Title: Frailty and physical fitness in elderly people: a systematic review and meta-analysis.

Short title: Meta-analysis on frailty and physical fitness in elderly people

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Abstract

Background: Frailty is an age-related condition that implies a vulnerability status affecting quality of life and independence of the elderly. Physical fitness is closely related to frailty, as some of its components are used for the detection of this condition.
Objectives. This systematic review and meta-analysis was conducted to investigate the magnitude of the associations between frailty and different physical fitness components and to analyse if several health-related factors can act as mediators in the relationship between physical fitness and frailty.
Methods. A systematic search was conducted of PubMed, SportDiscus, and Web of Science, covering the period from the respective start date of each database to March 2020, published in English, Spanish or Portuguese. Two investigators evaluated 1649 studies against the inclusion criteria (cohort and cross-sectional studies in humans aged ≥60 years old that measured physical fitness with validated tests and frailty according to the Fried Frailty Phenotype or the Rockwood Frailty Index). The quality assessment tool for observational cross-sectional studies was used to assess the quality of the studies.
Results. Twenty studies including 13527 participants met the inclusion criteria. A significant relationship was found between frailty and each physical fitness component. Usual walking speed was the physical fitness variable most strongly associated with frailty status, followed by aerobic capacity, maximum walking speed, lower body strength and grip strength. Potential mediators such as age, sex, body mass index or institutionalization status did not account for the heterogeneity between studies following a meta-regression.
Conclusions. Taken together, these findings suggest a clear association between physical fitness components and frailty syndrome in elderly people, being usual walking speed the most associated fitness test. These results may help to design useful strategies, to attenuate or prevent frailty in elders.
Systematic review registration. PROSPERO registration no. CRD42020149604 (date of registration: 03/12/2019)

Key points

1) Physical fitness components are strongly associated with frailty.
2) Usual walking speed is the physical fitness test most strongly associated with frailty status.

Declarations

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1. Introduction

The life expectancy of humans has continuously increased in most countries over the last century[1]. Nevertheless, there is a growing body of literature that recognizes that chronological age alone cannot account for the heterogeneity in structural, functional, and physiological changes associated to human ageing. It has been proposed that individuals with accelerated ageing are frail, and frailty itself can be detected, which can help in planning appropriate care and support[2,3].

The term "frailty" was first defined by Vaupel et al.[4] in 1979 as an actuarial concept that describes the unmeasured variability in the risk of death within individuals of the same age. Since then, scientific progress in frailty has possibly been retarded by the lack of consensus on its definition, which in turn has delayed the development of frailty screening, diagnostic tools and treatments.[5] Some progress, however, has been made in the last years. Among the available definitions, the World Health Organization (WHO)[1] defines frailty as "a progressive age-related decline in physiological systems that results in decreased reserves of intrinsic capacity, which confers extreme vulnerability to stressors and increases the risk of a range of adverse health outcomes."

The research on frailty biology began in 2001 when two scientific groups developed tools to quantify frailty in elders; the frailty index (FI) by Rockwood and Mitnitski[6] and the frailty phenotype (FP) by Fried and colleagues[7]. The number of tools for frailty detection in different populations has rapidly grown and more than twenty of them are currently available[8]. Even though there are wide differences between these tools, they all aim to detect vulnerable individuals at high risk for adverse outcomes related to a reduction of physiological compensation[9], such as disability, falls, worsening mobility, low quality of life, cognitive decline, hospitalization, nursing home admission or death[10].

Although the concepts differ, there is some common ground, as shown by the overlap in the variables for the identification of frailty[10]. One of these common links is the motor performance or physical fitness, related to the functional decline of the individuals and key markers for determining the risk of adverse outcomes[11,12].

In 1985, Caspersen[13] firstly defined being physically fit as "the ability to carry out daily tasks with vigor and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and to meet unforeseen emergencies". This definition was further refined to denote a set of attributes related to a person's ability to perform physical activities that require aerobic capacity, endurance, strength, or flexibility that is mostly determined by a combination of regular physical activity and genetically inherited ability[14].

Therefore, physical fitness is a multidimensional construct, operationalized as a set of measurable health- and skill-related attributes or components including cardiorespiratory fitness, muscular strength, flexibility, balance, agility (or dynamic balance) and walking speed[14]. All these components of physical fitness can be assessed by motor tests. It requires little time and provides information regarding activities associated with the daily living of elders[15].

There is a growing body of literature that identifies physical fitness as one on the main markers of health status at any age[14,16]. Health-related physical fitness, achieved through regular exercise and/or spontaneous physical activity, confers physiological and psychological benefits, and serves as a buffer against stress; all possible mechanisms that can protect against the development of stress-related disorders and chronic illness[17]. Studies over the past two decades have also provided important information on how physical fitness declines with age[18] and its association with cognitive impairment[19], physical dependence[20], institutionalization and death[21].

The study of the associations between frailty and physical fitness has recently gained the interest of the scientific community, however the real magnitude of these associations is not known yet.

Therefore, the present systematic review aims to 1) Describe the magnitude of the associations between frailty and different physical fitness components and 2) To analyse if several health-related factors can act as mediators in the relationship between physical fitness and frailty.

We hypothesized that all physical fitness components would be associated with frailty, and more specifically, that muscle strength will be the one with the strongest power of association. Our second hypothesis was that some health-related factors, such as age, sex and body mass index (BMI) might act as mediators in the magnitude of those associations.

2. Methods

This systematic review and meta-analysis was performed using the Cochrane handbook, the Conducting Systematic Reviews and Meta-Analyses of Observational Studies statements (COSMOS-E)[22] and following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[23] and the Meta-analyses Of Observational Studies in Epidemiology (MOOSE) [24]. The protocol was previously registered under the PROSPERO database (International Prospective Register of Systematic Reviews) with reference number CRD42020149604.

2.1. Data sources and search strategy

The electronic databases of PubMed (MEDLINE), SportDiscus and Web of Science were systematically searched covering the period from the respective start date of each database to March 2020. The first search in the three databases was carried out on September 2, 2019. Subsequently, two updates were made, on December 9, 2019 and March 7, 2020. The specific search strategy for PubMed was: ("Physical Fitness"[Mesh] OR "Physical Fitness" OR "Cardiorespiratory Fitness"[Mesh] OR "Cardiorespiratory Fitness" OR "Physical Functional Performance"[Mesh] OR "Physical Performance" OR "Muscle Strength"[Mesh] OR "Muscle Strength" OR "Postural Balance"[Mesh] OR "Postural Balance" OR Balance OR "Range of Motion, Articular"[Mesh] OR flexibility OR agility OR "Physical Endurance"[Mesh] OR "Physical Endurance" OR "Walking Speed"[Mesh] OR "Walking Speed") AND ("Frail Elderly"[Mesh] OR Frailty[Mesh] OR Frail*) AND ((English[lang] OR Portuguese[lang] OR Spanish[lang]) AND "aged"[Mesh Terms]). The search syntax included frailty and fitness-related terms and can be inspected in full in Electronic Supplementary Material Appendix S1.

The search was limited to English, Spanish and Portuguese languages and there was no restriction regarding the year of publication. Also, the search strategy was modified for each database, in order to maximize sensitivity. The search comprised the title, abstract and subject headings.

Additionally, the references of the included articles were checked to find potentially relevant studies. Two independent reviewers (DNV, AGC) screened the titles and abstracts of the articles and decided which of them needed further examination of the full text. Relevant articles were obtained in full and assessed against the inclusion and exclusion criteria described below. Inter-reviewer disagreements were resolved by consensus. Arbitration by a third expert reviewer was used for unresolved disagreements.

2.2. Inclusion criteria

The inclusion criteria were focused on the types of studies, participants and measures. 1) Types of study: Both cohort and cross-sectional studies were included. Randomized and non-randomized controlled trials were excluded from the present systematic review and meta-analyses; 2) Types of participants: humans aged ≥60 years old; 3) Types of measures: a) Physical fitness tested with validated field measurements or objective laboratory tests; b) Frailty status evaluated according to either the Fried Frailty Phenotype (FP)[7] or the Rockwood Frailty Index (FI)[25], which are both defined as diagnosis criteria.[8] 4) the results of the frail and non-frail subgroups should be reported independently.

2.3. Exclusion criteria

The following types of studies were excluded from the present review: 1) Studies in languages other than English, Spanish or Portuguese; 2) Unpublished studies, abstracts, dissertations, theses and book chapters; 3) Studies focusing exclusively on validating physical performance batteries to measure frailty; 4) Studies that focus in frail participants with a single specific pathology.

2.4. Operationalization of main concepts

Two tools have been proposed to measure frailty in this systematic review and meta-analysis.

The FI is based in a deficit accumulation approach. A count of deficits is taken, which are a collection of symptoms, signs, diseases, disabilities or test abnormalities. An increasing number of deficits raise the likelihood of being frail. It is expressed as the ratio between the actual number of deficits and the total possible number of deficits and is therefore a scalar measure ranging from 0 to 1. [25]

The FP was defined as a clinical syndrome in which three or more of the following criteria were present: unintentional weight loss (10 lbs / 4,5 kg in past year), self-reported exhaustion, weakness (measured by handgrip strength and adjusted for sex and body mass index), slow walking speed (adjusted for sex and standing height), and low physical activity. [7]

Physical fitness, a concept also referred to as physical capability or physical functioning, is an umbrella term defined as the ability to carry out daily tasks with alertness and vigor, without undue fatigue, and with enough energy reserve to meet emergencies or to enjoy leisure-time pursuits. [13] The physical fitness components included in the meta-analysis and their tests are explained in the Electronic Supplementary Material Appendix S2.

2.5. Risk of Bias Assessment

Each selected study was assessed for risk of bias (RoB) according to the 6 domains described in the COSMOS-E [22] and the risk of bias instrument for non-randomized studies of exposures[26]. The six RoB items were: 1) Bias due to confounding, 2) Bias in the selection of participants into the study, 3) Bias in the classification of exposures, 4) Bias due to missing data, 5) Bias in the measurement of outcomes, and 6) Bias in the selection of reported results. The researchers evaluated the studies and determined their RoB by responding to signaling questions from each of the six RoB items previously listed. The summary of the RoB results for all the included studies is presented in Table 1, whereas the complete details of the evaluation are available in Electronic Supplementary Material Appendix S3.

2.6. Meta analyses, sensitivity analyses, and meta regression analyses

Five separate random effects meta analyses were performed with those physical fitness variables for which the effect size could be calculated from the reported results in at least three different studies. This was possible for the following fitness variables: handgrip strength, lower body strength, usual walking speed, maximum walking speed and aerobic capacity. The meta-analyses were only performed with the results of FP scale, because only four studies report the FI with different fitness components and also it could be a potential source of bias. Group comparisons were performed calculating the Cohen's d effect size, using the frail group as the reference group. Additionally, heterogeneity between studies was assessed by I^2 statistics.

Independent variables potentially associated with physical fitness and frailty (age, sex distribution and BMI) were included as predictors in binomial meta-regression models. Analyses were performed with the R statistical programming language (version 3.6.1) using the 'metafor' package[27].

3. Results

3.1. Search summary

Fig. 1 shows the study selection process. The initial searches identified 1822 potentially relevant articles in the consulted databases and 7 additional articles were identified through reference lists. Following the review of titles and abstracts and the removal of duplicates, the total was reduced to 61 potentially relevant articles for inclusion. Of these articles, 20 met the selection criteria and were included in this systematic review and 14 of them in the meta-analysis. The 41 excluded articles are shown in the Electronic Supplementary Material Appendix S4 with their exclusion criteria.

3.2. Summary of study characteristics

From the twenty included studies (Table 2), those conducted in developing countries were predominant (n=13; 54%). Brazil presented a noteworthy number of studies on the topic (n=6; 25%), followed by the USA (n=4; 17%). Great differences in the sample size of the included studies were observed, ranging between 26 and 6560 participants.

The main characteristics of the individual studies included in this review are summarized in Table 2. The included studies differed with respect to the physical fitness components evaluated, therefore the individual study results were included in eleven separated tables (from Tables 3-14).

3.3. Risk of bias in studies

Risk of bias assessments for each study are presented in Table 1. All of them were judged to be at "Moderate" or "Serious" overall risk of bias. These judgments were largely due to the 'Bias due to confounding', 'Bias in selection of participants into the study', and 'Bias in selection of reported results' domains. These domains are mainly associated with the non-reporting of the confounding variables, the selection method and the unadjusted estimates and cofounders (adjusted estimates and their precision).

3.4. Muscle strength and frailty status

A total of thirteen studies reported measurements of muscle strength (Tables 3-6). Overall, low muscle strength values were significantly associated with presence of frailty. However, there were some differences depending on the specific test of muscular strength used or depending on the particular muscle region tested.

3.4.1 Dynamic strength

A total of eight studies were focused on lower body strength (Table 3). The meta-analysis of the association of frailty status and lower body strength was statistically significant with a high effect size (SMD -0.97, CI -1.41, -0.52, p< 0.01, significant heterogeneity, I^2=91%, p<0.01) (Figure 2). This suggests that belonging to the frailty group is associated with lower values of leg strength.

Theou et al.[28] used the FI and the 30-second fitness test. This study was not included in the meta-analysis due to the use of FI as a continuous variable. The results of this study showed that this leg strength test is highly correlated with the FI score (r=-0.62; p<0.001). The analysis of lower-limb muscle strength among frailty tertiles revealed great differences between the lowest tertile and both the highest tertile (SMD=-2.64) and the intermediate one (SMD=-1.18). In this case there were also significant differences between the intermediate and the highest tertile (SMD=-1.19).

According to Batista et al.[29], low scores of lower-limb muscle strength were correlated with a greater rate of participants presenting three or more frailty criteria. Specifically, this variable was significantly associated with the criteria of decreased walking speed (p<0.001) and reduced grip strength (p<0.05).

Regarding dynamic upper body strength (Table 4), Furtado et al.[30] found an inverse and moderate association with frailty (r=-0,617; p=0,001), using the FP as a score (1-5). Similarly, Theou et al.[28] found a moderate inverse correlation (r=-0.44, p=0.001) between frailty and arm curl in women.

3.4.2 Handgrip strength

Ten studies analyzed the association of frailty status and handgrip strength (Figure 3). The meta-analysis showed that non-frail elders had higher mean values (+4.8 Kg) compared to the frail ones (SMD -0.60, CI -0.78, 0.42, P< 0.01, significant heterogeneity, I^2=88%, p<0.01).

FI (Table 5) is also significatively related to handgrip strength in both dominant (r=-0.37, p=0.007) and non-dominant hand (r=-0.51, p<0.01). Differences in handgrip strength were found between the lowest and intermediate tertiles (SMD Non dominant=1.15, SMD Dominant=0.99) and between lowest and highest tertiles (SMD Non dominant=2.15, SMD Dominant=1.77).[28]

3.4.3 Other muscular isometric strength tests

Two studies[28,31] investigated the relationship between frailty and isometric strength in several muscle groups. Both studies measured the maximal isometric knee extensors strength, concluding that frail subjects showed significantly lower levels of strength. Likewise, in the FI tertiles, a significant difference was found between the lowest and highest frailty tertile groups (SMD = -1.53).

Moreover, Buckinx et al.[31] studied the association of frailty with other muscle groups, specifically knee flexors, ankle flexors, ankle extensors, hip abductor, hip extensors, elbow flexors and elbow extensors. These authors found that robust elderly had significantly higher values in all these tests compared with pre-frail and frail ones (Table 6).

3.5. Balance and frailty status

Four studies included results about the association between frailty status and static balance, measured with different protocols (Table 7). This methodological variability hindered the quantitative analysis of the results.

Tay et al.[32] used the side-by-side, semi-tandem and full-tandem standing tests from the Short Physical Performance Battery (SPPB) to assess the static balance. The authors concluded that prefrail/frail participants had significantly poorer static balance than robust ones only in the full-tandem test. In relation to the studies that used platforms, Kang et al.[33] described that the instability of the center of pressures (CoP), calculated as the root mean square of the deviations from the neutral position, was statistically higher in frail individuals. Moreover, they described a new index (C1) that summarizes the complexity of balance dynamics. This C1 index during quiet stance was also independently associated with frailty status ($p=0.017$). In the other CoP variables, the frail group showed similar oscillations and velocity when compared with the non-frail and prefrail groups.

In relation to dynamic balance or agility, all seven studies found a worse balance in the frail elderly compared with the non-frail groups (Table 8). Moreover, Theou et al.[28] showed that this variable is highly related with an increase of the FI score ($r=0.61$; $p<0.001$). Also, an analysis of the dynamic balance differences among frailty tertiles revealed great differences (all<0.05) between the lowest tertile and both the highest (SMD=-2.15) and the intermediate tertiles (SMD=-1.66).

Finally, three studies measured balance with mixed scales that include static and dynamic balance: Tinetti test[31], Berg Balance Scale[34] and BESTest[35] (Table 9). All of them concluded that a worst score in the scale is significantly associated with the frailty status.

3.6. Flexibility

In total, three studies analyzed the association between flexibility and frailty status using the flexibility tests reported by Rikli and Jones[36].

Tables 10 and 11 show the contradictory results reported for this fitness variable. Furtado et al.[30] reported significant differences between robust, prefrail and frail groups, both in lower and upper body flexibility. Similarly, Chang et al.[37], found that non-frail elderly had higher values of upper body flexibility than the frail group. Nevertheless, Tay et al.[32] did not find this association in upper nor lower body flexibility.

3.7. Walking speed

A total of fourteen sets of results (from twelve studies) analyzed the association between walking speed and frailty status (Tables 12-13).

Figure 4 shows the meta-analysis, including ten studies, of the association between frailty status and usual walking speed. The frailty group showed lower values of usual walking speed in comparison with the non-frail group (SMD -1.11, CI -1.52, 0.70, P< 0.01, significant heterogeneity, I^2=95%, P<0.01). Only one study reported non-significant differences [34].

In relation with FI, Theou et al.[28] determined that usual walking speed had the strongest correlation with FI (r=-0.80, p<0.01) among all the physical fitness tests. In the same way, walking speed is one of the performance measures that declined the most between all the tertiles (SMD lowest vs intermediate: -1.60; intermediate vs higher: -1.75 and lowest vs higher: -3.33). In this sense, Jung et al.[38] also concluded that FI is associated with usual walking speed either unadjusted (β = -0.589, P , 0.001) or after adjustment by age and sex (β = -0.534, P = 0.001). This study also associated usual walking speed to every item of the FP. Specifically, the exhaustion (β = -0.085, P = 0.001) and grip strength (β = -0.310, P= 0.001) items were associated with walking speed when the slow walking speed item was not included in the regression analysis.

The association between maximal walking speed and frailty was analyzed in 4 studies (Table 13). From three studies, the metanalysis (Figure 5) showed a statistically significant difference between frailty categories with a high effect size (SMD -0.97; 95% CI -1.25, -0.68, p< 0.01, non-significant heterogeneity, I^2=0%, p=0.55). As in usual walking speed, Theou et al.[28] found that maximum walking speed had a strong correlation with FI (r=-0.69, p<0.01) and varied significantly between all tertiles (SMD lowest vs intermediate: -1.43; intermediate vs highest: -1.82 and lowest vs highest: -3.21).

3.8. Aerobic capacity

Three studies analyzed the association between aerobic capacity and FP status (Table 14). Figure 6 displays the meta-analysis of this association, which showed a significant difference between the two groups, with a high effect size (SMD -1.01, CI -1.64, -0.38, P< 0.02, significant heterogeneity, I^2=75%, P<0.02). The heterogeneous results between Bastone et al.[39] and the other two studies can be explained by the differences in the selected protocols to measure the aerobic capacity. Tay et al.[32] and Langlois et al.[40] investigated this relationship using the 6-minute aerobic test (6MWT)[36], while Bastone et al.[39] implemented an incremental shuttle walk maximal test and measured maximal walking distance (included in the meta-analysis), peak oxygen consumption (VO^2peak), maximum heart rate and respiratory exchange ratio. In this sense, VO^2peak was also significantly associated with frailty, as the non-frail group presented a mean of 18.4 mL/kg/min and the frail group a mean of 13.7 mL/kg/min. In contrast, there were no significant differences in maximum heart rate or respiratory exchange ratio between the different frailty status groups.

3.9. Overall findings

Figure 7 presents a summary of the differences found between frailty categories for each fitness component analyzed. Taken together, these results suggest that all physical fitness tests are clearly associated with frailty status, with the usual walking speed being the physical fitness variable with a highest association with the frailty syndrome, followed by aerobic capacity, maximum walking speed, lower body strength and grip strength, respectively.

3.10. Heterogeneity in health-related factors

The I^2 statistic quantifies the amount of variation between studies that cannot be attributed to chance.[41] Most I^2 values obtained in the meta-analyses performed in this systematic review are considered high.

However, this high heterogeneity in the meta-analyses presented in this review could be due to differences in participant characteristics among the individual studies. Nevertheless, the characteristics included in the meta-regression (age, sex distribution, BMI and institutionalization status) could not explain this heterogeneity. Other health factors or environmental determinants of health such as cognitive impairment, comorbidity or plurimedication may have contributed to the increase of heterogeneity but these variables were not included in the studies.

4. Discussion

To the best of our knowledge, the present systematic review and meta-analysis is the first one that quantifies the association between physical fitness and frailty. Specifically, we tested the hypothesis that non-frail individuals would have better physical fitness than frail ones in every physical performance characteristic. Following the analysis of twenty studies, we found strong support for the acceptance of our hypotheses.

One of the most significant findings that emerged from this systematic review was that usual walking speed is the physical fitness component most closely associated to frailty, which partially contradicts the initial hypotheses that muscle strength will be the one with the strongest power of association. In addition, the frailty-associated decline of strength is steeper in dynamic lower body strength than in isometric handgrip strength.

All studies described an association between the different measures of body strength and frailty status. The results of the current meta-analysis found a larger difference between groups (frailty versus non-frailty status) in the lower body strength compared with the isometric grip strength. This could be explained by the relationship between functional independence and lower-limb muscle strength present at different frailty levels[42], which has been found to be more associated with frailty than grip strength. A possible reason for this difference could be connected with the fact that the daily activities do not require maximal effort, but rather sustained submaximal effort [20,28]. These results are in agreement with findings by Theou et al.[28], which showed that muscular endurance was a better predictor of frailty (strongly correlated with FI) than maximum muscular isometric and isotonic strength. In this sense, other studies have also found that lower muscle strength can be a better predictor of outcomes than handgrip strength[43]. However, other studies have supported that handgrip strength is an indispensable biomarker for identifying older adults at risk of poor health status[44]. Likewise, Batista et al.[29] showed that elderly people with signs of decreased walking speed and reduced grip strength presented lower scores for lower-limb muscle strength. They concluded that an evaluation of elderly individuals using only this test could simplify and quicken the categorization of patients at risk of frailty. However, according to our results, not only handgrip strength but also lower muscle strength are good biomarkers for the prediction of frailty risk.

Regarding balance, taking together the studies included in this systematic review, there is a frailty-associated decline in static and dynamic balance. It seems that balance measures like the Timed Up and Go test, SPPB-balance test or mixed balance tests (Tinneti, Berg Scale or BESTest) can discriminate between frail and non-frail groups classified by FP. Similarly, two studies[28,32] using the FI scale found a moderate deterioration in balance within the frail group. In contrast, there are contradictory results among the three articles that studied CoP variables and their association with FP. These results are an example of the contradictory scientific literature regarding the CoP. The latest literature review confirmed that CoP instability measures, such as the range of body sway and its velocity, increase with age[45]. Nonetheless, some authors like Maki et al.[46] found no differences in postural sway between older fallers and non-fallers, in opposition to others that indicated that there is a relationship between fall risk and CoP measures, especially in outdoor fallers (Pajala et al.[47]) and recurrent fallers (Melzer et al.[48]). This heterogeneity is probably due to the limited number of studies and the different measurement protocols.

As explained in the results, it is difficult to draw a clear conclusion regarding the relation between flexibility and frailty due to the small number of studies focusing on this topic. However, two of the available studies found significant differences between frail and non-frail groups. These findings differ from those by Tay et al.[32] who did not observe differences between groups, although these results need to be interpreted with caution, given that because the frail and prefrail groups were combined together. Globally, these heterogeneous studies could corroborate the ideas of Nuzzo JL[49] , who suggested that flexibility could be excluded as a major component of physical fitness, due to the limited predictive or concurrent validity in terms of health outcomes (e.g., mortality, falls, occupational performance), particularly when viewed in light of the other major components of fitness (i.e., body composition, cardiovascular endurance, muscle strength).

Usual walking speed is also a diagnostic criterion of frailty in both the FP and FI scales and it is therefore highly correlated with frailty. Nevertheless, there are some particular differences among gait variables and studies. Firstly, our meta-analysis shows that maximum walking speed is significantly associated with frailty status, but also that differences between groups in usual walking speed are greater. More specifically, Theou et al.[28] showed a higher correlation with the FI in preferred walking speed than in maximum walking speed. A possible explanation for this phenomenon might be that, as showed by Shinkai et al.[50], maximum walking speed is more sensitive when predicting the onset of functional dependence among younger people (<75 years), whereas usual walking speed is more sensitive among older people (≥75 years). Another previous study reported that usual walking speed, which is related to muscle quality, may play a mediating role between sarcopenia and dependence, given the association of the usual walking speed test with the daily-living walking speed.[51] Finally, one of the studies included in the meta-analysis reported non-significant differences between groups, probably because of the selected test. On this regard, most studies measured the usual walking speed on the floor, while Vieira et al.[34] did so on an instrumented mat.

The relation between aerobic capacity and frailty status seems to be confirmed in our meta-analysis. Notably, the aerobic capacity measured with a maximal incremental shuttle walk test seems to have a stronger association with frailty status than aerobic endurance measured by the 6-minute aerobic test from the Senior Fitness Test. There has been controversy about the physiological responses to the 6MWT, which has been described as both a maximal and a submaximal test for the elderly people.[52] Kern et al.[52] found that only 58% of their elderly patients fulfilled the criteria for maximal effort in the 6MWT. In addition, Bastone et al.[39] described a frailty-associated decline of peak VO^2. These results are consistent with those of Jackson et al. [47] who associated a peak VO^2 of 18 mL/kg/min with independent living as well as with those of Pulz et al.[54] who proposed a cut point of 15mL/kg/min as a key threshold for disability assessment.

Having discussed how physical fitness is associated to frailty, the second hypothesis considered the potential effect of other health-related factors, which could explain heterogeneity. It is somewhat surprising that no health-related factor (age, sex, institutionalization and BMI) could explain this heterogeneity and therefore they could not explain the magnitude of that association. Probably other health-related factors like chronic disabilities or cognitive impairment could explain this heterogeneity as shown by Bastone et al.[39]. For this reason, the summaries of estimates of our meta-analyses, which are an average of estimates across different populations should be considered with caution.

4.2 Study limitations

Our study has several potential limitations. Firstly, this meta-analysis is limited by the compromised study quality, given that all studies were judged to be at "Moderate" or "Serious" overall risk of bias. This aspect limits the strength of the conclusions and may lead to an overestimation of the observed associations. Secondly, heterogeneity was significant in the analyses of muscle strength, walking speed and aerobic capacity, probably because of the wide range of the health characteristics of the study samples. Finally, the difficulty encountered when trying to assess the prefrail group separately can also be a limitation since some studies decided to merge this group with the frail one.

4.3. Future perspectives

There are still many unanswered questions regarding the relationship between frailty and health-related physical fitness components. Further research should be undertaken to investigate the health-related factors that mediate the relationship between frailty and physical performance. An interesting topic for future research would be the potential mediation of cognitive impairment in the participant's understanding of the physical fitness tests. Also, in future research, it could be interesting to investigate different balance and aerobic capacity assessment protocols and the clinical and economic implications of using these physical fitness tools.

5. Conclusions

This systematic review and meta-analysis shows the associations between physical fitness components and the frailty syndrome. Body strength, balance, walking speed and aerobic capacity are clearly associated with frailty. These findings support the importance of usual walking speed as the physical fitness test that is most strongly associated to frailty status, followed by aerobic capacity, maximum walking speed, lower body strength and grip strength. These results may help to design useful strategies, as specific training programs, to attenuate or prevent frailty in elders. Age, sex, body mass index and institutionalization status cannot explain the heterogeneity found between studies; therefore, future research should establish the health-related factors that can mediate in the relationship between fitness and frailty status.

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Conflicts of Interest

David Navarrete-Villanueva, Alba Gómez-Cabello, Jorge Marín-Puyalto, Luis Alberto Moreno, Germán Vicente-Rodriguez and José Antonio Casajús declare that they have no conflicts of interest relevant to the content of this review.

Authorship Contributions

All authors contributed to the study conception and design. The literature search and data collection were performed by DNV and AGC. The data analysis was performed by DNV and JMP. The first draft of the manuscript was written by DNV and all authors critically revised and commented on the original manuscript. All authors read and approved the final manuscript.

Data availability

The authors declare that the data supporting the findings of this study are available within the article.

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Table 1 Risk of bias assessments of studies of the effects of frailty on physical fitness in elderly people

Studies	Bias due to counfunding	Bias due to selection of participants	Bias in classification of exposure (physical fitness)	Bias doe to missing data	Bias in measurement of outcomes (frailty)	Bias in selection of reported results	Study-level RoB Judgment
Kang et al. [33]	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Verghese and Xue [54]	Low	Serious	Low	Moderate	Low	Serious	Serious
Theou et al. [28]	Moderate	Serious	Low	Moderate	Low	Moderate	Serious
Montero-Odasso et al. [55]	Low	Serious	Low	Moderate	Low	Moderate	Serious
Langlois et al. [40]	Moderate	Moderate	Low	Low	Low	Serious	Serious
Batista et al. [29]	Serious	Serious	Low	Moderate	Low	Serious	Serious
Chang et al. [37]	Serious	Low	Low	Moderate	Low	Serious	Serious
Curcio et al. [56]	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Bastone et al. [39]	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Buckinx et al. [16]	Low	Serious	Low	Low	Low	Moderate	Serious
Furtado et al. [30]	Moderate	Low	Low	Low	Low	Low	Moderate
Marques et al. [35]	Serious	Moderate	Low	Moderate	Low	Moderate	Serious
Vassimon-Barroso et al. [57]	Serious	Low	Low	Moderate	Low	Serious	Serious
Vieira et al. [34]	Serious	Moderate	Low	Moderate	Low	Serious	Serious
Jung et al. [38]	Serious	Moderate	Low	Moderate	Low	Moderate	Serious
Meng et al. [58]	Low	Serious	Serious	Moderate	Low	Low	Serious
Tay et al. [32]	Moderate	Serious	Low	Moderate	Low	Moderate	Serious
Martins et al. [59]	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate
Jansen et al. [60]	Low	Moderate	Low	Moderate	Low	Moderate	Moderate
Chaudhary and Chowdhary [61]	Moderate	Low	Low	Moderate	Low	Moderate	Moderate

Fig 1. Flow diagram of the literature search and study selection for the meta-analysis.

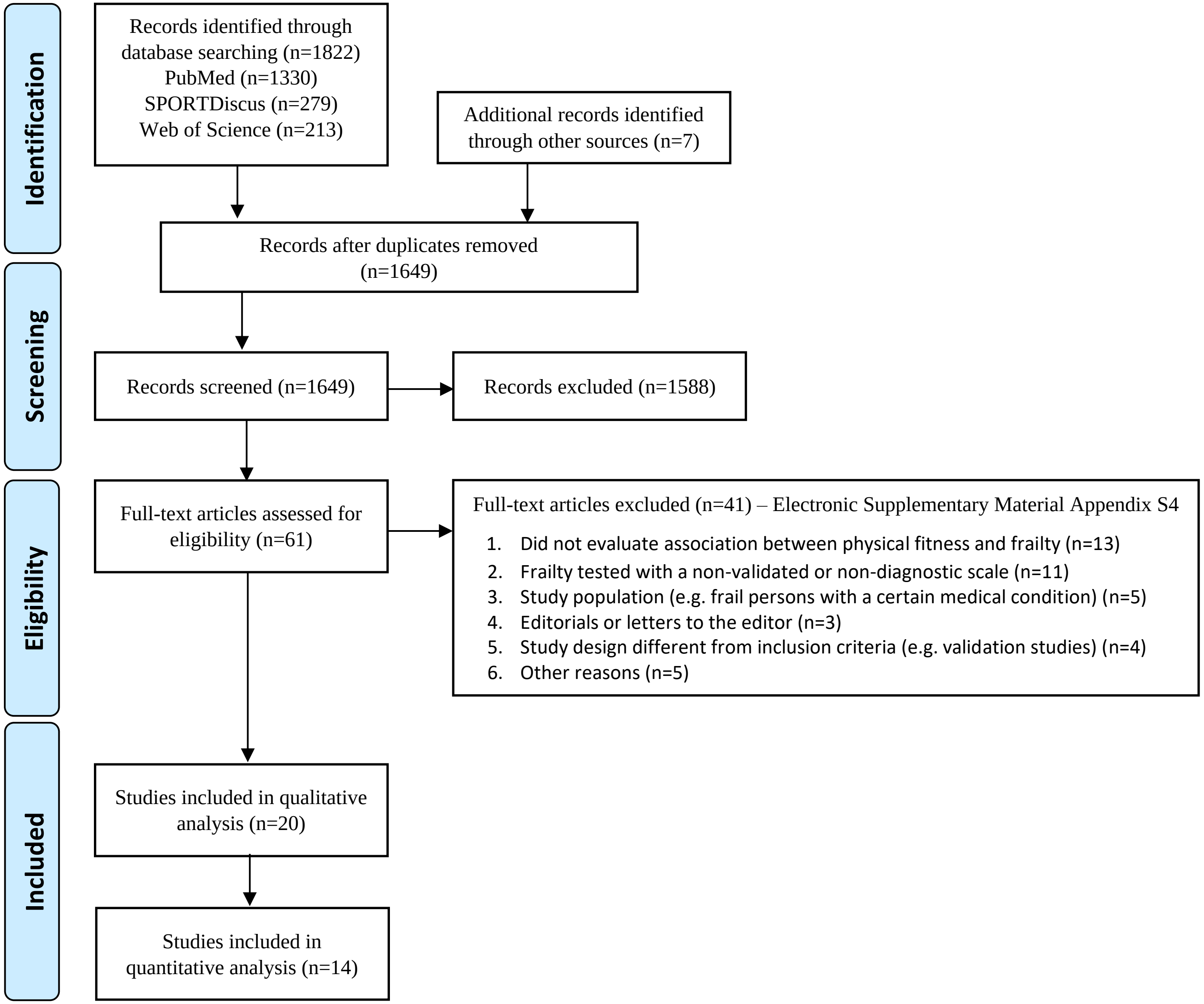

Table 2. Characteristics of the studies								
Study	**Country**	**Number of participants**	**% women**	**Age (years)**	**BMI (kg/m²)**	**Frailty Scale**	**% frail**	**Physical fitness outcomes**
Kang et al. [33]	USA	550	32.7	77.5 ± 5.5	27.2 ± 5.1	FP	9.0	MS, Bal, WS
Verghese and Xue [54]	USA	539	60.5	80.1 ± 5.2	NR	FP	19.7	MS, WS
Theou et al. [28]	Greece	53	100	76.4 ± 5.4	NR	FI	NR	MS, Bal, WS
Montero-Odasso et al. [55]	Canada	100	78	82.0 ± 5.4	26.3 ± 4.5	FP	20.0	WS
Langlois et al. [40]	Canada	83	78.3	72.1 ± 5.8	NR	FP	47.0	MS, Bal, WS, AC
Batista et al. [29]	Brazil	150	64.2	NR	NR	FP	55.3	MS
Chang et al. [37]	China	234	29.5	70.7 ± 8.4	23.5 ± 3.3	FP	39.4	MS, Bal, Flex
Curcio et al. [56]	Colombia	1878	52.2	70.9 ± 7.4	24.4 ± 4.5	FP	12.2	MS, WS
Bastone et al. [39]	Brazil	26	50	75.5 ± 6.5	25.7 ± 5.8	FP	50.0	AC
Buckinx et al. [16]	Belgium	662	72.5	83.2 ± 9.0	25.9 ± 5.5	FP	25.1	MS, Bal, WS
Furtado et al. [30]	Portugal	119	100	82.0±7.9	28.5 ± 5.0	FP	45.4	MS, Bal, Flex, WS, AC
Marques et al. [35]	Brazil	60	0	NR	27.8 ± 5.1	FP	33.3	Bal
Vassimon-Barroso et al. [57]	Brazil	42	62	77.1 ± 6.4	27.7 ± 5.1	FP	28.6	Bal
Vieira et al. [34]	USA	63	66.7	75.0 ± 7.0	29.5 ± 5.2	FP	NR	Bal, WS
Jung et al. [38]	Korea	1,348	55.5	75.7 ± 6.2	NR	FI	NR	WS
Meng et al. [58]	China	101	0	79.4 ± 7.7	NR	FP	12.9	MS, Bal, WS
Tay et al. [32]	Singapore	135	71.1	69.0 ± 7.4	25.4 ± 5.1	FI, FP	NR	MS, Bal, Flex, WS, AC
Martins et al. [59]	Japan	712	53.6	69.4 ± 4.5	22.5 ± 2.7	FP, FI, KCL	13.5	MA, WS
Jansen et al. [60]	Germany	112	80.4	78.8 ± 8.0	27.7 ± 6.0	FP	17.0	WS
Chaudhary and Chowdhary [61]	India	6560	49.5	NR	20.5 ± 5.3	FP	20.0	MS

Notes: **MS:** Muscle Strength, **Bal:** Balance, **Flex:** Flexibility, **WS:** Walking Speed, **AC:** Aerobic Capacity, **FP:** Frailty Phenotype, **FI:** Frailty Index, **KCL:** Kihon Checklist, **NR:** Not Reported. Values of continuous variables are expressed as mean ± standard deviation.

Table 3. Dynamic lower body strength according to frailty status

Study	Measurement	Cut points	Robust	Prefrail	Frail	p
			Non-Frail			
Kang et al. [33]	**5TC** (s)		11.1 ± 2.2	14.3 ± 3.9	18.3 ± 4.6	0.001
			12.43 ± 3.02			
Chang et al. [37]	**CS** (times)		12.9 ± 5.5		9.4 ± 6.1	<0.001
Curcio et al. [56]	**2TC** (s)		1.24 ± 0.28	1.54 ± 0.78	2.24 ± 1.32	0.001
			1.42 ± 0.63			
Meng et al. [58]	**5TC** (s)		1.05±0.29	0.90±0.39	0.66±0.39	<0.001
			0,94 ± 0,36			
Tay et al. [32]	**5TC** (s)		10.5 (8.3-12.3)	12.36 (9.7-16.6)		0.003
	CS (times)		14.4 ± 4.9	12.4 ± 3.7		0.036
Furtado et al. [30]	**CS** (times)		11 (10;12)	9 (7;11)	6 (5;8)	<0.001
Study	**Measurement**	**Cut points**	**Non-Frail**		**Frail**	**p**
Batista et al. [29]	**5TC (%)**	> 60 s	30.8		69.2	0.01
		60 - 16.7 s	40.6		59.4	
		16.69 - 13.7 s	64.3		35.7	
		< 13.69 s	78.6		21.4	
Study	**Measurement**		**Highest FI tertile**	**Intermediate FI tertile**	**Lowest FI tertile**	**r, p**
Theou et al. [28]	**CS** (s)		13.4±2.7	9.9±3.0*	6.7±2.3 *,†	-0.62, <0.001

r: partial correlation coefficients adjusted for age; **5TC**: five-times chair stand test; **2TC:** two-times chair stand test; **CS:** chair stand test (30s); **FI:** Frailty Index (Rockwood). The results were reported as mean ± standard deviation or as median (interquartile range).* Significantly different from the highest FI tertile, p ≤ 0.05 † Significantly different from the intermediate FI tertile, p ≤ 0.05

Table 4. Dynamic upper body strength according to frailty status

Study	Measurement	Robust	Prefrail	Frail	p
Furtado et al. [30]	**AC** (times)	13 (11;15)	11 (9;14)	9 (7;11)	P=<0.001
Study	**Measurement**	**Highest FI tertile**	**Intermediate FI tertile**	**Lowest FI tertile**	**r, p**
Theou et al. [28]	**AC** (times)	16.5±3.3	14.2±5.1	9.9±3.7*,†	–0.44, 0.001

r: partial correlation coefficients adjusted for age; **AC:** arm curl test; **FI:** Frailty Index (Rockwood). The results were reported as mean ± standard deviation or as median (interquartile range).* Significantly different from the highest FI tertile, p ≤ 0.05 † Significantly different from the intermediate FI tertile, p ≤ 0.05

Table 5. Handgrip strength according to frailty status						
Study	**Measurement**	**Hand measured**	**Robust**	**Prefrail**	**Frail**	**p**
			Non-Frail			
Verghese and Xue [54]	**HG** (kg)	Dominant hand	24.1±7.5		20.2±6.1	<0.001
Langlois et al. [40]	**HG** (kg)	Dominant hand	20.13±7.8		17.48±7.84	>0.05
Chang et al. [37]	**HG** (kg)	Right hand	24.1 ± 8.6		19.8 ± 9.1	<0.001
Curcio et al. [56]	**HG** (kg)	Dominant hand	25.8 ± 6.4	21.1±6.9	15.25±5.44	<0.001
			22.95 ± 6.7			
Buckinx et al. [16]	**HG** (kg)	The best of both hands	27.9 ± 16.6	18.1 ± 9.2	14.1 ± 6.68	<0.0001
			20.06 ± 10.7			
Meng et al. [58]	**HG** (kg)	Not defined	34.75 ± 4.21	26.49±6.6	23.37±5.15	<0.001
			28.84 ± 5.96			
Tay et al. [32]	**HG** (kg)	The best of both hands	23.8 ± 6.7	22.8 ± 8.2		0.517
Martins et al. [59]	**HG** (kg)	Dominant hand	29.5±8.3	28.8±8.2	26.5±6.9	0.135
			29.19 ± 8.26			
Chaudhary and Chowdhary [61]	**HG** (kg)	Not defined	26.07± 8.39	21.1± 10.8	14.78±11.0	NR
			22.7 ± 10.1			
Study	**Measurement**	**Hand measured**	**Highest FI tertile**	**Intermediate FI tertile**	**Lowest FI tertile**	**r, p**
Theou et al. [28]	**HG** (kPa)	Dominant hand	57.8±10.9	46.4±12.0*	38.4±10.9*	-0.37, 0.007
		Non-dominant hand	54.9±10.1	43.3±10.0*	31.4±11.6*,†	-0.21, 0.132

Notes: **r**: partial correlation coefficients adjusted for age**; HG:** Hand Grip Strength; **FI:** Frailty Index (Rockwood). The results were reported as mean ± standard deviation or as median (interquartile range). **NR:** Not reported.

* Significantly different from the highest FI tertile, $p \leq 0.05$ † Significantly different from the intermediate FI tertile, $p \leq 0.05$

Table 6. Other isometric or isotonic strength tests according to frailty status					
Study	**Measurement**	**Robust**	**Prefrail**	**Frail**	**p**
Buckinx et al. [16]	**IM: Knee flexors** (N)	108.9 ± 44.0	88.4 ± 35.8	68.1 ± 36.2	<0.0001
	IM: Knee extensor (N)	136.4 ± 52.3	103.6 ± 52.5	79.9 ± 41.1	0.0004
	IM: Ankle flexors (N)	100.2 ± 54.6	74.3 ± 34.5	64.1 ± 88.6	<0.0001
	IM: Ankle extensors (N)	113.7 ± 45.5	90.2 ± 55.7	70.3 ± 32.1	<0.0001
	IM: Hip abductors (N)	104.6 ± 39.9	73.1 ± 36.1	45.5 ± 35.9	<0.0001
	IM: Hip extensors (N)	111.7 ± 46.0	78.3 ± 43.9	45.1 ± 38.2	<0.0001
	IM: Elbow flexors (N)	116.2 ± 49.8	90.7 ± 38.3	72.4 ± 32.5	<0.0001
	IM: Elbow extensors (N)	81.5 ± 36.8	63.9 ± 27.6	52.6 ± 23.2	<0.0001
Study	**Measurement**	**Highest FI tertile**	**Intermediate FI tertile**	**Lowest FI tertile**	**r, p**
Theou et al. [28]	**IM: Knee extensors** (N)	27.2±7.0	22.5±5.9	18.2±4.5 *,†	-0.45, 0.001
	IT: Knee extensors (N)	9.8±2.2	8.5±2.1	6.2±1.2 *	-0.51, <0.001

Notes: **r**: partial correlation coefficients adjusted for age; **IM:** Isometric strength; **IT:** Isotonic strength; **FI:** Frailty Index (Rockwood). The results were reported as mean ± standard deviation or as median (interquartile range).

* Significantly different from the highest FI tertile, p ≤ 0.05 † Significantly different from the intermediate FI tertile, p ≤ 0.05

Table 7. Static balance according to frailty status					
Study	**Measurement**	**Robust**	**Prefrail**	**Frail**	**p**
Tay et al. [32]	**SPPB-BT: Side by side** (n>10s - %)	96 - 99	32 - 97		0.445
	SPPB-BT: Semi-tandem (n>10s - %)	96 - 99	32 - 97		0.267
	SPPB-BT: Tandem (n>10s - %)	84 - 86.6	22 - 66.7		0.036
Vassimon-Barroso et al. [57]	**CoP- Amplitude$_{AP}$** (mm)	21.71 ± 7.27	24.55 ± 8.01	24.03 ± 7.02	NR
	CoP- Amplitude$_{ML}$ (mm)	11.61 ± 4.71	12.12 ± 5.61	12.42 ± 4.14	NR
Marques et al. [35]	**CoP- Mean Velocity$_{AP}$** (mm/s)	0.4 ± 0.2	0.4 ± 0.1	0.4 ± 0.2	0.90
	CoP- Mean Velocity$_{ML}$ (mm/s)	0.3 ± 0.2	0.3 (0.1)	0.2 ± 0.1	0.90
Vassimon-Barroso et al. [57]	**CoP- Total Mean Velocity** (mm/s)	13.67 ± 5.05	14.33 ± 3.51	12.8 ± 2.87	NR
	CoP-RMS$_{AP}$ (mm)	4.91 ± 2.45	4.82 ± 1.83	4.84 ± 1.33	NR
	CoP-RMS$_{ML}$ (mm)	2.4 ± 0.81	2.53 ± 1.42	2.53 ± 0.89	NR
Kang et al. [33]	**CoP-RMS$_{AP}$** (mm)	4.45 ± 1.61	4.70 ± 1.75	5.52 ± 2.10 *,†	≤0.005

Notes: **SPPB-BT:** Short Physical Performance Battery Balance Test; **AP:** Anterior-Posterior; **ML:** Medial-Lateral; **Amplitude:** distance between the maximum and the minimum CoP displacement; **RMS:** Root mean square. The results were reported as mean ± standard deviation, as median (interquartile range) or as total n – percentage (in SPPB-BT results). **NR:** Not reported.* Significantly different from the highest FI tertile, p ≤ 0.05 / Significantly different from robust group, p ≤ 0.05 † Significantly different from the intermediate FI tertile, p ≤ 0.05 / Significantly different from prefrail group, p ≤ 0.05

Table 8. Dynamic balance according to frailty status					
Study	**Measurement**	**Robust**	**Prefrail**	**Frail**	**p**
		Non-Frail			
Langlois et al. [40]	**3TUG** (s)	9.74 ± 3.59		11.78 ± 3.59	0.022
Chang et al. [37]	**8FUG** (s)	8.1 ± 3.4		11.4 ± 6.3	<0.001
Buckinx et al. [16]	**3TUG** (s)	14.1 (10.4-16.8)	24.1 (14.4-28.0)	32.4 (22.2-44.4)	0.0001
Furtado et al. [30]	**8FUG** (s)	13 (11;15)	11 (9;14)	9 (7;11)	<0.001
Vassimon-Barroso et al. [57]	**3TUG** (s)	11.14 ± 1.99	14.08 ± 5.64	21.43 ± 8.33*,†	<0.01
Tay et al. [32]	**3TUG** (s)	9.33 (7.79–0.61)	10.69 (8.29 – 14.67)		0.031
Study	**Measurement**	**Lowest FI tertile**	**Intermediate FI tertile**	**Highest FI tertile**	**r, p**
Theou et al. [28]	**8FUG** (s)	6.8±1.2	9.6±2.4	19.8±8.3*,†	0.61, 0.000

__Notes:__ **r**: partial correlation coefficients adjusted for age; **3TUG:** 3-meter Timed Up and Go test; **8FUG:** 8-foot (2,45m) up-&-go test (SFT); **FI:** Frailty Index (Rockwood). The results were reported as mean ± standard deviation or as median (interquartile range).* Significantly different from the highest FI tertile, p ≤ 0.05 / Significantly different from robust group, p ≤ 0.05 † Significantly different from the intermediate FI tertile, p ≤ 0.05 / Significantly different from prefrail group, p ≤ 0.05

Table 9. Mixed balance according to frailty status					
Study	**Measurement**	**Robust**	**Prefrail**	**Frail**	**p**
Buckinx et al. [16]	**Tinetti**	26.6 ± 2.65	24.2 ± 5.10	17.1 ± 6.99	0.001
Vieira et al. [34]	**BBS**	55 ± 2	51 ± 4	50 ± 5	<0.05
Marques et al. [35]	**BESTest**	80.4 ± 14.7	74 ± 17.6	60.5 ± 14.2 *,†	<0.01

__Notes:__ **BBS:** Berg balance scale. The results were reported as mean ± standard deviation or as median (interquartile range). * Significantly different from the highest FI tertile, p ≤ 0.05 / Significantly different from robust group, p ≤ 0.05 † Significantly different from the intermediate FI tertile, p ≤ 0.05 / Significantly different from prefrail group, p ≤ 0.05.

Table 10. Upper body flexibility and frailty					
Study	**Measurement**	**Robust**	**Prefrail**	**Frail**	**p**
		Non-Frail			
Chang et al. [37]	**CSR**	−14.6 ± 16.8		−23.6 ± 15.3	<0.001
Furtado et al. [30]	**CSR**	35 (23;43.5)	38.75 (34.5;43.5)	32.25 (22.5;38.5)	<0.001
Tay et al. [32]	**CSR**	1.67 ± 10.5	0.77 ± 14.2		<0.370
Notes: **CSR:** chair sit-&-reach test (SFT). The results are reported as mean ± standard deviation or with median (interquartile range).					

Table 11. Lower body flexibility and frailty					
Study	**Measurement**	**Robust**	**Prefrail**	**Frail**	**p**
Furtado et al. [30]	**BST**	53 (39;70.5)	44 (37.5;60.5)	40.25 (31;51)	0.022
Tay et al. [32]	**BST**	6.51 ± 16.59	4.85 ± 25.27		0.720
Notes: **BST:** Back Stretch test (SFT). The results are reported as mean ± standard deviation or with median (interquartile range).					

Table 12. Usual Walking Speed and frailty

Study	Measurement	Robust	Prefrail	Frail	p
		Non-Frail			
Kang et al. [33]	**SPPB-UWS** (s)	3.9 ± 0.7	4.7 ± 1.2	6.7 ± 1.6	0.001
		4.23 ± 0.94			
Verghese and Xue [54]	**FP-UWS** (m/s)	1.03 ± 0.18	0.96 ± 0.17		0.001
Montero-Odasso et al. [55]	**FP-UWS** (m/s)	1.24 ± 0.13	0.95 ± 0.21	0.79 ± 0.19	<0.001
		1.04 ± 0.19			
Curcio et al. [56]	**FP-UWS** (m/s)		0.93 ± 0.22	0.69 ± 0.22	0.001
		1 ± 0.2			
Buckinx et al. [16]	**SPPB-UWS** (m/s)	26.6±2.65	0.75 ± 0.33	0.44 ± 0.18	0.001
		0.81 ± 0.34			
Vieira et al. [34]	**IM-UWS** (m/s)	1.25±0.24	1.02 ±0.18	1.0 ± 0.23	0.003
		105.4 ± 17.4			
Meng et al. [58]	**FP-UWS** (m/s)	1.05 ± 0.29	0.90 ± 0.39	0.66 ± 0.39	0.009
		0.94 ± 0.36			
Tay et al. [32]	**FP-UWS** (m/s)	1.38 ± 0.27	1.19 ± 0.35		0.001
Martins et al. [59]	**FP-UWS** (m/s)	1.4±0.2	1.4±0.2	1.3±0.2	0.135
		1.4 ± 0.2			
Jansen et al. [60]	**FP-UWS** (m/s)	1.18 ± 0.15	0.92 ± 0.22	0.64 ± 0.25	<0.001
		1.03 ± 0.19			

Study	Measurement	Highest FI tertile	Intermediate FI tertile	Lowest FI tertile	r, p
Theou et al. [28]	**FP-UWS** (m/s)	1.2±0.2	0.9±0.2*	0.5±0.3*,†	–0.8, <0.001

Notes: **r**: partial correlation coefficients adjusted for age; **FP-UWS:** Frailty Phenotype Usual Walking Speed (4,5m-15-foot walk test); **SPPB-UWS:** SPPB Usual Walking Speed**; 10m-UWS:** 10 meters Usual Walking Speed**; IM-UWS:** instrumented mat (GAITRite®, SN: Q209, CIR Systems Inc., Franklin, NJ, USA) Usual Walking Speed. The results are reported as mean ± standard deviation.* Significantly different from the highest FI tertile, p ≤ 0.05

† Significantly different from the intermediate FI tertile, p ≤ 0.05

Table 13. Maximum Walking Speed and frailty

Study	Measurement	Robust	Prefrail	Frail	p
		Non-Frail			
Montero-Odasso et al. [55]	**FP-MWS** (m/s)	1.55 ± 0.19	1.25 ± 0.26	1.06 ± 0.22	<0.001
		1.34 ± 0.24			
Langlois et al. [40]	**UMWS** (m/s)	1.5±0.23		1.30±0.23	0.001
Jansen et al. [60]	**10m-MWS** (m/s)	1.47 ± 0.22	1.13 ± 0.27	1.07 ± 0.12	<0.001
		1.27 ± 0.25			
Study	**Measurement**	**Highest FI tertile**	**Intermediate FI tertile**	**Lowest FI tertile**	**r, p**
Theou et al. [28]	**FP-MWS** (m/s)	1.5±0.3	1.1±0.3*	0.6±0.3 *,†	–0.71, <0.001

Notes: **FP-MWS:** 4,5m maximum walking speed**, UMWS:** mean score of comfortable and maximum, **10m-MWS:** 10 meters Maximum Walking Speed**. r:** partial correlation coefficients adjusted for age. The results are reported as mean ± standard deviation.

* Significantly different from the highest FI tertile, p ≤ 0.05

† Significantly different from the intermediate FI tertile, p ≤ 0.05

Table 14. Aerobic capacity and frailty

Study	Measurement	Robust	Prefrail	Frail	p
		Non-Frail			
Bastone et al. [39]	**ISWT** (m)	310.0 ± 92.6		130.0± 82.4	<0.001
	VO_2peak (mL/kg/min)	18.4 ± 4.8		13.7 ±3.6	0.003
	MHR (b/min)	133.4 ± 15.1		118.5 ± 23.1	0.063
	RER	1.1 ± 0.1		1.1 ± 0.1	0.63
Langlois et al. [40]	**6MWT** (m)	487.1 ± 86.1		413.3 ± 86.0	0.001
Tay et al. [32]	**6MWT** (m)	449.4 ± 121.2	376.8 ± 143.7		0.006

Notes: **6MWT**: 6-minute walk test, **ISWT**: Incremental Shuttle Walk Test (maximal test), **MHR:** Maximum Herat Rate, **RER:** Respiratory Exchange Ratio. The results are reported as mean ± standard deviation.

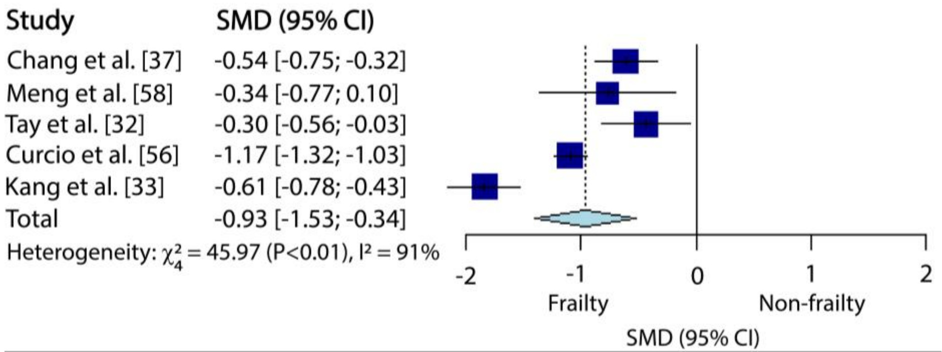

Fig. 2. Meta-analysis of lower body strength test and frailty status.

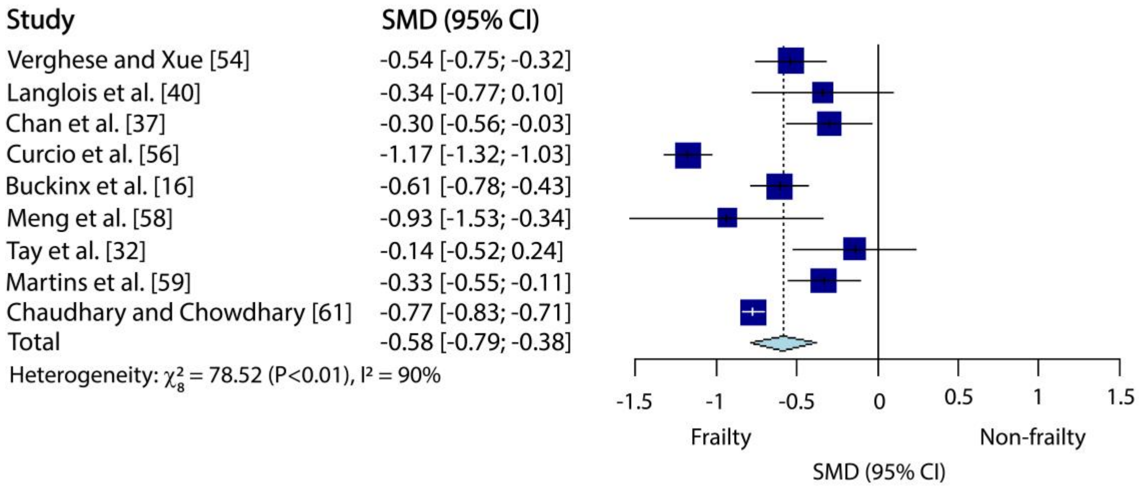

Fig. 3. Meta-analysis of handgrip strength test and frailty status.

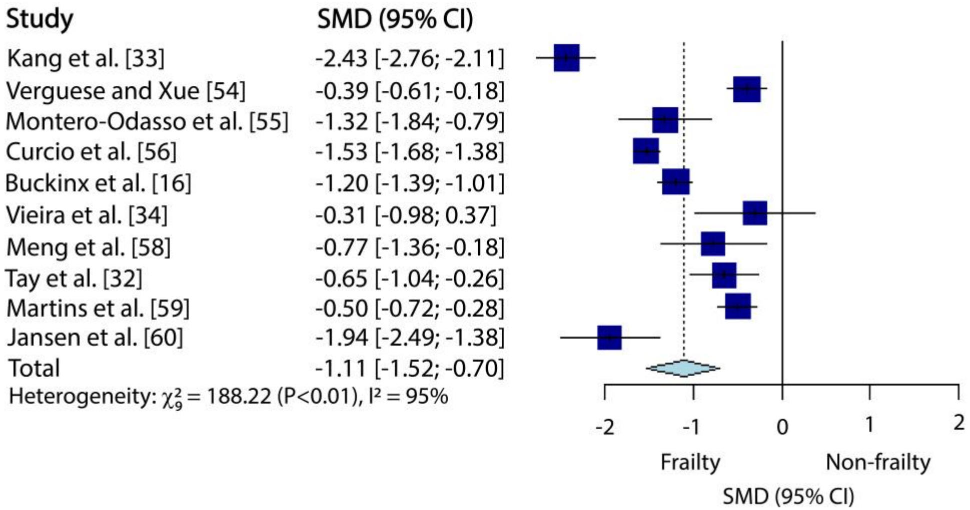

Fig. 4. Meta-analysis of usual walking speed and frailty status.

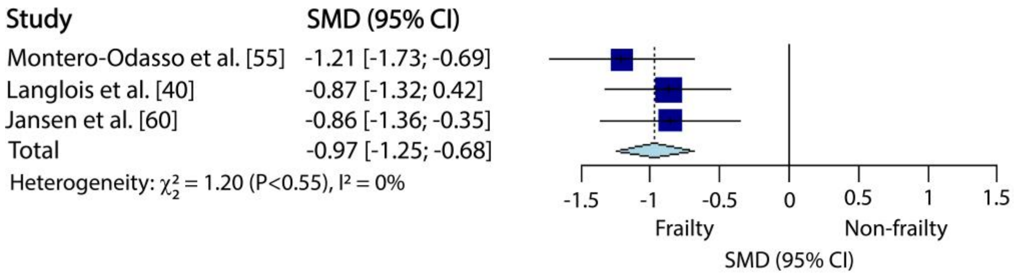

Fig. 5. Meta-analysis of maximal walking speed and frailty status.

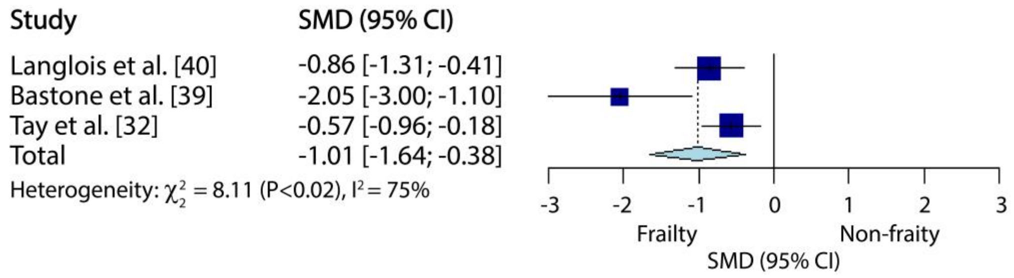

Fig. 6. Meta-analysis of aerobic capacity and frailty status.

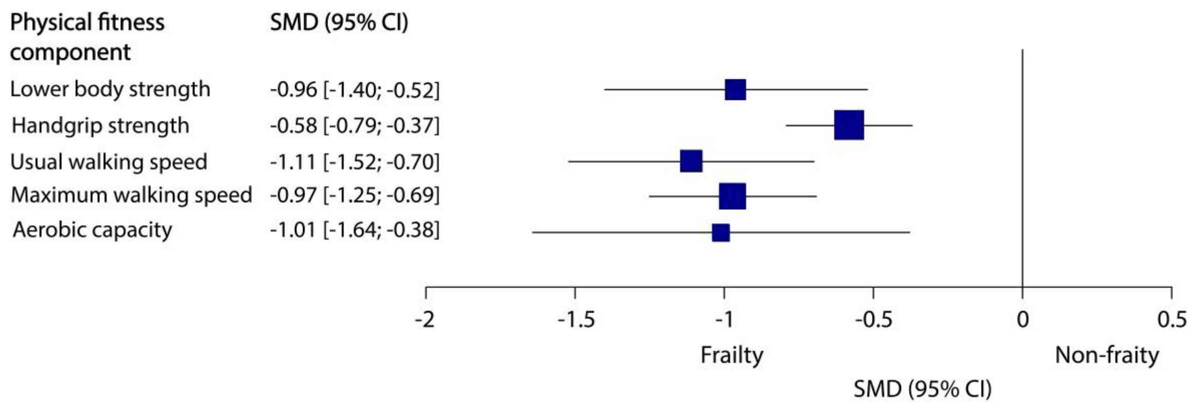

Fig. 7. Global Meta-analysis of physical fitness components and frailty status.