Cogitare Enfermagem

REVIEW

GAIT SPEED ASSOCIATED WITH CLINICAL FACTORS IN THE ELDERLY IN PRIMARY HEALTH CARE: INTEGRATIVE REVIEW*

HIGHLIGHTS

1. Clinical factors contribute directly to changes in gait speed.
2. Several chronic diseases are associated with reduced gait speed.
3. There is variation in gait over the years investigated.

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ABSTRACT

Objective: to analyze national and international scientific production on gait speed associated with signs, symptoms, and clinical factors in elderly people in primary health care. **Method:** integrative literature review carried out in five data sources (Virtual Health Library, Embase, Web of Science, Cumulative Index To Nursing And Allied Health Literature (CINAHL), and PubMed) with publications from January 2017 to June 2023. **Results:** 13 publications met the eligibility criteria, with a predominance of studies in English. Studies indicated that reduced gait speed is associated with fractures ($p<0.05$), dementia ($p<0.01$), cardiovascular ($p<0.001$) and neuropsychiatric ($p<0.01$) diseases, falls ($p<0.05$) and polypharmacy ($p<0.001$). **Conclusion:** altered gait speed patterns in the older people are related to various clinical factors, reinforcing the need for further studies and the guiding role of the geriatric nursing team in the health of the older person.

KEYWORDS: Aged; Walking Speed; Primary Health Care; Signs and Symptoms; Signs and Symptoms.

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INTRODUCTION

The physiological changes common to the aging process, added to the presence of chronic diseases, can result in negative health conditions for the aged[1]. Gait is known to be a predictor of functional decline, hospitalizations, and mortality since it is essential for carrying out everyday tasks. Thus, when reduced, it can influence neuromuscular control and physical activity levels and lead to situations such as sarcopenia and a decline in functionality[1].

In a cross-sectional study of 385 elderly people in Juiz de Fora, Minas Gerais, researchers found that 20.8% of the samples had reduced gait speed (VM)[3]. Reduced gait speed (GS) may be related to clinical factors such as chronic non-communicable diseases (CNCD), hospitalizations, continuous use of medication, falls, and conditions that influence the increased incidence of fractures, institutionalization, and death[2]. Furthermore, it is known that these factors influence conditions related to neuromuscular and cardiorespiratory control and the level of physical activity, contributing to a reduction in GS (VM)[1].

It is therefore important to verify which factors are associated with reduced GS, so that the multi-professional team, especially gerontological nursing, can develop actions to prevent conditions related to reduced gait speed in the elderly, especially in primary health care (PHC). This study aimed to analyze national and international scientific production on gait speed associated with signs, symptoms, and clinical factors in older people in primary health care (PHC).

METHOD

This is an Integrative Review (IR) of the literature, based on six stages: 1) identification of the topic and selection of the research question; 2) search and selection of the literature, establishment of inclusion/exclusion criteria; 3) categorization of the studies; 4) evaluation of the studies included in the IR; 5) interpretation of the results; and 6) synthesis of knowledge[4].

For the first stage, the association between clinical factors and GS in elderly people in PHC was identified as the theme. To draw up the research question, the PCC strategy was applied, in which the letter P corresponds to the population (aged people), C for the concept (gait speed associated with signs, symptoms, and clinical factors), and C for Context (Primary Health Care). The following research question was chosen: What is the panorama of national and international scientific production on gait speed associated with signs, symptoms, and clinical factors in elderly people in primary health care?

In the second stage, the following data sources were chosen to search for articles: Virtual Health Library Portal (VHL), Embase (Elselvier), Web of Science (WOS), Cumulative Index To Nursing And Allied Health Literature (CINAHL) and PubMed. To establish the search strategies, keywords from the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) were used, combined using the Boolean operators "AND" and "OR" (Chart 1).

Chart 1 - Search strategies applied to the integrative review. Curitiba, Paraná, Brazil, 2023.

DATABASE	SEARCH STRATEGIES
BVS	*(Idoso) OR (Aged) AND (Velocidade de Caminhada) OR (Marcha) OR (Walking Speed) OR (Gait) OR (Gaits) AND (Atenção Primária à Saúde) OR (Primary Health Care) AND (Sinais Clínicos) OR (Sintomas Clínicos) OR (Signs and Symptoms)*
Embase	*(Aged) AND (Walking Speed) OR (Gait) AND (Primary Health Care)*
Web of Science	*(Aged) AND (Walking Speed) OR (Gait) AND (Primary Health Care) AND (Signs and Symptoms)*
CINAHL	*(Aged) AND (Walking Speed) OR (Gait) AND (Primary Health Care) AND (Signs and Symptoms)*
PubMed	*(Aged) AND (Walking Speed) OR (Gait) AND (Primary Health Care)*

Source: The authors (2023).

The bibliography used for the selection of articles included in the IR corpus was managed using the Mendeley® computer program. The following inclusion criteria were established for scientific productions: a) published between January 2017 and June 30, 2023; check if it is different from the tables and abstract; b) available in full; c) open access; d) covering the aged public; e) published in Portuguese, English or Spanish. The exclusion criteria were a) editorials, reviews, experience reports, theoretical reflections, dissertations, theses, and monographs; b) being repeated in the databases, with only the first version found being kept; c) not answering the review question.

For the third stage, a Microsoft Excel® 2016 spreadsheet was created to categorize the articles included in the review, according to the pre-established criteria. The following information was extracted: author(s)/year of publication, journal, country, study design, sample/number of participants, objective(s), main study results, and level of scientific evidence.

The level of evidence of the studies included in the review was based on the classification proposed by the Oxford Center for Evidence-Based Medicine[5], consisting of five hierarchical levels of evidence according to the type of study (Chart 2).

Chart 2 - Classification of levels of evidence by type of study. Curitiba, Paraná, Brazil, 2023.

LE	TYPES OF STUDIES
1 a	Systematic Review (with homogeneity) of Randomized Controlled Clinical Trials (RCTs).
1 b	RCTs with a narrow confidence interval (CI).
1 c	Studies with "All or Nothing" therapeutic results and sensitivity and specificity close to 100%. Controlled case series study.
2 a	A systematic review (with homogeneity) of cohort studies.
2 b	Individual cohort study (including lower quality RCTs, e.g. follow-up below 80%). Cohort study with poor randomization quality, control, or no long follow-up, cross-sectional cohort study.
2 c	Observation of therapeutic outcomes (outcomes research); Ecological studies. Outcomes research (observation of therapeutic results or clinical evolution).
3 a	A systematic review (with homogeneity) of case-control studies.
3 b	Individual case-control studies.
4	Case reports (including lower quality cohorts or case-control studies).
5	Expert opinion without explicit critical evaluation, physiology studies, bench research, and "first principles". Opinion of respected authorities or experts. Non-systematic literature review.

Legend: RCTs - Randomized Controlled Clinical Trials; CI - Confidence Interval; LE - Level of Evidence.
Source: *OXFORD CENTRE EVIDENCE-BASED MEDICINE* (2009)[5].

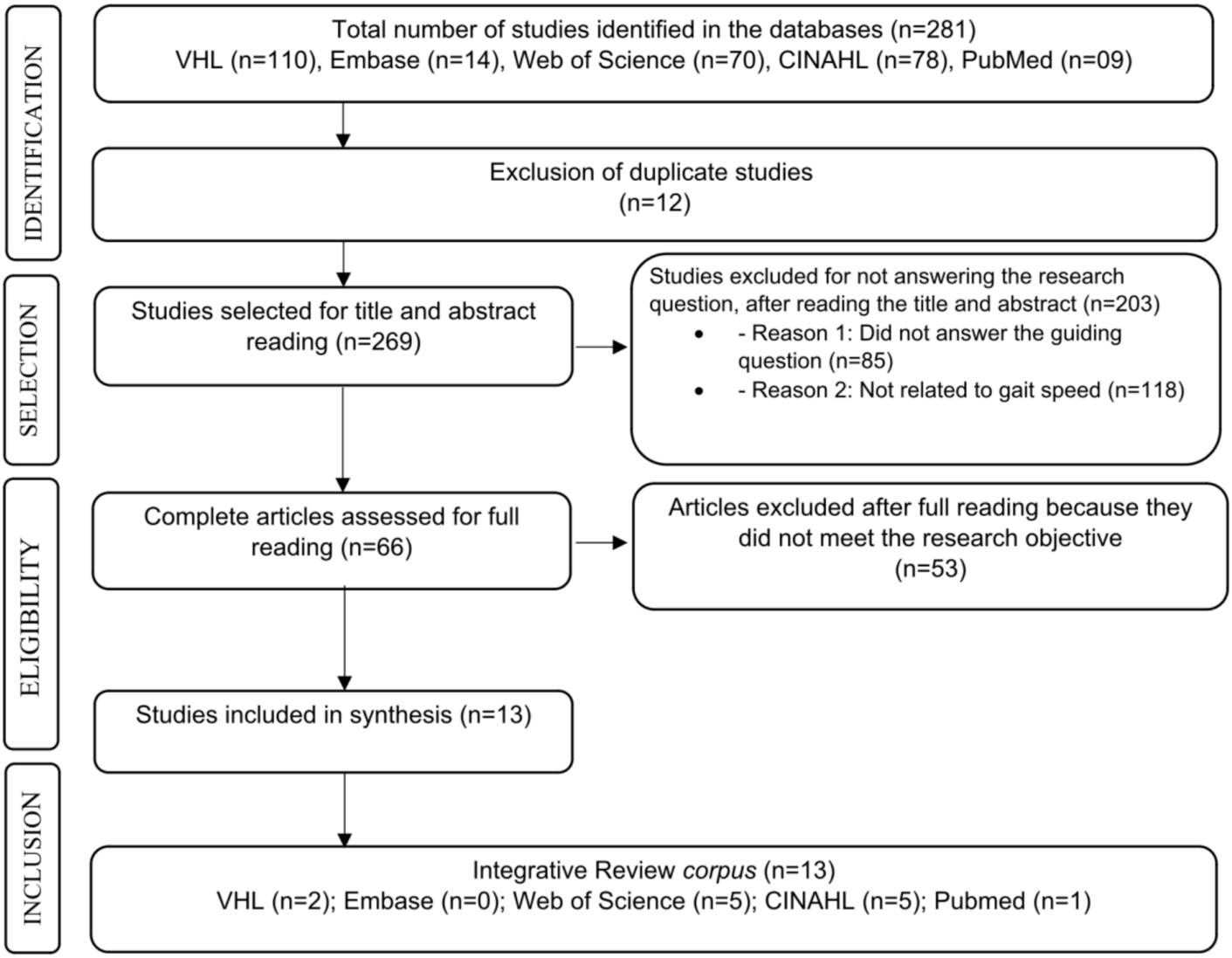
For the fourth stage of the IR of the literature, the studies were evaluated by analyzing the content of the articles included, using three reviewers. The fifth stage involved interpreting the studies, which were transcribed and presented descriptively and in graphs and tables. The sixth stage is the presentation of the summary of the review, which corresponds to the conclusion of this study.

The *Preferred Reporting Items for Systematic Reviews and Meta-analyses* (PRISMA)[6] were used to represent the article selection process and the composition of the literature IR corpus.

RESULTS

The initial search of the selected databases resulted in 281 articles. To select the studies, the titles and abstracts were read, followed by the full texts. Twelve publications were excluded for being duplicated between databases: 203 for not answering the research question when reading the title and abstract, and 53 for not answering the research question after reading the full text. Thus, 13 publications met the eligibility criteria and made up the analysis *corpus*, as shown in the flowchart of the selection of articles and composition of the integrative review *corpus* (Figure 1).

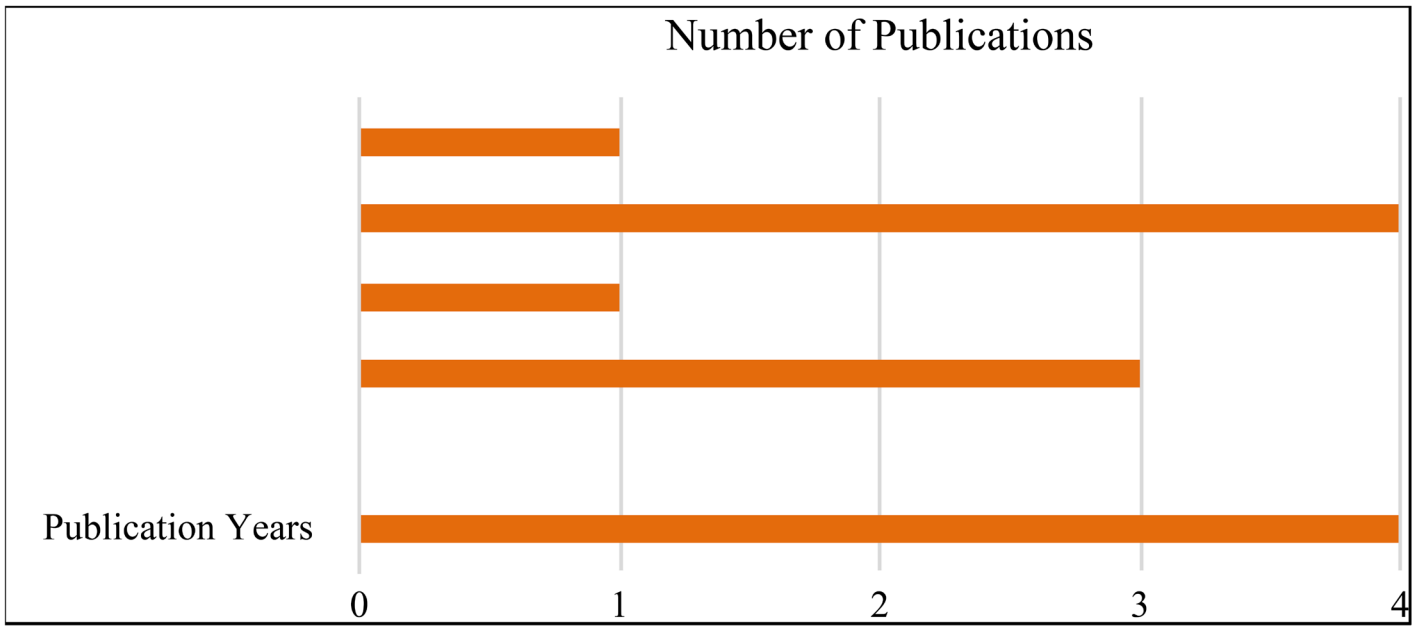
Figure 1 - Flowchart of article selection and composition of the integrative review corpus. Curitiba, Paraná, Brazil, 2023.



Source: The authors (2023).

The thirteen articles selected to make up the IR corpus were published between 2017 and 2022, with the highest number of publications in 2017 and 2021 (n=4; 30.8%, respectively) (Figure 2).

Figure 2 - Distribution of the number of scientific productions that made up the corpus of the integrative review according to year of publication. Curitiba, Paraná, Brazil, 2023.



Source: The authors (2023).

The English language predominated (n=12; 92.3%), while one article was in Portuguese (7.7%). As for the countries of origin of the publications, three (23.1%) were developed in Sweden, two (15.4%) in China, two (15.4%) in Japan and one (7.7%) in Australia, France, Brazil, Norway, Finland, and Turkey, respectively.

As for the design of the studies, all were quantitative (n = 13; 100%), with a predominance of cohort studies (n= seven; 53.8%), followed by cross-sectional studies (n=six; 46.15%). Regarding the level of evidence in the studies, five (38.5%) were classified as 2b and the remaining eight (61.5%) as 2c. This classification, according to the *Oxford Centre for Evidence-Based Medicine*[5], gives the studies analyzed an adequate design and scientific credibility.

For the GS assessment, eight (61.5%) used a distance of 6 meters to perform the test, followed by two (15.4%) with a distance of 4 meters. One (7.7%) study assessed a distance of 14 meters, 2.5 meters, and 2.4 meters, respectively.

Chart 3 summarizes the main characteristics of the articles included in the integrative review.

Quadro 3 - Summary of the characteristics of the articles included in the integrative review. Curitiba, Paraná, Brazil, 2023.

Author/Year	Title	Objective(s)	Language	Design	Sample(n)	Main results	LE*
MATHEW *et al.*, 2017[7]	Gait outcomes of older adults receiving subacute hospital rehabilitation following orthopaedic trauma: a longitudinal cohort study.	To describe gait speed at admission and discharge from inpatient rehabilitation in aged people recovering from orthopedic trauma and factors associated with gait speed performance and discharge destination.	English	Cohort	n=746	Of the 746 aged, 76.4% of those who were able to complete the gait speed test on admission and discharge were able to improve their gait by 0.10m/s. Only 1.3% had a clinically significant decrease in gait. As for factors associated with gait speed, patients with pelvic fractures (p<0.01) and multiple fractures (p<0.01) had faster gait speeds than aged people with femoral fractures.	2c
DUMURGIER *et al.*, 2017[8]	Gait Speed and Decline in Gait Speed as Predictors of Incident Dementia.	To investigate the association between gait speed and dementia, using repeated gait assessments before the onset of dementia.	English	Cohort	n=3.663	3,663 people took part, 296 of whom developed dementia, with an incidence of 12.3/1000 person-years. In a model adjusted for age and sex, lower walking speed was associated with the risk of dementia (p<0.001). In addition, regardless of initial walking speed, those with slower walking speed had a higher risk of dementia (p=0.009).	2b
HEILAND *et al.*, 2017[9]	Cardiovascular risk burden and future risk of walking speed limitation in older adults.	Explore longitudinally the association between cardiovascular risk factor burden and limitations in walking speed, balance, and getting up from a chair and see if these associations vary according to age and cognitive status.	English	Cohort	n=1.441	Of the 1,441 aged participants, 326 developed limitations in walking speed, and cardiovascular risk was associated with limitations in walking speed in those aged less than 78 years. In addition, greater cardiovascular risk was significantly associated with the advanced decline in walking speed (p<0.001).	2c

(continued)

WELMER *et al.*, 2017[10]	Cognitive and physical function in relation to the risk of injurious falls in older adults: a population-based study.	To quantify the effect of cognitive and physical deficits independently on the risk of falls, to verify whether this risk is modified by global cognitive impairment, and to explore whether the risk varies according to the length of follow-up.	English	Cohort	n=2.495	Among the 2,495 participants, 167 had at least one fall during the three-year follow-up period, 310 during the five-year follow-up period, and 571 during the 10-year follow-up period. Decreased walking speed increased the risk of falling by 38% over the three years. Slow walking speed was associated with the risk of falling over the 3- and 10-year periods in people with cognitive impairment (p<0.05).	2b
LENARDT *et al.*, 2019[11]	Gait speed and occurrence of falls in the long-lived elderly.	To analyze the relationship between gait speed and the occurrence of falls in long-lived aged people.	Portuguese	Cross-sectional	n=243	Of the 243 aged people, 50 (20.7%) had reduced GS, and 111 (45.7%) had fallen in the last 12 months. Of the aged with reduced GS, 30 (60%) had fallen in the last year. Reduced GS was significantly associated with falls in the last 12 months (p=0.023).	2c
ISHIZAKI *et al.*, 2019[12]	Association of physical performance and self-rated health with multimorbidity among older adults: results from a nationwide survey in Japan.	To examine the association of physical performance measures and self-rated health with multi-morbidity among Japanese aged ≥60 years using cross-sectional data from a national longitudinal survey.	English	Cross-sectional	n=2.525	Of the 2,525 participants who answered the survey without assistance, the most prevalent chronic disease was hypertension (44.1%), followed by low back pain (25.7%) and cataracts (24.7%). Multi-morbidity predominated in 44% of the aged and was statistically significantly associated with handgrip strength (p=0.006) and self-rated health (p<0.001), but not with gait speed (p=0.479).	2c

(continued)

VETRANO *et al.*, 2019[13]	Walking speed drives the prognosis of older adults with cardiovascular and neuropsychiatric multimorbidity.	Analyzing jointly the effect of cardiovascular multi-morbidity and functional impairment, and the effect of neuropsychiatric multi-morbidity and functional impairment, all-cause and cause-specific mortality.	English	Cohort	n=3.363	After 3 years of follow-up, compared to patients with preserved walking speed and no cardiovascular or neuropsychiatric diseases, the mortality risk ratios were 1.88 (1.29-2.74), 3.85 (2.60-5.70) and 5.18 (3.45-7.78), respectively, during the three-year follow-up. The presence of one or two cardiovascular diseases increases the chances of mortality, regardless of walking speed. On the other hand, slow walking speed concomitant with the presence of neuropsychiatric disease was associated with mortality over 3 years (p<0.01).	2b
TANAKA *et al.*, 2020[14]	Relationship of low muscle mass and obesity with physical function in community dwelling older adults: Results from the Nagahama study.	To investigate the influence of obesity and low muscle mass on physical function among community-aged people.	English	Cross-sectional	n=1.922	Of the 1,922 participants, 1,279 were women with an average age of 67.7 years. It was observed that obese individuals with a low body mass index (BMI) had a lower walking speed when compared to non-obese individuals with a normal (eutrophic) BMI.	

(continued)

LIN *et al.*, 2021[15]	Using hand grip strength to detect slow walking speed in older adults: the Yilan study.	Objective 1: To determine whether handgrip strength is the best explainable correlate for walking speed in aged Asian community dwellers compared to several candidate variables, and to what extent handgrip strength correlates with walking speed. Objective 2: To determine the optimal cut-off values for handgrip strength to detect slow walking speed.	English	Cross-sectional	n=301	Of the 301 aged, 55% were women, and the average age was 73.9 years. It was observed that older, female participants with low levels of schooling and who did not practice physical activities had slower gait speeds when compared to the other participants. Concerning clinical factors, individuals with diabetes, hypertension, heart disease, a history of stroke, arthritis in the lower limbs, and depression had a slower gait. Walking speed was associated with age, height, weight, handgrip strength, and muscle mass. In the Stepwise multiple linear regression analysis, handgrip strength was found to be the most explainable factor related to walking speed among all the participants.	2c
ZHOU *et al.*, 2021[16]	A prospective cohort study of the risk factors for new falls and fragility fractures in self-caring elderly patients aged 80 years and over.	To prospectively analyze risk factors for new falls and fragility fractures in self-care-aged people and find suitable assessment tools for community screening and follow-up interventions.	English	Prospective Cohort	n=290	290 people aged 80 or overtook part in the study. After 12 months, 87 of them had new falls. This incidence was negatively correlated with Activities of Daily Living (ADL) (p = 0.008) and the Time Up and Go (TUG) test >12 s (p = 0.021). It was also possible to observe 33 new fractures related to the frailty condition, which was associated with new falls (p = 0.000). However, new fractures due to frailty were negatively associated with bone mineral density of the lumbar vertebrae (p = 0.012) and walking speed (p = 0.000).	2b

(continued)

LAUKLI *et al.*, 2021[17]	Frailty assessment of older adults, first-time applicants of public home care service in Norway.	Objective 1: To estimate the prevalence of frailty in aged people applying for public home care services for the first time. Objective 2: To examine the suitability of gait speed and Short Physical Performance Battery as screening tools for frailty defined by Fried et al. adapted for a general population >70 years old in Norway.	English	Cross-sectional	n=116	The study included 116 participants. Regarding frailty, 61.2% of those investigated were considered frail, 29.3% as pre-frail, and 8.6% as robust. Mean gait speed was lower in frail than in pre-frail individuals, and lower in pre-frail than in robust individuals (p<0001). No robust-aged individual had a gait speed <0.8 m/s.	2c
OHLIN *et al.*, 2021[18]	Low or declining gait speed is associated with risk of developing dementia over 5 years among people aged 85 years and over.	To investigate the longitudinal association between gait speed, change in gait speed, and development of dementia over five years in people aged 85 and over.	English	Cohort	n=296	A total of 296 aged participants were assessed at baseline, of whom 98 developed dementia after 5 years of assessment. Gait speed at baseline was associated with dementia both in the unadjusted model of the analysis (p <0.001) and the adjusted model (age, gender, and dependence in activities of daily living) (p =0.045). Variation in gait speed was only associated with dementia in the adjusted model (p =0.015).	2b
OZKOK *et al.*, 2022[19]	Associations between polypharmacy and physical performance measures in older adults.	To examine the associations of polypharmacy with certain physical performance measures used to assess ambulation.	English	Cross-sectional	n=392	Of the 392 participants, 62.5% had polypharmacy, for whom a slower walking speed was also observed when compared to patients without polypharmacy (p <0.001). In addition, patients using five or more medications required more time to perform the Timed Up and Go (TUG) test. In the analysis adjusted for age, gender, and BMI, polypharmacy was still associated with walking speed (p=0.03).	2c

Legend: LE - Level of Evidence (2009)5.

Source: The authors (2023).

DISCUSSION

Of the articles analyzed, all pointed out that certain clinical factors directly influence changes in the gait speed pattern[7-19]. Changes in GS performance related to clinical factors are due to the decrease in the body's physiological reserve resulting from the aging process since it can be accompanied by functional losses that affect individuals[19].

In a longitudinal study of 746 aged people (≥ 60 years) from a tertiary hospital in Australia, considering the moments of rehabilitation and hospital discharge, it was found that patients with femoral fractures had slower GS when compared to those with pelvic fractures and multiple fractures during rehabilitation. Pelvic fractures (p <0.05), multiple fractures (p <0.05), and femur fractures (p <0.01) were associated with reduced GS. It is known that orthopedic injuries associated with frailty can result in conditions such as functional incapacity and subsequent fractures. Thus, orthopedic trauma can influence GS, which makes it important to investigate this condition for better rehabilitation of the aged[7].

GS is also considered to be directly associated with dementia since it involves motor, sensory, and neurocognitive pathways. A cohort study carried out in three French cities with 3,663 community-aged people (≥65 years) investigated the association between GS and dementia. After 9 years of follow-up, in an analysis adjusted for age and gender, those who developed dementia had slower GS (p <0.001). Furthermore, the rate of GS reduction was 80% higher among the aged who developed dementia[8].

A cohort study of 296 community-dwelling aged people in Sweden and Finland, with a five-year interval between assessments, showed that 98 participants developed dementia over the years (period investigated). GS at baseline (p =0.045) and reduced gait performance (p =0.015) were associated with dementia[18]. The association between dementia and reduced GS can be explained by vascular issues, since a stroke, for example, can interrupt neuronal circuits involved in motor response, contributing to reduced gait and dementia[8].

Cardiovascular diseases have also been shown to be associated with variations in GS performance. In a cohort study carried out between 2001 and 2004, with data extracted from the Swedish National Study on Aging in Kungsholmen involving 1,441 aged (≥60 years) households, 326 of them developed walking limitations over the years, and the risk of cardiovascular disease was significantly associated with a rapid decline in GS (p <0.001)9. The increase in atherosclerotic plaques can narrow arteries and decrease blood perfusion to the muscles during the aging process, compromising mobility and affecting gait[9].

Different data was found in a cohort study, which also used data from the Swedish National Study on Aging in Kungsholmen, including 3,241 aged people. It indicated that patients with one or two cardiovascular diseases had a higher chance of mortality, but there was no association with gait performance since reduced GS is considered multifactorial. Slow GS, on the other hand, was associated with neuropsychiatric diseases and increased the chances of mortality (p <0.01) over a three-year period[13].

Concerning falls, a cohort study carried out with data from the study, of 2,495 aged people, found that 167 people fell in three years of follow-up, 310 in five years of follow-up, and 571 in ten years, respectively. Thus, worse walking speed scores significantly increased the risk of falls over three years, with slow GS being associated with the risk of falls in aged people without cognitive impairment (p <0.05)[10].

Also, noteworthy is a prospective study that included 290 long-lived elderly people (≥80 years), which showed that, over 12 months, 87 (30%) people had new falls, in which aged people with slow GS were more likely to have falls (p <0.001)[16]. Similar data was found in a national cross-sectional study carried out with 243 aged people in the South of Brazil, in which 20.7% of the participants had reduced GS and 45.7% had falls in the last 12 months. In this study, reduced GS was significantly associated with falls (p =0.023)[11].

It was also observed that obesity was associated with lower mean GS. In a cross-sectional study of 1,922 community-dwelling aged people (≥60 years), both obese aged people and those with a low Body Mass Index (BMI) had slower GS when compared to non-obese people and those with a normal (eutrophic) BMI (p =0.003)[14]. These data corroborate the cross-sectional study using data from the Yilan Study in Taiwan, in which walking speed was significantly associated with the variables age, height, weight, handgrip strength, and muscle mass (p <0.001). However, in this study, multiple linear regression analysis indicated that handgrip strength was the most explainable factor for detecting slow GS15, given their relationship as markers of physical frailty.

Considering that GS is considered a component of the physical frailty phenotype, a crosssectional study carried out in Norway with 116 aged people found that the prevalence of frailty among those investigated was 62.2%. Individuals considered to be frail had lower mean GS when compared to pre-frail individuals, and these, in turn, also had lower mean GS when compared to non-frail individuals (p <0.001)[17].

GS can also be influenced by polypharmacy (continuous use of five or more medications). In a cross-sectional study of 392 elderly people in Turkey, it was found that the prevalence of polypharmacy was 62.5% and that the aged who used five or more drugs had slower mean GS when compared to the other participants (p<0.001)[19]. It is known that drug interactions, as well as polypharmacy, can affect slowing GS, including issues related to balance, which have an impact on reducing speed to avoid falls[20].

In addition, changes in GS patterns are associated with chronic diseases, but not with multi-morbidity. Although multi-morbidity had a high prevalence (44%) among 2,525 older Japanese people, it was not found to be associated with altered GS in those investigated (p=0.479)[12]. This condition can be explained by the fact that people with multi-morbidity also have a greater treatment burden, avoiding health conditions and consequently reducing GS.

Considering the clinical factors associated with variations in GS in aged people, it is important for the multidisciplinary team working in primary health care to be aware of the conditions related to gait alterations, to avoid possible negative health outcomes arising from this condition.

A limitation of the IR was the lack of international longitudinal articles addressing reduced GS in the aged in primary health care.

CONCLUSION

There are several clinical factors associated with altered GS patterns in aged people, such as fractures, dementia, cardiovascular diseases, falls, polypharmacy, and chronic diseases. These factors can result in conditions such as "sarcopenia", loss of functionality, and dependence, resulting in a loss of quality of life and autonomy for the aged.

The multi-professional health team, especially gerontological nursing, plays a key role in preventing and monitoring clinical conditions to avoid and/or postpone the reduction in GS of aged people. In addition, it is of extreme importance to use instruments aimed at assessing the health of these individuals, related to clinical factors and markers of physical frailty, especially gait speed, given the possibility of early identification of these conditions for better management and gerontological care.

In this sense, by identifying the clinical factors associated with gait alterations, it is possible to plan new studies on the subject, searching for scientific evidence to better care for the aged. In addition, nursing, based on scientific evidence, plays a central role in the care of the aged in PHC.

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Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work - **Spekalski MV dos S, Boldt P, Domingues MPS, Silva JG da, Betiolli SE**. Drafting the work or revising it critically for important intellectual content - **Spekalski MV dos S, Hammerschmidt KS de A, Lenardt MH, Betiolli SE.** Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - **Spekalski MV dos S, Betiolli SE**. All authors approved the final version of the text.

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