip strength measured with a dynamometer and a value <12.2 kgf was defined as frailty. Fatigue was evaluated by the question "Do you feel full of energy?" derived from the short form of the Geriatric Depression Scale, and a negative answer was defined as fatigue. A reduction in walking speed was assessed by the 3-meter walk test (if necessary, a mobility aid was allowed) and the older adult was classified as frail when he/she could not take the test. Low PA was evaluated by the question "Do you perform any of the following activities: dancing, walking, rural work or gardening?" The older adult was classified as frail when he/she did not perform at least one activity. The frailty phenotype was classified in the studies of Duarte et al.²⁷ and Ribeiro et al.²⁹ as follows: frail (3 or more

criteria); pre-frail (1 or 2 criteria), and robust (not meeting any of the criteria).

Herr et al.²⁸ also evaluated frailty based on the five criteria ³, but the data were obtained with a standardized questionnaire applied by face-to-face interview (73.3%), telephone interview (14.5%), or mail (12.2%). A low level of PA was defined when the elderly person does not perform any regular exercise and/or outdoor activity and/or is unable to move from bed to chair without assistance (bedridden or unable)²⁸.

The studies of Gu et al.³⁰ and Dupre et al.³¹ assessed frailty using a frailty index (FI) proposed by the authors themselves. This index involves several items such as self-reported health status, cognitive state, disability, hearing and visual capacity, depression, heart

rate, and several chronic diseases. Physical activity was evaluated by the question "Do you exercise regularly?".

Table 1 shows the main results of the reviewed studies. Three studies²⁷⁻²⁹ reported the prevalences of the frailty criteria: low PA level (78% to 72.5%), weakness (84.2% to 66%), slow walking speed (77.6% to 48.4%), fatigue (43.8% to 42%), and weight loss (23.8% to 6%). In addition, approximately 95% of the centenarians were classified as frail and pre-frail in these studies. One study28 identified that 71.4% of frail centenarians live in nursing homes²⁷ and there was an association between low PA level and living in an institution (OR 1.58, 95%CI 1.12–2.23, p<0.001) and functional disability (≥2 ADL) (OR 2.99,95% CI 2.14-4.18, p>0.001). Ribeiro et al.29 also found a significant association (p<0.001) between frailty and functional status of centenarians and showed that frail older adults are more likely to have depression than pre-frail individuals (OR 3.92,95% CI 1.48-10.4, p<0.006).

Gu et al.30 observed that the FI varies according to age group and sex. A strong negative association was observed between FI and regular exercise when younger older adults were compared to centenarians both in women (65 to 79 years, OR 0.66, p<0.001; ≥100 years, OR 0.28, p<0.001) and men (65 to 79 years, OR 0.70, p<0.001; \geq 100 years, OR 0.23, p<0.001)³⁰ (Table 1). Dupre et al.³¹, investigating the FI (in quartiles) in male and female centenarians, also found that frailty varies according to sex and age group (female: 65 to 79 years - least frail 62.8/ most frail 3.7; ≥100 years – least frail 3.6/ most frail 48.2; male: 65 to 79 years – least frail 63.5/ most frail 8.2; ≥100 years – least frail 1.9/ most frail 22.8). Men exercised more than women but this practice decreased with increasing FI in men and women (least frail: male 51.5 / female 39.5; most frail: male 17.3 / female 6.7) (Table 1).

Evaluation of methodological quality

Concerning the methodological quality of the studies included in this review, four articles were classified as poor quality²⁷⁻³⁰ and one article as regular³¹ (Table 2). Regarding the domains of the

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checklist, most studies received low scores for internal validity and confounding variables. Only one study 31 scored in the selection bias domain. Regarding the power of the study, 60% of the studies included in this review scored in this domain^{28-30,31}.

DISCUSSION

This review showed that frailty increases with age²⁷⁻³¹ in men and women 30,31 and that women are frailer than men in all age groups³⁰. In addition, frailty is associated with the functional status of centenarians²⁷⁻²⁹ and frail older adults are more likely to have depression than pre-frail individuals²⁹.

Based on the frailty phenotype³, most centenarians in this review were classified as pre-frail and frail, i.e., the older adults met at least one physical frailty criterion in the assessments³²⁻³⁴. The prevalent phenotypic characteristics³ in centenarians were low PA level, weakness, and slow walking speed²⁷⁻²⁹. One study³⁵ identified low PA level and slowness as the two most common criteria among pre-frail and frail older adults. Neurological deterioration is a predominant characteristic of the centenarian population, which affects physical functions of the lower limbs, reducing muscle strength and gait speed and thus increasing the risks of physical frailty in adults older than 85 years of age³⁶.

Regarding scientific evidence on PA in centenarians, studies²⁷⁻²⁹ have identified a low level of PA in this population, particularly among older adults living in nursing homes^{27,28} who exhibit functional disability28 and are pre-frail and frail27-29. Concerning the low PA level of older adults who live in nursing homes and have functional disabilities^{27,28}, a review showed that 50% of individuals older than 80 years have muscle weakness or functional deficits and that 68% of them live in nursing homes³⁷. Institutionalized older adults are more dependent on ADLs than communitydwelling older adults³⁸. Taken together, the results show that

> 0 0 0 0 0

Internal validity External Reporting Internal validity - bias - confounding **Power** Total validity Study Quality (selection bias) score 10 12 13 22 23 24 25 27 15 16 19 20 Gu et al., 0 11 200930 Dupre 0 0 0 16 et al., Regular

Table 2: Summary of domain scores of the checklist for the evaluation of methodological quality (Downs and Black, 199823).

Poor

Ribeiro et al.. O 0 0 O 0 O 10 Poor 201829 Herr et al., 0 0 0 0 0 11 Poor 201828

Legend: #Item from 0 to 2 points

200931 Duarte et al.,

201427

0

09

Poor

advanced age is associated with frailty²⁷⁻³¹ and frail older adults have limitations in ADLs³⁵.

This review identified that both male and female centenarians with a higher FI exercise less than younger older adults. Regarding age group, a study involving older adults with a mean age of 74 years showed that high-intensity PA was associated with a lower risk of frailty and pre-frailty²¹. On the other hand, a study involving centenarians found that a higher FI was correlated with lower exercise participation, demonstrating that the participation in exercise decreases with advancing age, with a consequent increase in physical inactivity and frailty.

Concerning gender and exercise, this review found that male centenarians exercise more than females³¹. Studies indicate that the differences between genders are related to acquired risks, the responses of the immune system, and hormones³⁹⁻⁴¹. Furthermore, female centenarians are frailer than males³⁰, a fact that may explain why men exercise more than women. Given these findings, the practice of PA by older adults is important, even at an advanced age such as in centenarians since PA plays an important role in the prevention of frailty⁴² and depression⁴³. This review found that frail centenarians are more likely to have depression than pre-frail individuals. Within this context, the World Health Organization⁴³ recommends PA as part of the treatment of depression in people with an inactive lifestyle, as is the case of centenarians who exhibit a low level of PA.

Another aspect considered in this review is the method used to assess PA level. Analysis of the five studies demonstrated a lack of consensus since they evaluated this factor through indirect questions²⁷⁻³¹, adaptations of the original instrument²⁷⁻²⁹, and even considering functional disabilities in ADLs²⁸. It is necessary to highlight the difference between the concepts of PA and functional disability. Physical activity is any body movement produced by skeletal muscles that will result in energy expenditure greater than resting levels⁴⁴, while functional disability is the difficulty of an individual or need for support to carry out daily tasks⁴⁵. Further discussion and consensus are therefore necessary to define the most appropriate instrument for the assessment of PA in the oldest-old, giving priority to direct measures. For example, one study conducted on centenarians measured the PA level using a pedometer as a direct measure, which records the number of steps/day⁴⁶.

The selected studies were conducted in European (Portugal, France, Switzerland, Denmark, and Sweden) and Asian countries (China and Japan). A review⁴⁷ indicates that scientific evidence is limited for low- and middle-income countries and that frailty is an important aspect to be investigated considering its public health implications. Within this context, there is a lack of studies on frailty and PA conducted in developing countries, especially those involving the centenarian population.

The publication year of the reviewed articles started in 2009. It is believed that this period is related to the increase in the global

number of centenarians in the last decade¹ and to the need for investigations to better understand the characteristics of this population in terms of frailty²⁻⁻³¹ and active lifestyle⁴⁶. Another aspect to be highlighted is that the articles identified were observational studies. Studies involving the oldest-old are challenging and difficulties exist in recruiting them for epidemiological⁴⁶ and experimental studies. Hence, there is a need for further research on centenarians to explain the causes and effects of physical exercise on frailty so that more effective intervention strategies can be proposed for this population.

Concerning methodological quality, most of the reviewed studies²⁷⁻³¹ had a poor classification. This finding can be explained by the study design since all were observational studies, i.e., the studies scored low or not at all in the "internal validity – bias" and "confounding variable – selection bias" domains. We, therefore, recommend conducting experimental studies that can demonstrate the causal relationship between variables. Among the domains receiving the lowest scores, the "confounding variable – selection bias" domain was only addressed in the cohort study³¹. It is noteworthy that most studies are observational; however, they are not poor studies, only their scores are below those of experimental studies.

The strengths of this systematic review include the fact that no restrictions were imposed in terms of search period or main languages. However, experimental studies involving this population were found to be scarce. Therefore, one limitation of this study is the small number of included articles, which consequently does not allow for the performance of a meta-analysis. Furthermore, this small number of articles is due to the eligibility criteria used in this review, which prioritized studies that involved centenarians, demonstrating the scarcity of studies investigating frailty and PA in this population.

Conclusion

In summary, this review demonstrated that frailty increases with age and that most centenarians were classified as pre-frail and frail. The prevalent phenotypic characteristics were low PA level, weakness, and slow walking speed. Frailty is associated with the functional status of centenarians and frail older adults are more likely to have depression than pre-frail individuals. Most older adults with a low PA level live in nursing homes, have a functional disability, and are pre-frail and frail. Male and female centenarians with a higher FI practice less physical exercise than younger older adults and men exercise more than women.

Studies investigating frailty and PA in centenarians that have better methodological quality and that use robust and standardized assessment instruments are recommended. In addition, experimental studies that explore the causal relationship between these variables should be conducted.

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