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WHAT IS THE EVIDENCE FOR ASSOCIATIONS BETWEEN GAIT SPEED AND GRIP STRENGTH WITH FRAILTY IN HEALTHY OLDER ADULTS? A SYSTEMATIC REVIEW

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MSc Physiotherapy

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ABSTRACT

Background

Frailty is a common age-related syndrome that is associated with an increased susceptibility to adverse health outcomes, which include disability, dependency, hospitalisations, requirement for long-term care, falls and death. The prevalence of these adverse outcomes are projected to increase with the increasing elderly population, which poses major problems to healthcare systems. There is a need for feasible screening tools that can identify elderly people at risk of frailty on a large scale so that targeted preventative interventions can be implemented.

Objective

To determine whether gait speed and grip strength are significant indicators of frailty and its associated adverse-health-related outcomes in healthy older adults.

Search Strategy

To identify studies the electronic databases MEDLINE, CINAHL, PubMed, PEDro and Cochrane Library were systematically searched under defined search terms and combinations. The reference lists of included studies were hand-searched to identify any more studies that may be relevant to the research question.

Study Selection

The search was limited to RCTs and cohort studies in the English language, and included publications between January 2000 and March 2018. Studies that examined the associations for gait speed and/or grip strength with frailty in relation to healthy adults over the age of 60 were included.

Data collection and analysis

The included studies were critically appraised using the CASP checklist for cohort studies, and data collection headings were adapted from a previous systematic review in this area by den Ouden et al. (2011).

Main Results

The key findings of this review were that gait speed was associated with an increased risk of future disability, hospitalisations, mortality, requirement for care and falls, and the majority of evidence reported that grip strength was associated with an increased risk of future disability. The associations between gait speed and an increased risk of future disability also appeared to be stronger and more consistent than that of grip strength

Conclusion

Gait speed appears to be an indicator of future disability; mobility limitation, hospitalisations, mortality and falls, and grip strength appears to be an indicator of future disability. Additionally, gait speed seems to be a stronger indicator of future disability than grip strength.

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1. INTRODUCTION

1. INTRODUCTIN

Frailty is a common syndrome associated with ageing (Thompson 2016). It is characterised by a decline in physiological reserve over time as well as an increased susceptibility to adverse health outcomes, which include; disability, dependency, hospitalisations, requirement for long-term care, falls and death (Fried et al. 2004; Thompson 2016). Frailty is also associated with an increased risk of postoperative complications after surgery, and an increased length of hospital stay (Lee et al. 2015). The existence of frailty is globally recognised as a syndrome; however, there is no consensus on a gold-standard definition (Pialoux et al. 2012). According to the well-recognised phenotype developed by Fried et al. (2001), individuals can be categorised as being either robust, pre-frail or frail. Frailty is categorised by the presence of five characteristics; slow walking speed, unintentional weight loss, decreased grip strength, self-reported exhaustion and low physical activity levels (Fried et al. 2001). Individuals with none of these characteristics are categorized as robust, those with one or two are classified as pre-frail, and those with three or more are classified as frail (Fried et al. 2001). The presence of pre-frailty is often over-looked by general practitioners due to either the slight nature of the specific deficits, or them being attributed to natural ageing; as well as the physician's general focus on identifying particular diseases or medical issues (Lee et al. 2017). Due to improvements in healthcare and lifestyles, there is an increasing elderly population in the UK (Hayter 2017). There are currently 11.8 million people living in the UK who are over the age of 65, a figure which is projected to increase to more than 16 million by 2035 (Age UK 2017). However, it is not solely the increasing elderly population which poses challenges to the healthcare system, but rather the correlation between ageing and frailty (Wou and Conroy 2013). It is estimated that the prevalence of frailty is between 3-6% in those aged 65-70, and more than 16% in those over the age of 80 (Shamliyan et al. 2012). In those over the age of 85, it is estimated that 37% of men and 31% of women are frail (Shamliyan et al. 2012). Healthcare costs in relation to long-term care are expected to significantly increase by 2025, largely owing to a projected 25% increase in the amount of individuals who will be living with an age-related disability (Boseley 2017).

There is some evidence to suggest that measurements of gait speed and grip strength are associated with frailty in older adults (Vermeulen et al. 2011). Use of gait speed and grip strength as performance indicators may have particularly important implications for clinical practice (Vermeulen et al. 2011). Frailty is a syndrome that is progressive and potentially reversible (Pialoux et al. 2012), and there is the potential to identify at-risk individuals so that preventative interventions can be implemented (Vermeulen et al. 2011). Identifying groups of at-risk elderly people would allow interventions to be implemented at a population level (Abellan Van Kan et al. 2009). Interventions such as high intensity exercise have been shown to be safe and effective (Binder et al. 2002; Theou et al. 2011). Preventing the onset or progression of frailty can consequently reduce the prevelance of disability, as well as the other associated adverse outcomes (Monteserin 2010; Vermeulen et al. 2011). Diagnosis of specific medical conditions has limited scope for identifying individuals at risk of frailty (Waite et al. 1994). There is a need for screening measures that can be implemented in healthcare systems that are psychometrically sound and feasible, so that at-risk individuals can be identified on a large scale (Lee et al. 2017). The reason why physical performance measures are not already widely incorporated into primary care settings for screening may potentially be due to the viewpoint that assessment would have space, time or equipment restrictions (Guralnik et al. 1989; Studenski et al. 2003).

There have been a number of different screening tools proposed over the years for assessing frailty, however, there is no consensus on the most suitable tool, and most are either too time-consuming or have questionable validity (Abellan Van Kan et al. 2009). The Comprehensive Geriatric Assessment (CGA) is a commonly used method of assessing frailty in primary care and is widely considered as the gold standard (Hamaker et al. 2012; Pialoux et al. 2012). This assessment considers patients' physical, medical and psychological states by means of a multi-dimensional protocol (Pialoux et al. 2012). The CGA allows targeted interventions to be tailored to patients' particular deficits to improve both physical and cognitive function, leading to reduced healthcare costs and hospitalisation rates (Pialoux et al. 2012). However, due to the time consumption, administrative constraints, and costs, the CGA is not feasible for use on a wide scale for routine screening in primary care networks, reinforcing the need for more efficient screening measures (Pailoux et al. 2012). Tools for measuring handgrip strength (e.g. dynamometer) and gait speed (e.g. 4m walk test) are cheap, simple, and feasible for use in primary care settings (Lee et al. 2017).

The term sarcopenia refers to the progressive muscle wasting that is associated with ageing (Roubenoff and Hughes 2000). This consequently leads to a loss of muscle strength (Proctor et al. 1998). These changes combined with the decrease in exercise tolerance that is associated with ageing lead to a decline in functional capacity (Evans 1995). Theoretically speaking, gait speed is a representation of multi-dimensional functional status, and slow gait speed may therefore be indicative of a deterioration in well-being (Abellan Van Kan et al. 2009). An individual's ability to mobilise underlines a number of different functions that are required for independence (Studenski 2009). Slowing seems to be a universal hallmark of the ageing process, and is thought to involve the deterioration of multiple organ systems (Ferrucci et al. 2000; Brach et al. 2009). Locomotion requires stability, co-ordinated timing, and strength, and involves the integration of the central and peripheral nervous systems, the joints and muscles, visceral structures including the heart and lungs, and the blood (Studenski 2009). Dysfunction of any of these components can contribute to a reduced gait speed, and these factors may theoretically explain why such a simple measure can potentially be used to predict the adverse health-related outcomes that are associated with frailty (Studenski 2009). Age-related declines in physiological mechanisms such as a decrease in the number of motor units, muscular activation dysfunctions, or the a decrease in the number of type 2 muscle fibres among other changes may also contribute towards to a reduced gait speed and decreased muscle strength, and an increase the risk of frailty (Abellan Van Kan et al. 2009).

A decline in upper limb strength is also associated with functional decline in the ageing population (Al Snih et al. 2002). Age-related physiological and behavioural changes such as decreased hormone levels, reduced BMI, disease, poor nutrition and reduced activity levels contribute to a decrease in muscle strength (Al Snih et al. 2002). In order to have the capacity to carry out activities of daily living (ADLs), a certain level of muscle strength is required (Rantanen et al. 1999). Muscle strength above this strength requirement threshold is referred to as reserve capacity, and provides a degree of allowance for strength loss before functional decline occurs (Rantanen et al. 1999). Therefore, the higher the baseline strength, the greater the safety margin before adverse outcomes develop (Rantanen et al. 1999), which theoretically explains how early intervention could potentially prevent or delay the onset of frailty and its complications. Handgrip strength is a commonly used method of assessing muscle strength (Taekema et al. 2011). It is widely recognised as a physical performance indicator for both upper body and global muscular strength (Visser et al. 2000). Handgrip strength also correlates well with lower-limb strength when properly controlled using a standardised protocol and a validated dynamometer (Cruz-Jentoft et al. 2010). A decline in grip strength is a major element of sarcopenia and frailty (Granic et al. 2016). Grip strength testing has also been found to have a good predictive validity for future adverse outcomes in the elderly population (Bohannon 2008).

Screening for frailty can help to reduce the prevalence of adverse health outcomes by allowing targeted interventions to be tailored to the patient’s specific deficit, which would consequently reduce healthcare costs (Monteserin 2010). Additionally, identifying those at-risk individuals can be important for maintaining an individual's quality of life (Buckinx et al. 2015). Preventing the onset of frailty can reduce healthcare costs by ultimately reducing the rates of hospitalisations and institutionalisations (Buckinx et al. 2015). Prevention of frailty and its associated complications is a realistic therapeutic goal in the elderly population and can be very beneficial for the individual, their families and society as a whole (Buckinx et al. 2015). The prevalence of falls and the associated injuries among the elderly population are a major issue in the UK (NICE 2013). Approximately one third of adults over the age of 65 and half of those over the age 80 fall at least once annually (NICE 2013). Due to the high prevalence of medical conditions such as osteoporosis in the elderly population, even low impact traumas can cause severe injuries (e.g. hip fracture) (Hartholt et al. 2012). The ratio of falls to fall-related injuries in the elderly population is approximately 3:1 (Hartholt et al. 2012). Consequently, one third of falls require medical treatment and hence incur healthcare costs (Hartholt et al. 2012). It is estimated that the cost of falls to the NHS is about £2.3 billion per year (NHS 2017). As well as the astronomical healthcare costs, there is also significant distress, trauma, loss of functional ability, increased fear of falls, and an increased morbidity and mortality associated with falls (NHS 2017). Because an increased risk of falls is an adverse outcome of frailty (Xue 2011), these factors highlight how beneficial implementing screening measures for identifying frailty on a large scale could potentially be for society as whole.

2. LITERATURE REVIEW

2. <u>LITERATURE REVIEW</u>

There is limited research that has evaluated the associations of gait speed and/or grip strength in relation to frailty directly. The systematic reviews and cohort studies included in this literature review have examined either one or both of these physical performance measures in relation to frailty or any of its associated adverse-health related outcomes. As previously highlighted in Section 1, frailty is characterised by an increased susceptibility to adverse outcomes, including disability and mortality, among others (Thompson 2016). Therefore, studies assessing these outcomes were included due to their associations with frailty. For the purpose of this systematic review, the broad term adverse outcome(s) (or adverse health-related outcomes) is an umbrella term which includes one or more of the following outcomes; disability, dependency, functional decline, mobility limitation, hospitalisations, care requirement, falls and mortality.

2.1 Contextual Background

Two previous systematic reviews have examined both of these physical performance indicators in relation to frailty (den Ouden et al. 2011; Vermeulen et al. 2011). Both reviews found that there were associations between gait speed and grip strength with disability in older adults (den Ouden et al. 2011; Vermeulen et al. 2011). Vermuelen et al. (2011) concluded that both slow gait speed and weak grip strength predict future disability, with gait speed being the more powerful predictor. Den Ouden et al. (2011) concluded that both slow gait speed and weak grip strength indicate an increased risk of developing disability. However, there is a need to conduct an updated systematic review since there has not been one completed in this area that includes both of these physical performance indicators since 2011. There is also new literature that has become available in this area since the previous reviews were conducted which needs to be included in an updated review.

However, as well as there being a need for an up-to-date systematic review, there were also a number of weaknesses in the two reviews that already exist. In order to assess the methodological quality of the systematic reviews and cohort studies included in this literature review, the Critical Appraisal Skills Programme (CASP) systematic review checklist and CASP Cohort study checklist were used respectively (CASP 2017a; CASP 2017b). These checklists, are shown in Appendix A and Appendix B respectively, and have been validated in order to ensure standardisation of critical appraisal of the available evidence (Baker 2014). They both consider the validity, results and relevance of the study (CASP 2017a; CASP 2017b). A limitation of the review by Vermeulen et al. (2011) was that the data from the different studies were not pooled together properly due to large variations in both the measurement protocols and how ADL disability was quantified. In the review by den Ouden et al. (2011) there was some contrasting evidence as regards to how significant the predictive correlations between handgrip strength and disability were, and further evaluation of more recently published literature will be beneficial confirm the findings of this review. Additionally, another weakness of the review by den Ouden et al. (2011) was that there were only a small number of RCTs (randomized controlled trials) included, which have a 1b level of evidence (CEBM 2017). Another systematic review that includes more RCTs would yield a higher evidence level (CEBM 2017).

2.2 Gait Speed and Frailty

Use of gait speed as a screening measure in the elderly population has become an area of increasing interest in recent years (Matsuzawa et al. 2013). Although there are a number of appealing advantages of implementing gait speed as a screening measure in clinical settings, including its efficiency, feasibility and cost-effectiveness, the evidence for its predictive capability is still brought into question (Abellan Van Kan et al. 2009; Lee et al. 2017). The capacity of gait speed for identifying healthy individuals who are a numbers of years from becoming frail is still an area of developing research (Sternberg et al. 2011). In total, four previous systematic reviews have examined the associations between gait speed and frailty/adverse outcomes in healthy older adults, two of which have already been discussed in Section 2.1

In 2009, an expert panel from the International Academy on Nutrition and Ageing (IANA) task force conducted a systematic review on the capacity of usual gait speed to predict adverse outcomes in community-dwelling elderly (Abellan Van Kan et al. 2009). This review included 27 studies published before March 2009 (Abellan Van Kan et al. 2009). It was concluded that gait speed was a strong predictor of disability, institutionalisations, mortality and falls and was just as sensitive as other batteries of tests when compared over time (Abellan Van Kan et al. 2009). The evidence was substantial enough for the authors to recommend gait speed for use as a single-item screening tool in clinical settings (Abellan Van Kan et al. 2009). The expert panel found that the optimal cut-off point for identifying at-risk individuals was ≤0.8 m/s (Abellan Van Kan et al. 2009). This review scored relatively highly when assessed with the CASP checklist; however, one limitation was that only one electronic-database was included in the search strategy (Abellan Van Kan et al. 2009), which may have consequently excluded potentially important studies from the review. Additionally, there is a need to include more up-to-date evidence in an updated review as this review was carried out in 2009 (Abellan Van Kan et al. 2009).

Another systematic review performed by Clegg et al. (2014) examined the diagnostic accuracy of a number of different physical performance indicators, including gait speed and timed-up-and-go (TUG), for detecting frailty. The authors concluded that both gait speed and TUG are indicators of frailty (Clegg et al. 2014). However, it was also concluded that both measures had a high sensitivity, but limited specificity, and are not accurate enough for to be used as single-item screening tests in clinical settings as limited specificity could potentially lead to false-positives (Clegg et al. 2014). These findings are in contrast to those of the previously mentioned review by Abellan Van Kan et al. (2009) in relation to gait speed. The review by Clegg et al. (2014) scored relatively moderately on the CASP checklist, but did have some weaknesses. There were only three studies included in this review; only one of which included gait speed and one of which included TUG (Clegg et al. 2014), bringing the methodological quality of the review into question due to limited synthesis of literature from different studies. In addition, there was no report of hand-searching reference lists for studies or personal contact with experts, and therefore important studies may have been excluded (Clegg et al. 2014).

2.3 Grip Strength and Frailty

Handgrip strength is another physical performance indicator which has developing interest for its use in clinical settings (Dodds et al. 2016). As previously highlighted, weak grip-strength occurs in conjunction with sarcopenia, and has been found to be indicative of adverse outcomes such as hospitalisations, disability and mortality (Alfaro-Acha et al. 2006; Cawthon et al. 2009; Dodds et al. 2016). There have been three previous reviews that have compiled information relating to the associations between grip strength and frailty/adverse outcomes, two of which have already been discussed in Section 2 .1. The other relevant systematic review was performed by Bohannon (2008), which examined the capacity of grip strength for predicting future adverse outcomes. It was concluded that handgrip strength testing has a good predictive validity for mortality and disability, and the authors recommended its use for screening on a wider scale (Bohannon 2008). However, this review did not focus exclusively on healthy older adults, and also included studies of young and middle-aged people, as well as people living with chronic conditions (Bohannon 2008). Therefore, the transferability of the findings to the focus population of this review is questionable, and a new review that focuses on healthy older adults will be beneficial. Additionally, a number of weaknesses were identified when the CASP checklist was applied. The reliability of the search is questionable as only one reviewer carried out the entire search of all databases and abstract screening (Bohannon 2008). In addition, the author did not assess the methodological quality of any of the included studies (Bohannon 2008), and therefore the qualities of the studies are questionable. Furthermore, the final search for this review was conducted in June 2006 (Bohannon 2008), and there is a need for more up-to-date material to be included in an updated review.

Some contrasting literature has emerged since the three previous systematic reviews that included grip strength were conducted. A 3-year follow-up by Legrand et al. (2014) examined the capacity of grip strength and two other performance indicators for predicting disability, hospitalisations and mortality in adults over the age of 80. The findings of this study did not agree with those of the previous systematic reviews, and no significant associations were found between grip strength and future disability (Legrand et al. 2014). The authors did however conclude that grip strength is a strong predictor of mortality and hospitalisations (Legrand et al. 2014). A weakness of this study was that only baseline data for grip strength was used in the analysis, and the dynamic interactions of the variables were not assessed (Legrand et al. 2014). Additionally, the follow-up of 33 months was relatively short (Legrand et al. 2014), and may not have been adequate to gain a true picture of the relationships between the variables. Huang et al. (2010) carried out an 18-month prospective cohort study to examine the predictive capacity of a number of different performance indicators; including grip strength, gait speed and TUG, for detecting older adults at risk of future ADL disability. It was concluded that all three of these physical performance indicators predicted ADL disability, and would prove beneficial in screening non-disabled populations to identify at-risk individuals (Huang et al. 2010). However, because this study was carried out over a relatively short duration, and had a small sample size (n=110), the internal validity is questionable (Huang et al. 2010).

2.4 Overview of the Current Evidence Base and Rationale for this Systematic review

Although there is a relatively large body of literature that analyses the associations between gait speed and/or grip strength with frailty or its associated complications, some contrasting evidence exists. There is still some debate in the literature as to whether or not the predictive properties of gait speed are strong enough for it be used as a single-item screening tool in clinical practice. Contrasting literature also exists regarding the capacity of grip strength to predict disability. Additionally, the limitations in the methodologies of the previous systematic reviews and cohort studies bring the validity of their results into question. In addition, the transferability of the findings of one of the previous reviews that examined grip strength is also questionable (Bohannon 2008). These factors and inconsistencies combined with the fact there has not been a review examining both of these physical performance indicators in relation to frailty since 2011, support the need for an updated systematic review that focuses on healthy older adults.

3. RESEARCH QUESTION AND OBJECTIVE

3. RESEARCH QUESTION AND OBJECTIVE

Research Question: 'What is the evidence for associations between gait speed and grip strength with frailty in healthy older adults?'

Objective: To determine whether gait speed and grip strength are significant indicators of frailty and its associated adverse-health-related outcomes in healthy older adults.

4. METHODOLOGY

4. METHODOLOGY

4.1 Search Strategy

To identify studies the electronic databases MEDLINE, CINAHL, PubMed, PEDro and Cochrane Library (see Table 4.1) were systematically searched under the identified search terms and combinations (see Table 4.2). Each of these databases were selected based on their relevance to healthcare. Selection of keywords was based on their descriptions of the population, the measurement and the outcome. Two similar systematic reviews were searched in order to assist with selection of keywords (den Ouden et al. 2011; Vermeulen et al. 2011). The combinations in Table 4.2 were searched for the databases PubMed, MEDLINE, CINAHL and Cochrane Library. Due to the specificity of the search protocol for PEDro, the search criteria were different from the other databases. The PEDro search terms were (Problem: frailty AND Sub-discipline: gerontology AND Method: clinical trial) and (Problem: muscle weakness AND Sub-discipline: gerontology AND Method: clinical trial). The initial search was carried out on 2 December 2017 and the final search on 19 April 2018.

Table 4.1- Electronic Databases Searched

Database	Database Link
PubMed	www.ncbi.nlm.nih.gov
CINAHL	www.ebscohost.com
MEDLINE	www.ebscohost.com
PEDro	www.pedro.org.au
Cochrane Library	www.cochranelibrary.com

For a summary of search terms, keywords/combinations and number of hits for each database see Table 4.3. The search was limited to the English language and included publications between January 2000 and March 2018 in order to exclude out-dated studies. Search terms were discussed with the University librarian before final selection. Further filtering of the search results was required for the databases PubMed, CINAHL and MEDLINE in order to reduce the number of hits and refine the results. The PubMed search results were further refined by: ‘text availability- free full text’, ‘species- human’, ‘aged- 65+ years’, and ‘search fields- title/abstract’. Further filtering criteria for CINAHL and MEDLINE were the very similar as they were both searched via EBSCOhost Research Databases. However, the ‘Subject: Major Headings’ were different for each database. The filtering criteria for both databases excluding ‘subject: major headings’ were: ‘what I have found?- academic journals’, and ‘age- 65+ years’. The ‘Subject: Major Headings’ for each database were as follows:

- CINAHL- ‘functional status’, ‘frail elderly’, ‘ageing’, ‘gait’, ‘physical mobility’, ‘grip strength’, and ‘physical performance’.
- MEDLINE- ‘ageing’, ‘gait’, ‘frail elderly’, ‘mobility limitation’, and ‘hand strength’.

Table 4.2- Keywords and Combinations used in the Search

	Keywords	Combination
Population	1. Elderly	23. (#1 OR #2 OR #3 OR #4 OR #5)
	2. Age* OR Aging	
	3. Older people	
	4. Over 60	
	5. Geriatric	
Measurement	6. Gait AND (Speed OR Velocity)	24. (#6 OR #7 OR #8 OR #9 OR #10)
	7. Walk* AND (Pace OR Speed OR Velocity)	
	8. Grip strength	
	9. Physical Performance	
	10. Dynamom*	
Outcome	11. Frail*	25. (#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20)
	12. Disab*	
	13. Activities of daily living	
	14. Functional decline	
	15. Mobility limitation	
	16. Physical mobility	
	17. Weight loss	
	18. Physical Activity	
	19. Exhaustion	
	20. Balance	
Population, Measurement and Outcome		26. (#23 AND #24 AND #25)
Study Design	21. Random* Control*	27. (#21 OR #22)
	22. Cohort	
Population, Measurement, Outcome and Study Design		28. (#26 AND #27)

Table 4.3- Databases searched, Keywords used and Number of Hits

Database	Keywords/Combinations	No. of Hits
PubMed	Combination #28	627
CINAHL	Combination #28	351
MEDLINE	Combination #28	612
Cochrane Library	Combination #26	67
PEDro	(Problem: frailty AND Sub-discipline: gerontology AND Method: clinical trial) and (Problem: muscle weakness AND Sub-discipline: gerontology AND Method: clinical trial)	107

4.2 Inclusion Criteria

The included studies were limited to study designs of RCTs and cohort studies. Sample characteristics of the included studies were limited to healthy older adults over the ages of 60, and included both male and female participants. Also included were studies published in the English language with full-text available between January 2000 and March 2018. Studies that included gait speed and/or grip strength were also included. Definitions of key terms and variables including participants, gait speed, grip strength and frailty are described in Sections 4.4 and 4.5. Studies that included one or more of the following outcomes were included: disability, dependency, mobility limitation or functional decline. For studies that did not include any of these outcomes, the criteria for their inclusion was to include two or more of the following outcomes; care requirement, hospitalisations, falls and mortality

4.3 Exclusion criteria

Studies focusing on a patient group with a specific co-morbidity (e.g. dementia, stroke, Parkinson's, cardiac conditions, Alzheimer's etc.) were excluded. Also excluded were cohort studies with a cross-sectional design due to their poor level of evidence for assessing cause and effect (Mann 2012). Conference abstracts, dissertations, and expert opinion papers were also excluded from this systematic review as they are limited resources conducted by sole researchers, and their methodological qualities are lower than RCTs or cohort studies (CEBM 2017). Prospective cohort studies with a follow-up period of less than two years were also excluded in order to eliminate any studies that have not allowed enough time to examine the true associations between the variables. Also excluded were studies that only included composite gait speed measures that did not examine the direct associations between gait speed and frailty/adverse outcomes.

4.4 Definition of Terms

4.4.1 Participants

This systematic review was limited to healthy older adults, both male and female who were over the age of 60. Because the majority of the included studies consisted of large sample sizes of elderly people, it was impossible to ensure all of the participants were ‘healthy’. Therefore, for the purpose of this systematic review, only studies that did not include cohorts of individuals who were selected due to the presence of a common chronic condition were considered relevant.

4.5 Frailty Determinants and Outcomes

The frailty determinants that were analysed in this systematic review were gait speed and grip strength, and the outcomes were frailty and its associated adverse health-related outcomes.

4.5.1 Gait Speed

For the purpose of this review, gait speed was defined as the distance walked in a specified period of time (Kharb et al. 2011). Slow gait speed is one of the five components of Fried’s frailty phenotype (Fried et al. 2001), and has been found to be predictive of frailty (Vermeulen et al. 2011). The unit of measurement used is metres per second (m/s) (Novaes et al. 2011). As highlighted in the introduction section, gait speed is a cheap, quick and feasible physical performance measure (Peel et al. 2012). The most commonly used distances for measuring gait speed in clinical practice are 4m, 6m and 10m (Graham et al. 2008). There are a number of different methods of assessing gait speed that have been validated for use in the elderly population including (not an exhaustive list); usual gait speed, fast gait speed, TUG and timed 10-

metre walk test (Wolf et al.1999; Clegg et al. 2014; Kim et al. 2016). Both usual and fast gait speed have been validated over a number of different distances (Kim et al. 2016).

4.5.2 Handgrip Strength

Grip strength is a widely used method of measuring muscle strength, and a poor grip strength has been found to have a good capacity for predicting adverse outcomes in older adults (Bohannon 2008). Poor muscle strength is also a component of Fried's frailty phenotype (Fried et al. 2001). Grip strength is commonly tested using a dynamometer (Roberts et al. 2011). As previously highlighted in Section 1, some of the advantages of grip strength as an outcome measure are its low cost, simplicity and feasibility (Lee et al. 2017). Another advantage of grip strength measures is their portability (Bohannon 2008), and the most commonly used device, the Jamar hand dynamometer is research-validated (Hamilton et al. 1992), and has a well-established intra-rater, inter-rater and test-retest reliability (Roberts et al. 2011). Good handgrip strength testing practice involves calibrating the dynamometer and taking the best score from a number of trials to minimise bias (Fess 1987; Roberts et al. 2011).

4.5.3 Frailty

Frailty is a common syndrome associated with ageing (Thompson 2016). It is characterised by a decline in physiological reserve over time as well as an increased susceptibility to adverse outcomes, which include; disability, dependency, hospitalisations, requirement for long-term care, falls and death (Fried et al. 2004; Thompson 2016). Due to the lack of relevant studies that directly measured frailty as an outcome, studies that measured a number of different outcomes that are associated with frailty were included in this systematic review. Therefore, relevant studies with the following outcomes were included; frailty, disability, dependency functional decline, mobility limitation, falls, hospitalisations, care requirement and mortality. Some examples of validated disability and functional decline measures include (not an exhaustive list) the Katz ADL Scale, the Lawton-Brody Instrumental ADL Scale, the Rosow-Breslau Scale and the Physical Function scale (Brorsson and Asberg 1984; Wallace and Shelkey 2007; Bohannon and DePasquale 2010; Kucharska-Newton et al. 2017).

4.6 Study Selection

Study selection was carried out using Covidence (www.covidence.org), which is an online tool used for organising searches for systematic reviews. Titles and abstracts of the search results from each database were exported to Covidence. Prior to title and abstract screening, all duplicates were identified and removed by Covidence. All studies were initially screened by title and abstract and either ‘yes’, ‘no’ or ‘maybe’ were selected accordingly. ‘Yes’ was denoted to studies that met all the inclusion criteria, ‘maybe’ for studies that likely met all the inclusion criteria, and ‘no’ for studies where it was immediately evident that all the inclusion criteria were not met.. All studies that were denoted ‘yes’ or ‘maybe’ were then screened by full text to ensure all inclusion criteria were met and to decide upon studies to be included in this systematic review. Any queries on whether a study should be included or excluded were discussed with the dissertation supervisor. The reasons for excluding studies that were screened by full-text were recorded. The reference lists of included studies were hand-searched to identify any more studies that may be relevant to the research question. A PRISMA flow diagram was then devised via Covidence to report on included and excluded studies (Aparasu and Bentley 2014). See Figure 5.1 in the results section for the PRISMA flow diagram of the study selection process.

4.7 Data Extraction

One investigator carried out the data extraction independently. It is common practice for two investigators to carry out data extraction, but for the purposes of this dissertation, there was only one researcher due to University requirements. The data extraction tables included sample characteristics (sample size, age and percentage female), study design, outcome(s), frailty determinant(s), factors controlled for, and association measures (see Table 4.4). These criteria were adapted from data extraction headings used in the similar previous systematic review by den Ouden et al. (2011). This was a rigorous systematic review that scored a high methodological quality when quality assessed using the CASP systematic review checklist (den Ouden et al. 2011). Additionally, the review by den Ouden et al. (2011) examined very similar variables to this review, and extracted all of the appropriate data from the included studies.

Table 4.4- Data Extraction

Authors	Study design	Participants	Outcome(s)	Frailty Determinant(s)	Factors controlled for	Association Measures
Study 1						
Study 2						
Study 3						
Study 4						
Study 5						
Study 6						

4.8 Quality Assessment

The CASP checklist for cohort studies was used to critically appraise the included studies (CASP 2017a). Because none of the RCTs in the searches met the eligibility criteria, the CASP checklist for RCTs was not required for this systematic review. The CASP checklist for cohort studies has been established from guidelines composed by JAMA (1994) relating to medical literature (CASP 2017a). It has been devised to assess the methodological quality of cohort studies, with a particular emphasis on analysing the validity of the studies (CASP 2017a). This critical appraisal tool includes a number of methodological items, as seen in Table 4.5. The questions mainly consist of yes/no/can't tell answers (CASP 2017a). This checklist provides succinct questions, which comprehensively address all areas required for appraisal of the related studies (Nadelson and Nadelson 2014). This cohort appraisal tool provides a guided framework for answering questions, and provides systematic way of analysing the studies under three different sections: the internal and external validity, the results, and the relevance (CASP 2017a).

Quality appraisal of studies needs to clarify whether or not there is bias, what the findings of the study are, and how this can be applied in a real-world clinical context (Burls 2009). The CASP checklist for cohort studies comprehensively addresses these areas (CASP 2017a). This checklist has been validated in order to ensure standardisation of critical appraisal of the available evidence (Baker 2014). In addition, this tool has been designed so that it can be applied to studies relating to healthcare (CASP 2017a). Therefore, this appraisal checklist is appropriate for critically appraising the included studies in this review. Before selecting the CASP checklist for cohort studies for this review, the Cochrane collaboration's tool was also considered. However, because this tool exclusively focuses on bias, and does not take the results of the studies or their relevance to clinical practice into account (Higgins and Green 2011), the CASP tool was deemed to be more appropriate. The CASP cohort study checklist has no particular scoring scale (CASP 2017a). Scaled systems may simplify critical appraisal, but their use in quality assessment has a questionable evidence base (Higgins and Green 2011). It is difficult to rationalise how different items weigh in comparison to one another, and quantifying each with an equal individual score may therefore be inaccurate (Higgins and Green 2011). Scaled systems have been shown to be unreliable methods of assessing validity (Higgins and Green 2011).

Table 4.5- CASP Cohort Study Checklist (CASP 2017a)

		Study 1	Study 2	Study 3	Study 4	Study 5	Study 6
(A) Validity	1. Did the trial address a clearly focused issue?						
	2. Was the cohort recruited in an acceptable way?						
	3. Was the exposure accurately measured to minimise bias?						
	4. Was the outcome accurately measured to minimise bias?						
	5. (a)Have the authors identified all important confounding factors?						
	5. (b)Have they taken account of the confounding factors in the design and/or analysis?						
	6. (a)Was the follow up of subjects complete enough?						
	6. (b)Was the follow up of subjects long enough?						
(B) Results	7. What are the results of this study?						
	8. How precise are the results?						
	9. Do you believe the results?						
(C) Relevance	10. Can the results be applied to the local population?						
	11. Do the results of this study fit with other available evidence?						

5. RESULTS

5. RESULTS

5.1 Studies Selected

The results of the search strategy indicated in Table 4.2 had a combined total of number of hits of 1764. As described in the methodology, duplicates were removed by Covidence, and the studies were screened by title (and abstract if necessary). 1339 studies did not meet the eligibility criteria and were excluded. 33 studies were considered likely to be relevant to this review, and their full texts were retrieved. 21 of these studies did not meet the eligibility criteria and were excluded. See Table 5.1 for a list of the excluded studies after full-text review, and the reasons for exclusion. 12 studies met all of the eligibility criteria and were included in this systematic review. See Figure 5.1 for the PRISMA flow diagram reporting on the study selection process. The results of the data extraction are shown in Table 5.2.

Table 5.1-Studies Excluded and Reasons for Exclusion after Full-text Review

Author	**Reason for exclusion**
Al Snih et al. (2002)	Wrong outcome: mortality and co-morbidities were only outcomes
Steffen et al. (2002)	Wrong outcome: did not include frailty or any of its adverse outcomes
Paterson et al. (2004)	Wrong patient population: included participants under the age of 60.
Perera et al. (2006)	Wrong patient population: included stroke survivors and older adults who had a mobility disability at baseline
Hardy et al. (2007)	Wrong outcome: only included mortality
Van Iersel et al. (2008)	Wrong patient population: 45% of participants had dementia
Huang et al. (2010)	Follow-up period less than 2 years
Sallinen et al. (2011)	Wrong study design: cross-sectional
Studenski et al. (2011)	Wrong outcome: only included survival
Verghese et al. (2011)	Wrong study design: cross-sectional
Viccaro et al. (2011)	Follow up period less than 2 years
Yoshimura et al. (2011)	Wrong patient population: included participants under the age of 60
Stevens et al. (2012)	Wrong study design: cross-sectional
Woo et al. (2012)	Did not show results or discuss individual associations between gait speed or grip strength with ADL disability- Only reported Cardiovascular Health Study score associations
Bouillon et al. (2013)	Wrong outcome: only included hospitalisations
Castell et al. (2013)	Wrong study design: cross-sectional
Deshpande et al. (2013)	Wrong patient population: included participants under the age of 60
Sugiura et al. (2013)	Wrong outcome: only included higher level competence
Cooper et al. (2014)	Wrong patient population: included participants under the age of 60
Granic et al. (2016)	Wrong outcome: did not include frailty or any of its adverse outcomes
Buckinx et al. (2016)	Wrong patient population: Nursing home residents

PRISMA Flow Diagram

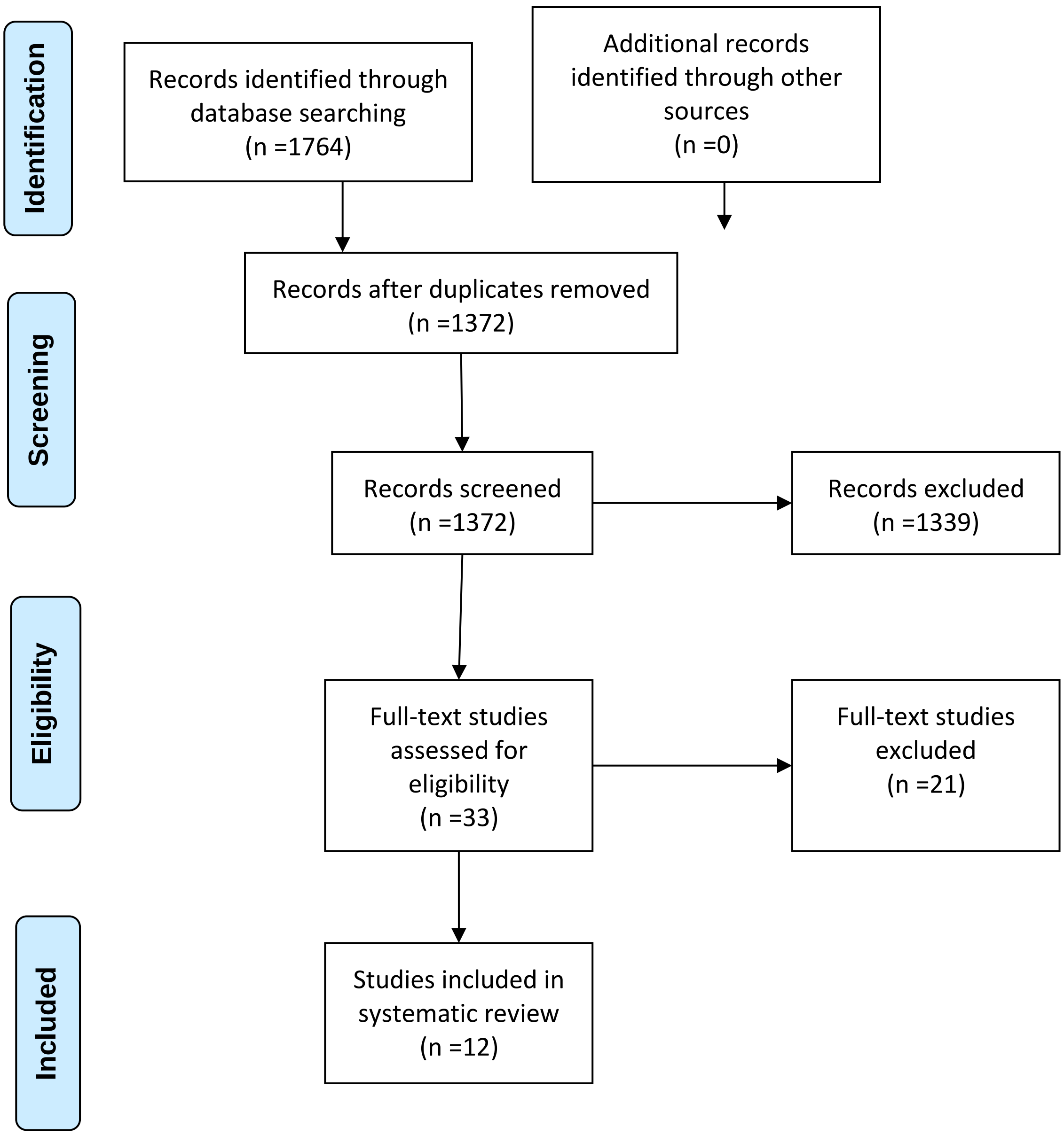

Figure 5.1- PRISMA flow diagram of the study selection process

Table 5.2- Data Extraction

Authors	Study design	Participants			Outcome(s)	Frailty Determinant(s)	Factors controlled for	Association Measures
		Sample Size (n)	Mean Age (Yrs) ± SD	% Female				
Sarkisian et al. (2000)	Prospective Cohort (8 year follow-up)	6632	73±4.9	100	Functional decline	Fast gait speed, grip strength	Age, education, smoking status, chronic conditions, cognitive function, presence of spinal fracture, enrolment site	Slow fast gait speed (≤1 m/s) predicted functional decline in basic activities [Q4 v Q1: OR= 2.29, (95% CI=1.66-3.17)] and functional decline in vigorous activities [Q4 v Q1: OR= 1.76, (95% CI=1.44-2.16)]. Weak handgrip strength predicted functional decline in vigorous ADLs [Q4 v Q1: OR=1.21, (95% CI= 0.99-1.49)] but no statistically significant associations found between weak grip strength and functional decline in basic ADLs.
Shinkai et al. (2000)	Prospective Cohort (6 year follow-up)	940	≥65;	Does not specify	ADL dependence	Gait speed (usual and fast), grip strength	Age, sex, number of comorbidities (diabetes, stroke, arthritis, CVD)	Both slow usual gait speed [Q4 v Q1: HR=2.43, (95% CI=1.42-4.17)] and slow fast gait speed [Q4 v Q1: HR= 5.15, (95% CI=2.71-9.77)] predicted ADL dependence Weak grip strength also predicted future ADL dependence [Q4 v Q1: HR= 2.51, (95% CI=1.50-4.20)]
Studenski et al. (2003)	Prospective Cohort (3 year follow-up)	487	74.1± 5.7	43.7	Hospitalisations, functional decline	Usual gait speed	Age and baseline function	Slow gait speed predicted hospitalisations and functional decline-41% of those who had slow gait speed (<0.6m/s) at baseline were hospitalised one or more times. 69% of slow gait speed group developed functional decline in at least one personal care items compared to 12% of the low risk gait speed group (>1 m/s)
Al Snih et al. (2004)	Prospective Cohort 7 year (follow-up)	2493	72	57.9	ADL disability	Grip strength	Age, marital status, chronic conditions, BMI, depression, cognitive state	Weak grip strength predicted ADL disability in both men [Q4 v Q1, HR=1.90, (95% CI=1.14-3.17)] and women [Q4 v Q1, HR=2.28, (95% CI=1.59-3.27)]

Cesari et al. (2005)	Prospective Cohort (4.9 year follow-up)	3047	74.2± 2.9	51.5	Mobility limitation, mobility disability, hospitalisations, mortality	Usual gait speed	Age, race, sex enrolment site, smoking status, cognitive state, physical activity level, BMI, chronic conditions [diabetes, HTN, CVD]	Slow usual gait speed group (<1m/s) had a rate ratio of 2.20(95% CI=1.76-2.74) for mobility limitation, 2.29(95% CI=1.63–3.20) for mobility disability, 1.48(95% CI=1.02–2.13) for hospitalisations and 1.64(95% CI=1.14–2.37) for death when compared to those in the low risk usual gait speed group (≥1m/s)
Montero-Odasso et al. (2005)	Prospective Cohort (2 year follow-up)	102	79.6± 4.0	71.3	Care requirement, nursing home placement, hospitalisations, falls, fractures, mortality	Usual gait speed,	Age, sex, comorbidities, prior falls, BMI, cognitive state and depression	Slow usual gait speed (<0.7m/s) predicted hospitalisations [RR=5.9, (95% CI=1.9–8.5)], care requirement [RR=9.5, (95% CI=1.3–2.5)], and falls [RR=5.4 (95% CI=2.0–4.3)] when compared to low risk gait speed group (>1.1 m/s). No significant associations between usual gait speed and fractures or mortality.
Rothman et al. (2008)	Prospective Cohort (8 year follow-up)	754	78.4± 5.3	64.6	chronic ADL disability, nursing home placement, traumatic falls, mortality	Fast gait speed, grip strength	Age, race, sex, education, amount of comorbidities, decreased body weight, self-reported exhaustion, low physical activity levels, muscle weakness, depression, cognitive impairment	Slow fast-gait speed predicted chronic ADL disability [HR =2.97, (95% CI=2.32–3.80)], nursing home placement [HR=3.86, (95% CI=2.23–6.67)], and traumatic falls [HR=2.19, (95% CI=1.33–3.60)]. Slow fast gait speed also indicated an increased risk of mortality [HR=1.7, (95% CI=1.2–2.3)]. No independent associations found between grip strength and any of the included adverse outcomes
Cesari et al. (2009)	Prospective Cohort (6.9 year follow-up)	3024	73.6± 2.9 .	51.6	Mobility limitation, mobility disability, hospitalisations, mortality	Usual gait speed	Age, race, sex, enrolment site, smoking status, cognitive state, physical activity level, depression, BMI chronic conditions (CVD, OA, PAD, pulmonary disease, diabetes, HTN,, CVD	Slow usual gait speed group (<1m/s) had an increased risk of mobility limitation [HR=2.49, (95% CI=2.23–2.78)], mobility disability [HR=2.45, (95% CI=2.10–2.86)], hospitalisations [(HR=1.38, (95% CI=1.13–1.68)] and mortality [HR=1.63, (95% CI=1.37–1.93)] when compared to low risk usual gait speed group (≥1m/s)

Artaud et al. (2015)	Prospective Cohort (11 year follow-up)	3,814	73.2± 4.6	61	3 disability domains: mobility disability, instrumental ADL disability, basic ADL disability	Fast gait speed	Age, sex, relationship between age and time	The HR (hazard ratio) per SD (-0.22 m/s) slower than mean baseline fast gait speed (1.54 m/s) was 1.77 (95% CI=1.60–1.94) for developing disability. Additionally, the mean yearly fast gait speed decline was 0.017m/s, and the HR per one SD (-0.13 m/s) increased yearly rate of decline in fast gait speed was 1.38 (95% CI=1.10–1.73) for developing disability
Heiland et al. (2016)	Prospective Cohort (mean follow-up 5.8 years)	1971	73.7± 10.8	63.7	ADL dependence	Usual gait speed	Age, sex, education, duration of follow-up, amount of comorbidities, cognitive impairment	High-risk group for usual gait speed group (<0.8m/s) had an increased risk [OR=8.4. (95% CI=5.2-13.3)] of ADL dependence when compared to low risk group (>1 m/s)
Perera et al. (2016)	Pooled analysis of 7 Cohorts	27220 (Total)	≥65	Varies for each study	Washing/dressing dependence, mobility limitation	Usual gait speed	Age, sex, race, BMI, prior hospitalisation, chronic conditions (diabetes, arthritis, cancer, heart disease)	Higher baseline usual gait speed was associated with a decreased risk of dependence and mobility limitation. Participants divided into sub-groups set at intervals set at every 0.2 m/s based on baseline usual gait speed results from <0.4 m/s to ≥1.4 m/s. Risk ratio per 0.1m/s faster baseline gait speed was 0.68 (95% CI=0.57–0.81) for men and 0.74 (95% CI=0.66–0.82) for women for washing/dressing dependence, and 0.75 (95% CI=0.68–0.82) for men and 0.73 (95% CI=0.67–0.80) for women for mobility limitation
Stessman et al. (2017)	Dynamic Prospective Cohort (25 year follow-up)	327, 384, 1187, and 406 in 1990, 1998, 2005 and 2010 respect-ively	70,78,85 and 90 in 1990, 1998, 2005 and 2010 respect-ively	48, 51.3, 54.8, and 51.7 in 1990, 1998, 2005 and 2010 respect-ively	ADL dependence, mortality	Grip strength	Sex, education, health status (self-report), BMI, smoking status, physical activity level, chronic conditions (ischaemic heart disease, hypertension, diabetes), depression, cognitive impairment	Weak baseline grip strength predicted ADL dependence between the ages of 78 and 85 [OR=2.68, (Q4 v Q1, 95% CI=1.04–6.89) and between 85 and 90 [Q4 v Q1, OR=2.31, (95% CI=1.01–5.30)]. Weak grip strength was also associated with a significantly higher incidence of mortality in Q1 when compared to Q2, Q3 and Q4.
SD= standard deviation, ADL= activities of daily living, CI= confidence interval, OR= odds ratio, HR= hazard ratio, RR= relative risk, CVD= cardiovascular disease, HTN= hypertension, OA= osteoarthritis, PAD= peripheral artery disease, BMI= body mass index								

5.2 Study Design

Eleven of the twelve included studies had a prospective cohort design, and the other study by Perera et al. (2016) was a pooled analysis of prospective cohorts. None of the RCTs or other types of cohort studies screened met all of the eligibility criteria for inclusion in this review. The duration of follow-up varied for each included study, ranging from 2 years (Montero-Odasso et al. 2005) to 25 years (Stessman et al. 2017).

5.3 Participants

5.3.1 Sample Size

The smallest sample size for an individual study was 102 (Montero-Odasso et al. 2005), and the largest was 6632 (Sarkisian et al. 2000). It is also important to note that the sample size of 27220 for the pooled analysis carried out by Perera et al. (2016) seen in Table 5.2 is the combined total for the seven included cohorts in that study. The mean sample size of the eleven individual prospective cohorts included was 2167. This a relatively large average sample size, which is a good aspect of the methodological strength of the studies included in this review.

5.3.2 Age

None of the selected studies included participants under the age of 60. Three of the included studies did not report the mean age ± SD, and were reported as either ≥65 (Shinkai et al. 2000; Perera et al. 2016) or the mean age (Al Snih et al. 2004). Additionally, the dynamic prospective cohort work by Stessman et al. (2017) was homogenous for age, and therefore participants were the same age at each data collection stage of the cohort study. The mean age of the ten included studies that reported an average age was 74.18 years.

5.3.3 Percentage Female

Most of the included studies had a majority female population. Only in the study by Studenski et al. (2003) and the sample of the dynamic prosprective cohort work by Stessman et al. (2017) taken in 1990 were females the minority. The proportion of females ranged from 43.7 percent (Studenski et al. 2003) to 100 percent (Sarkisian et al. 2000). The study by Shinkai et al. (2000) did not report the amount of females included.

5.4 Outcomes

5.4.1 Adverse Health-Related Outcomes

At least one form of an adverse health-related outcome of frailty was included in each of the included studies. For the purpose of this systematic review, an adverse health-related outcome is an umbrella term that includes any of the following: disability, dependency, mobility limitation, functional decline, hospitalisations, care requirement, falls or mortality. Because of the lack of studies that directly measured frailty as an outcome and the diversity of outcome measures available, the included studies used a wide-range of outcomes. Each of these outcomes were associated with frailty. See Table 5.2 for the outcomes used in each study.

5.4.1.1 ADL Disability

Nine of the twelve included studies measured either ADL disability or dependence, dependence for bathing or dressing, or functional decline. The operational term used for ADL disability varied from study to study. Some studies used ADL disability, some used ADL dependence, others used functional decline, and one study used chronic ADL disability. Each of these outcomes were mainly defined using a number of ADL tasks, and a new inability to perform at least one of these tasks on follow-up quantified either disability, dependency, or functional decline. Because all of these terms essentially quantify the same outcome (with slight variations), their results were grouped together under the umbrella term ‘disability’ for the purpose of this systematic review. The Katz ADL scale was used in six of the included studies to measure either ADL disability or dependence (Shinkai et al. 2000; Al Snih et al. 2004; Rothman et al. 2008; Artaud et al. 2015; Heiland et al. 2016; Stessman et al. 2017). Another established measure of ADL disability used in the study by Artaud et al. (2015) was the Lawton-Brody Instrumental ADL scale (Wallace and Shelkey 2007). Studenski et al. (2003) measured functional decline using part of the functional status section from the National Health Interview Survey (NHIS) and the Physical Function Scale of the Short Form Health Survey (SF-36). In the pooled analysis by Perera et al. (2016), only two ADL items were considered: bathing and dressing. The results of the seven included cohort studies were pooled together for these two tasks based on dependence (Perera et al. 2016). Summary of the ADL disability/functional decline outcomes of the included studies are as follows; Katz ADL scale (n=6), Lawton-Brody Instrumental ADL scale (n=1), NHIS functional status section (n=1), Physical Function Scale (n=1), bathing or dressing dependence (n=1).

5.4.1.2 Mobility Disability/Limitation

Four of the included studies in this systematic review analysed either mobility disability or mobility limitation (Cesari et al. 2005; Cesari et al. 2009; Artaud et al. 2015; Perera et al. 2016). Artaud et al. (2015) quantified mobility disability using the Rosow-Breslau Scale. Persistent lower extremity limitation and/or persistent severe lower extremity limitation were used as outcomes in three of the included studies (Cesari et al. 2005; Cesari et al. 2009; Perera et al. 2016). All items were quantified by level of difficulty walking a quarter mile or climbing stairs (Cesari et al. 2005; Cesari et al. 2009). Persistent severe lower extremity limitation and the results of the Rosow-Breslau Scale were categorised as mobility disability (Cesari et al. 2005; Cesari et al. 2009) and therefore was also categorised under the umbrella term ‘disability’ in the results for the purpose of this review. The other included mobility items were categorised as ‘mobility limitation’. Summary of the mobility disability/limitation outcomes of the included studies are as follows; mobility limitation (n=3) and mobility disability (n=3).

5.4.1.3 Other Adverse Health-Related Outcomes

The remaining adverse health-related outcomes that were included in the studies in this systematic review included the following; mortality, hospitalisations, care requirement, nursing home placement, falls and fractures (See Table 5.2). Mortality was quantified in five studies (Cesari et al. 2005; Montero-Odasso et al. 2005; Rothman et al. 2008; Cesari et al. 2009; Stessman et al. 2017), and hospitalisations was included in four studies (Studenski et al. 2003; Cesari et al. 2005; Montero-Odasso et al. 2005; Cesari et al. 2009). Nursing home placement and falls were both included in two studies (Montero-Odasso et al. 2005; Rothman et al. 2008), and care requirement and fractures were both included in one study (Montero-Odasso et al. 2005).

5.5 Frailty Determinants

5.5.1 Gait Speed

Ten of the twelve included studies in this systematic review measured a variation of gait speed. Seven measured usual gait speed (Shinkai et al. 2000; Studenski et al. 2003; Cesari et al. 2005; Montero-Odasso et al. 2005; Cesari et al. 2009; Heiland et al. 2016; Perera et al. 2016), and four measured fast gait speed (Sarkisian et al. 2000; Shinkai et al. 2000; Rothman et al. 2008; Artaud et al. 2015). Heiland et al. (2016) used the term self-selected gait speed. Although the exact instructions given to the participants were not documented in the protocol (Heiland et al. 2016), it can be reasonably assumed that self-selected gait speed is the same measure as usual gait speed. Five of the ten studies did not report the number of trials carried out (Sarkisian et al. 2000; Rothman et al. 2008; Artaud et al. 2015; Heiland et al. 2016; Perera et al. 2016), bringing the internal validity into question. The remaining five studies reported two or more trials, and used either the best time or the average (Shinkai et al. 2000; Studenski et al. 2003; Cesari et al. 2005; Montero-Odasso et al. 2005; Cesari et al. 2009).

Variability existed between the measurement protocols of the included studies that examined gait speed. Three of the included studies began recording gait speed from a static start (Cesari et al. 2005; Cesari et al. 2009; Perera et al. 2016). There is contrasting evidence in the literature regarding static-start gait speed assessments (Guralnik et al. 2000). The validity of these measures has been questioned due to the lack of allowance for acceleration (Guralnik et al. 2000). Lindemann et al. (2008) suggests that a distance of 2.5m is required for frail elderly to reach their steady state gait speed. However, the results of a systematic review by Peel et al. (2012) found no statistically significant differences when comparing static and moving-start gait speed measures. Therefore, the results of these three studies may potentially need to be interpreted with caution. Sarkisian et al. (2000), Rothman et al. (2008) and Heiland et al. (2016) did not specify whether a static or moving start was examined, and therefore results may need to be interpreted with caution. Both Studenski et al. (2003) and Montero-Odasso et al. (2005) allowed participants to walk 1m before timing began. Again, this may not be enough for frail elderly to meet their steady state gait velocity (Lindemann et al. 2008). Shinkai et al. (2000) and Artaud et al. (2015) both allowed three metres walking distance before the start-line.

Only five of the ten studies reported instructing the participants to continue for a specified distance after the end line to exclude deceleration from the test-time (Shinkai et al. 2000; Cesari et al. 2005; Montero-Odasso et al. 2005; Cesari et al. 2009; Artaud et al. 2015). The remaining five studies did not report allowing for this in their protocols, and their results may potentially need to be interpreted with caution. The distances used for gait speed measurement in the included studies ranged from 2m to 8m, and the most commonly used distances were 6m (n=6) and 4m (n=3). Rothman et al. (2008) used a different type of fast gait speed measure which involved walking 10 feet back and forth at maximal pace on a flat surface. Subjects who took longer than ten seconds to finish were categorised as having a slow gait speed (Rothman et al. 2008). However, the author of the current review was unable to find any evidence for validation of this measure in the literature, and therefore the results may need to be interpreted with caution. Additionally, the protocol was significantly different from the other gait speed measures used in the included studies as it involved turning in the assessment (Rothman et al. 2008).

5.5.2 Associations between Gait Speed and Frailty

See Table 5.2 for results of the association measures of the included studies that examined gait speed.

5.5.2.1 Fast gait speed and frailty

All four of the studies that included fast gait speed testing found associations between a slow fast gait speed and adverse outcomes (Sarkisian et al. 2000; Shinkai et al. 2000; Rothman et al. 2008; Artaud et al. 2015). Each of the four studies found that a slow fast gait speed was an indicator of disability. One of the studies also reported predictive associations for a slow fast gait speed with falls, care requirement and mortality (Rothman et al. 2008). In the 11-year follow-up study Artaud et al. (2015), a validated hierarchal disability indicator was used to quantify disability by pooling the results of the three individual disability scales used together

(Barberger-Gateau et al. 2000). It was found that a slow fast gait speed (≤1.49 m/s) was a strong predictor of future disability, and identified at-risk individuals up to 7 years before the onset of disability (Artaud et al. 2015). The HR (hazard ratio) per SD (-0.22 m/s) slower than mean baseline fast gait speed (1.54 m/s) was 1.77 (95% CI=1.60–1.94) for developing disability (Artaud et al. 2015). Additionally, the mean yearly fast gait speed decline was 0.017m/s, and the HR per one SD (-0.13 m/s) increased yearly rate of decline in fast gait speed was 1.38 (95% CI=1.10–1.73) for developing disability (Artaud et al. 2015).

In the 6-year follow-up study by Shinkai et al. (2000) which examined both fast and usual gait speed, it was found that both were predictive of ADL dependence. Those in the lowest quartile (Q1) for fast gait speed (≤1.81m/s) had the highest incidence of ADL dependence, with a HR of 5.15(95% CI=2.71-9.77) when compared to the highest quartile (Q4) (Shinkai et al. 2000). Interestingly, Shinkai et al (2000) concluded that fast gait speed was the most sensitive test for those aged 65-74 for predicting ADL dependence, and usual gait speed was the most sensitive for those aged ≥75. Of all the frailty criteria examined (including grip strength) in the 8-year longitudinal study by Rothman et al. (2008), a slow fast-gait speed (>10 seconds) was the most powerful predictor of chronic ADL disability [HR =2.97, (95% CI=2.32–3.80)] and nursing home placement [HR=3.86, (95% CI=2.23–6.67)]. Additionally, a slow fast gait speed also predicted traumatic falls [HR=2.19, (95% CI=1.33–3.60)], and indicated an increased risk of mortality [HR=1.7, (95% CI=1.2–2.3)] (Rothman et al. 2008). Similarly, in the 8-year prospective cohort study by Sarkisian et al. (2000), a slow fast gait speed (≤1 m/s) predicted functional decline in basic ADLs [Q4 v Q1: OR (odds ratio) =2.29, (95% CI=1.66-3.17)] and functional decline in vigorous ADLs [Q4 v Q1: OR=1.76, (95%CI=1.44-2.16)]. However, there was no consensus between the four included studies that examined fast gait speed on what cut-off speed defined slowness. The cut-offs used ranged from ≤1 m/s to ≤1.81 m/s. Rothman et al. (2008) used a cut-off time of 10 seconds rather than a cut-off speed.

5.5.2.2 Usual Gait speed and Frailty

All seven of the studies that examined usual gait speed also found associations between a slow gait speed and adverse outcomes. Six studies reported associations between slow usual gait speed and at least one of the following outcomes: disability (n=6) and mobility limitation (n=3) (Shinkai et al. 2000; Studenski et al. 2003; Cesari et al. 2005; Cesari et al. 2009; Heiland et al. 2016; Perera et al. 2016). Additionally four studies found associations between a slow usual gait speed and one or more of the following outcomes: hospitalisations (n=4), mortality (n=3), care requirement (n=1), and falls (n=1). (Studenski et al. 2003; Cesari et al. 2005; Montero-Odasso et al. 2005; Cesari et al. 2009). As mentioned in Section 5.5.2.1, Shinkai et al. (2000) found that slow usual gait speed predicted ADL dependence. Those in the lowest gait speed quartile (≤1.08m/s) had a HR of 2.43(Q4 v Q1, 95% CI=1.42-4.17) for ADL dependence (Shinkai et al. 2000). Similarly, in the 5.8-year follow-up study by Heiland et al. (2016) it was also found that a slow usual gait speed indicated future ADL dependence. The high-risk group for usual gait speed (<0.8m/s) had an increased risk of ADL dependence [OR=8.4. (95% CI=5.2-13.3)] when compared to low risk group (>1 m/s) (Heiland et al. 2016).

The pooled analysis by Perera et al. (2016) found that a slow usual gait speed (<0.4 m/s) predicted bathing/dressing dependence, mobility limitation, and mortality after the 3-year follow-up period. The results were described in terms of a higher baseline usual gait speed being associated with a decreased risk of dependence and mobility limitation (Perera et al. 2016). Participants were divided into sub-groups at intervals set at every 0.2 m/s based on baseline usual gait speed results from <0.4 to ≥1.4 m/s (Perera et al. 2016). The reported risk ratio per 0.1m/s faster baseline gait speed was 0.68 (95% CI=0.57–0.81) for men and 0.74 (95% CI=0.66–0.82) for women for washing/dressing dependence, and 0.75 (95% CI=0.68–0.82) for men and 0.73 (95% CI=0.67–0.80) for women for mobility limitation (Perera et al. 2016).

Strongest associations were reported between slow usual gait speed (<0.4 m/s) and mobility limitation, with an incidence of 40% in men and 47% in women on follow-up (Perera et al. 2016). The incidence of washing/dressing dependence was 10% of men and 15% of women in the slowest gait speed group (Perera et al. 2016).

Montero-Odasso et al. (2005) found that a slow usual gait speed (<0.7m/s) predicted a number of adverse events including care requirement [RR (relative risk) =9.5, (95% CI=1.3–2.5)], falls [RR=5.4, (95% CI=2.0–4.3)] and hospitalisations [RR=5.9, (95% CI=1.9–8.5)]. In contrary to the other studies that included mortality, no significant associations were found between a slow gait speed and mortality (Montero-Odasso et al. 2005). In the 3-year longitudinal study by Studenski et al. (2003) it was reported that a slow usual gait speed (<0.6m/s) was associated with an increased occurrence of hospitalisations, and predicted functional decline. 41% of the high-risk gait speed group (<0.6m/s) were hospitalised one or more times, compared to 11% of the low risk group (>1 m/s) on follow-up (Studenski et al. 2003). Additionally, 69% of the high-risk group developed a new difficulty in at least one personal care item compared to 12% of the low-risk group (Studenski et al. 2003).

Both studies by Cesari et al. (2005) and Cesari et al. (2009), found that a slow usual gait speed (<1 m/s) was associated with an increased risk of each of the adverse outcomes included. In the 4.9-year follow-up study by Cesari et al. (2005) it was found that the slow usual gait speed group (<1 m/s) had a rate ratio of 2.20(95% CI=1.76-2.74) for mobility limitation, and 2.29(95% CI=1.63–3.20) for mobility disability. In addition, the slow gait speed group had a rate ratio of 1.48(95% CI=1.02–2.13) for hospitalisations and 1.64(95% CI=1.14–2.37) for mortality when compared to those in the low risk group (≥1m/s) (Cesari et al. 2005). Similarly, in the 6.9-year prospective cohort study by Cesari et al. (2009), the high-risk usual gait speed group (<1m/s) had an increased risk of mobility limitation [HR=2.49, (95% CI=2.23–2.78)] and mobility disability [HR=2.45, (95% CI=2.10–2.86)] when compared to the low risk group (≥1m/s). They also had an increased risk of hospitalisations [(HR=1.38, (95% CI=1.13–1.68)] and mortality [HR=1.63, (95% CI=1.37–1.93)] (Cesari et al. 2009). There was no consensus on what cut-off speed defined a slow usual gait speed between the included studies, and the cut-points used ranged from <0.4 m/s to ≤1.08 m/s.

5.5.3 Handgrip Strength

Five of the studies included in this review measured grip strength (Sarkisian et al. 2000; Shinkai et al. 2000; Al Snih et al. 2004; Rothman et al. 2008; Stessman et al. 2017). Dynamometers were used in all five studies to measure maximal grip strength. However, variability existed between the protocols for measuring and calculating grip strength of the included studies. Shinkai et al. (2000) and Al Snih et al. (2004) used the highest reading of two trials in the dominant hand. Sarkisian et al. (2000) used the average strength score of both hands. Rothman et al. (2000) used the average of three trials in the dominant hand, and Stessman et al. (2017) used the highest of three trials in the dominant hand. Each study that included grip strength recorded two or more trials. None of the five studies reported any information on checking the calibration of the dynamometer used. Therefore the results of these studies may potentially need to be interpreted with caution, as calibration is essential for ensuring accuracy and consistency of results, and devices should be checked for calibration prior to testing (Chavan et al. 1975). Both Shinkai et al. (2000) and Rothman et al. (2008) failed to report a standardised arm position protocol, or any measures taken to ensure intra-rater reliability between administrators, bringing the internal validity into question. The importance of a standardised protocol was highlighted in a study by Spijkerman et al. (1991), in which participants were instructed to position themselves in whatever position they felt comfortable in for grip strength testing, and the results were significantly different when compared to using a standardised protocol.

A different type of dynamometer was used in each of the five studies. In a study by Guerra and Amaral (2009) that compared three different dynamometers to the Jamar dynamometer, which was used by Al Snih et al. (2004), including the Preston dynamometer, which was used by Sarkisian et al. (2000), found that none of the three dynamometers produced results that were comparable that of the Jamar device when applied to the elderly population. All devices had been calibrated prior to testing (Guerra and Amaral 2009). This may indicate that some of the instruments used in the included studies of this review may potentially be less accurate than others. Shinkai et al. (2000) does not report the type of dynamometer used, and the author of the current review was unable to find any evidence in the literature for validation of the devices used in the studies by Sarkisian et al. (2000), Rothman et al. (2008) and Stessman et al. (2017). Al Snih et al. (2004) used the Jamar hand dynamometer, which as previously discussed, is research-validated (Hamilton et al. 1992), and is considered the gold-standard when a standardised protocol is used (Roberts et al. 2011).

5.5.4 Associations between Handgrip Strength and Frailty

See Table 5.2 for results of the association measures of the included studies that examined grip strength. Four of the five included studies that examined handgrip strength found statistically significant associations between grip strength and disability (Sarkisian et al. 2000; Shinkai et al. 2000; Al Snih et al. 2004; Stessman et al. 2017). However, one of these four studies only found significant associations between a weak grip strength and functional decline in vigorous ADLs, and not basic ADLs (Sarkisian et al. 2000). In addition, of the two studies that included mortality (Rothman et al. 2008; Stessman et al. 2017), only one found statistically significant associations with weak grip strength (Stessman et al. 2017). In the 7-year follow-up study by Al Snih et al. (2004), it was found that a weak grip strength predicted future ADL disability. The HR for those in weakest quartiles for grip strength was 1.90 (Q4 v Q1, 95% CI=1.14-3.17) for men (<22kg), and 2.28 (Q4 v Q1, 95% CI=1.59-3.27) for women (<14kg) (Al Snih et al. 2004). Similarly, Shinkai et al. (2000) found that weak grip strength predicted ADL dependence (Q4 v Q1: HR= 2.51, [95% CI=1.50-4.20)]. The cut-off points for the lowest quartiles were ≤27kg for men and ≤16kg for women (Shinkai et al. 2000). In the 25-year dynamic prospective cohort work by Stessman et al. (2017) (baseline age=70 years), it was also reported that weak baseline grip strength predicted ADL dependence between the ages of 78 and 85 [Q4 v Q1, OR=2.68, 95% CI=1.04–6.89) and between 85 and 90 [Q4 v Q1, OR=2.31, (95% CI=1.01–5.30)]. Weak grip strength was also associated with a significantly higher incidence of mortality in Q1 when compared to Q2, Q3 and Q4 (Stessman et al. 2017). The baseline cut-off for weak grip strength for those in the lowest quartiles was <30kg for men and <18kg for women (Stessman et al. 2017).

In the study by Sarkisian et al. (2000), weak grip strength was found to be associated with an increased risk of functional decline in vigorous ADLs [Q4 v Q1: OR=1.21, (95% CI= 0.99-1.49)], but no statistically significant associations were found for functional decline in basic ADLs over the course of the 8-year follow-up. This study included females only and the cut-point for those in the lowest grip strength quartile was <15kg (Sarkisian et al. 2000). In contrast to the other studies, the 8-year longitudinal study carried out by Rothman et al. (2008) did not find any significant associations between grip strength and chronic ADL disability, or any of the other included adverse outcomes. The average cut-point for weak grip strength used in this study was <30.5kg for men and <19kg for women (Fried et al. 2001; Rothman et al. 2008). There was no consensus on cut-points to define weak grip strength between the five included studies that examined grip strength. The cut-points used ranged from <22kg to <30.5kg for men, and from <14kg to <19kg for women. No two studies used the same cut-off point.

5.6 Quality Assessment

For the results of the quality assessment, see Table 5.3. The pooled analysis by Perera et al. (2016) was not quality assessed, as it was not appropriate for appraisal by any of the CASP checklists. Because the CASP checklist does not use a scoring scale; the results are discussed under the checklist's three sub-sections; validity, results and relevance.

5.6.1 Validity

All eleven assessed studies scored a 'Y' (yes) for the initial two questions relating to whether or not the authors focused on a clearly focused issue and whether or not the cohort was recruited in an acceptable way. Only four of the studies scored a 'Y' for the third question on whether or not the exposure was measured accurately. The seven other studies scored a 'CT' (can't tell) mainly due to either lack of detail in the studies' protocols or no evidence being found for validation of the measure used. The reasons have been discussed in Sections 5.5.1 and 5.5.3. Only four of the included studies scored a 'Y' for the fourth validity question on whether or not the outcome was accurately measured to minimise bias. The remaining seven studies scored a 'CT' due to no evidence being found in the literature for validation of the outcome used. The reasons are discussed in more detail in Sections 6.1 and 6.2. Nine of the eleven studies identified all the important confounding factors, and nine of the eleven studies also took all of the confounding factors in the design/analysis into account. See Table 5.2 for the confounding factors adjusted for in each study. The internal validity of the study by Studenski et al. (2003) is particularly questionable, as the authors have not adjusted for chronic conditions, even though participants living with comorbidities were not excluded. All of the appraised studies had a complete enough follow-up, and all except the study by Montero-Odasso et al. (2005), which scored a ‘N’ (no) for question 6.(b), had a long enough follow-up. The study by Montero-Odasso et al. (2005) had a 2-year follow up, which may not have been sufficient to examine associations with mortality.

5.6.2 Results

Descriptions and summaries of the results for each study are indicated in Tables 5.2 and 5.3 respectively. The results of all eleven studies had a degree of accuracy to 95% confidence interval (CI). All studies scored a ‘Y’ for whether or not the results were believed by the reviewer.

5.6.3 Relevance

All eleven studies scored a ‘Y’ for both relevance questions relating to whether or not the results can be applied to the local population, and whether the results fit with other available evidence.

Table 5.3- Quality Assessment

	CASP quality appraisal																
	Authors		**Validity**								**Results**			**Relevance**			
			1. Did the trial address a clearly focused issue?	2. Was the cohort recruited in an acceptable way?	3. Was the exposure accurately measured to minimise bias?	4. Was the outcome accurately measured to minimise bias?	5. (a)Have the authors identified all important confounding factors?	5. (b)Have they taken account of the confounding factors in the design and/or analysis?	6. (a)Was the follow up of subjects complete enough?	6. (b)Was the follow up of subjects long enough?	7. What are the results of this study?	8. How precise are the results?	9. Do you believe the results?	10. Can the results be applied to the local population?	11. Do the results of this study fit with other available evidence?		
	Sarkisian et al. (2000)		Y	Y	CT	Y	Y	Y	Y	Y	Slow gait speed and weak grip strength predicted functional decline. However, weak grip strength did not predict decline in basic ADLs.	95% CI	Y	Y	Y		
	Shinkai et al. (2000)		Y	Y	CT	CT	Y	Y	Y	Y	Both slow gait speed and weak grip strength predicted ADL dependence	95% CI	Y	Y	Y		
	Studenski et al. (2003)		Y	Y	Y	CT	N	N	Y	Y	Slow gait speed predicted functional decline and hospitalisations	95% CI	Y	Y	Y		
	Al Snih et al. (2004)		Y	Y	CT	CT	Y	Y	Y	Y	Weak grip strength predicted ADL disability	95% CI	Y	Y	Y		
	Cesari et al. (2005)		Y	Y	Y	CT	Y	Y	Y	Y	Slow gait speed indicated an increased risk of mobility limitation, mobility disability, hospitalisations and mortality	95% CI	Y	Y	Y		

	Montero-Odasso et al. (2005)		Y	Y	Y	Y	Y	Y	Y	N	Slow gait speed predicted care requirement, hospitalisations and falls. No associations with fractures/mortality	95% CI	Y	Y	Y	
	Rothman et al. (2008)		Y	Y	CT	CT	Y	Y	Y	Y	Slow gait speed predicted chronic ADL disability, nursing home placement, traumatic falls and mortality. No associations for grip strength with adverse outcomes	95% CI	Y	Y	Y	
	Cesari et al. (2009)		Y	Y	Y	CT	Y	Y	Y	Y	Slow gait speed indicated an increased risk of mobility limitation, mobility disability, hospitalisations and mortality	95% CI	Y	Y	Y	
	Artaud et al. (2015)		Y	Y	CT	Y	N	N	Y	Y	Slow fast gait speed indicated an increased risk of disability.	95% CI	Y	Y	Y	
	Heiland et al. (2016)		Y	Y	CT	CT	Y	Y	Y	Y	Slow gait speed indicated an increased risk of ADL dependence	95% CI	Y	Y	Y	
	Perera et al. (2016)		Study not quality assessed as pooled analysis not appropriate for assessment with CASP tools													
	Stessman et al. (2017)		Y	Y	CT	Y	Y	Y	Y	Y	Weak grip strength predicted ADL dependence and indicated an increased risk of mortality	95% CI	Y	Y	Y	
Y= Yes, N= No, CT= Can’t Tell, CI= confidence interval																

5.7 Summary of Results

All ten of the studies that examined a variation of gait speed found that there were associations between gait speed and at least one adverse outcome that are associated with frailty. All nine studies that examined the associations between gait speed and disability, and all three studies that examined the associations between gait speed and mobility limitation, found that a slow gait speed was associated with an increased risk of these outcomes. Additionally, three of the four studies that included gait speed and mortality, and all four studies that included gait speed and hospitalisations, also found that a slow gait speed was associated with an increased risk of these outcomes. An increased risk of requirement for care and falls was also reported, although the number of studies that examined these variables were limited (n=2). There was no consensus between the studies on what cut-off speeds defined either a slow usual gait speed or a slow fast gait speed. Some contrasting evidence was reported regarding grip strength. Four of the five grip strength studies that included disability found statistically significant associations, but Sarkisian et al. (2000) only found associations with future functional decline in vigorous ADLs, and not in basic ADLs. Additionally, only one of the two studies that included mortality found significant associations with grip strength. The majority of the evidence found that a weak grip strength was associated with an increased risk of disability. However, the predictive associations between gait speed and disability appeared to be more powerful and more consistent than that of grip strength. Additionally, there was no consensus between the five studies on what cut-off points define a weak grip strength.

6. DISCUSSION

6. DISCUSSION

The objective of this systematic review was to determine whether gait speed and grip strength are significant indicators of frailty and its associated adverse-health-related outcomes in healthy older adults. The key findings of this review were that slow gait speed was associated with an increased risk of future disability, hospitalisations, mortality, requirement for care and falls, and the majority of evidence reported that weak grip strength was associated with an increased risk of future disability. The associations between gait speed and an increased risk of future disability also appeared to be stronger and more consistent than that of grip strength.

6.1 Associations between Gait Speed and Frailty

6.1.1 Fast Gait Speed and Frailty

All four of the included studies that evaluated the associations between fast gait speed and disability found statistically significant associations (Sarkisian et al. 2000; Shinkai et al. 2000; Rothman et al. 2008; Artaud et al. 2015). Three of these studies examined the associations between several different physical performance indicators (including grip strength) and disability (Sarkisian et al. 2000; Shinkai et al. 2000; Rothman et al. 2008). Each of these three studies concluded that fast gait speed was the most powerful predictor of disability compared to the other indicators. In the 11-year follow-up study by Artaud et al. (2015), it was concluded that monitoring changes in fast gait speed by regular testing is important for older adults, as an accelerated fast gait speed decline indicated an increased probability of disability, regardless of what the baseline speed was. Rothman et al. (2008) also concluded that a slow fast gait speed was the most powerful predictor of falls and nursing home placement when compared to the other examined performance indicators, and was the second strongest predictor of mortality after low physical activity levels (Rothman et al. 2008). As previously highlighted, no consensus between the included studies on what speed defined a slow fast gait speed was found.

However, it is important to note that each of these four studies scored a ‘CT’ for the third CASP checklist question on whether or not gait speed was measured accurately to minimise bias. The reasons have been highlighted in Section 5.5.1. Additionally, the studies by Shinkai et al. (2000) and Rothman et al. (2008) both scored a ‘CT’ for whether or not the outcome was accurately measured to minimise bias. Both of these studies used modified versions of the Katz ADL scale to measure ADL disability. However, the author of this review was unable to find any evidence of validation of these modified scales in the literature. Therefore, although all four of these studies agree that a slow fast gait speed is associated with an increased risk of disability, their results may potentially need to be interpreted with caution. However, there was a consensus of findings between the four studies in terms of the associations between fast gait speed and disability, and each of the studies scored relatively highly on the CASP checklist, and relatively strong associations were reported. Therefore, despite the limitations, it is reasonable to conclude that fast gait speed is a good indicator of future risk of disability, and could potentially be used as a screening measure in clinical settings. The associations for gait speed with falls, requirement for long-term nursing home stays and mortality are discussed in Section 6.1.3.

6.1.2 Usual Gait Speed and Frailty

All seven studies that analysed the associations between usual gait speed and adverse outcomes found statistically significant associations. All six studies that included usual gait speed and disability found that usual gait speed is an effective tool for identifying elderly people at risk of disability (Shinkai et al. 2000; Studenski et al. 2003; Cesari et al. 2005; Cesari et al. 2009; Heiland et al. 2016; Perera et al. 2016). Additionally, Cesari et al. (2005), Cesari et al.

(2009) and Perera et al. (2016) all concluded that usual gait speed predicts mobility limitation in older adults. All four studies that examined the associations between usual gait speed and hospitalisations found that a slow gait speed is an indicator of hospitalisations (Studenski et al. 2003; Cesari et al. 2005; Montero-Odasso et al. 2005; Cesari et al. 2009). Of the three studies that examined the associations between usual gait speed and mortality (Cesari et al. 2005; Montero-Odasso et al. 2005; Cesari et al. 2009), all except study by Montero-Odasso et al. (2005) found that a slow usual gait speed is an indicator of mortality. However, it is important to note that this study had a relatively small sample size (n=102) and short follow-up period (two years) (Montero-Odasso et al. 2005), which may not have been adequate to gain an accurate picture of the true associations with mortality. Montero-Odasso et al. (2005) also concluded that slow usual gait speed predicts falls and requirement for care.

As well as the previously highlighted limitation of the study by Montero-Odasso et al. (2005), there were also limitations of the other six included studies that examined usual gait speed. Both Shinkai et al. (2000) and Heiland et al. (2016) scored a ‘CT’ on the CASP checklist for whether or not gait speed was measured accurately enough to minimise bias. The reasons have been highlighted in Section 5.5.1**.** In addition, the author of the current systematic review was unable to find any evidence in the literature for validation of at least one outcome in each of these six studies. These included the modified versions of the Katz ADL scale used by Shinkai et al. (2000) and Heiland et al. (2016), the modified NHIS functional decline measure used by Studenski et al. (2003), and the washing/dressing dependence scale used by Perera et al. (2016). Additionally, no evidence was found for validation of the mobility limitation outcomes used by Cesari et al. (2005), Cesari et al. (2009) and Perera et al. (2016). In addition, Studenski et al. (2003) did not adjust for comorbidities in the analysis. Therefore, the results of all seven of the included studies that examined usual gait speed may potentially need to be interpreted with caution. However, all studies scored relatively highly on the CASP checklist, and there was a consensus between a relatively good number of studies regarding the associations for usual gait speed with disability, mobility limitation, hospitalisations. Therefore, it is reasonable to conclude that usual gait speed is a good indicator of disability, mobility limitation and hospitalisations. The conclusions drawn on the associations for gait speed with mortality, falls and requirement for care are discussed in section 6.1.3.

6.1.3 Overview of Gait Speed and Frailty

All nine studies that examined gait speed and disability, all four studies that included gait speed and hospitalisations, and all three studies that included gait speed and mobility limitation found significant associations, the majority of which were relatively strong. Therefore, despite the limitations, it is reasonable to conclude that gait speed is a good indicator of these three outcomes. Although there was less evidence for the associations between gait speed and falls, both studies concluded gait speed was a predictor of falls (Montero-Odasso et al. 2005; Rothman et al. 2008), and this was in line with the findings of a previous systematic review by Abellan Van Kan et al. (2009). Therefore, it would not be unreasonable to conclude that gait speed is also an indicator of falls. However, future research should examine gait speed and falls in more detail to confirm these findings. The only one of the four studies that included gait speed and mortality that did not find significant associations had a short follow period which may not have been adequate to gain a true picture of the associations (Montero-Odasso et al. 2005). The other three studies found that gait speed is an indicator of mortality, which is in accordance with the findings of the previous review by Abellan Van Kan et al. (2009). Additionally, the methodological qualities of these three studies were also relatively high. Therefore, it would not be unreasonable to conclude that gait speed is also an indicator of mortality despite the previously highlighted limitations. Because there was limited evidence for the associations for gait speed with requirement for care/nursing-home stays, the author of this review has reservations about accepting these findings. Future research including studies with larger sample sizes and longer follow periods should examine these variables in more detail.

6.2 Associations between Grip strength and Frailty

As previously highlighted in Section 5.5.4**,** Rothman et al. (2008) was the only one of the five included studies that examined grip strength and disability not to find significant associations between a weak grip strength and an increased risk of disability. The other four other studies found that weak grip strength is an indicator of disability (Sarkisian et al. 2000; Shinkai et al. 2000; Al Snih et al. 2004; Stessman et al. 2017). However, Sarkisian et al. (2000) found that a weak grip strength only indicated future functional decline in vigorous ADLs, and not in basic ADLs. There was contrasting evidence for associations between grip strength and mortality. Only two of the included grip strength studies included mortality, with Stessman et al. (2017) finding grip strength is a significant predictor of mortality and Rothman et al. (2008) finding no significant associations.

However, it is important to note that each of the included studies that examined grip strength had limitations. All five studies scored a ‘CT’ on the CASP checklist for whether or not grip strength was measured accurately to minimise bias. The reasons have been underlined in Section 5.5.3. Additionally, Shinkai et al. (2000), Al Snih et al. (2004) and Rothman et al. (2008) all used modified versions of the Katz ADL scale as outcomes for which the author of this review was unable to find any evidence of validation for in the literature. Therefore, the results of all five of the studies that have examined grip strength may potentially need to be interpreted with caution. However, the methodological qualities of each of these studies were relatively high, and there was a consensus between the majority of studies on the associations between grip strength and disability, which was in accordance with the findings of a previous review by

Bohannon (2008). Therefore, despite the limitations, it would not be unreasonable to conclude that grip strength is an indicator of disability, and handgrip dynamometry could potentially be used for screening in clinical settings. The evidence for associations between grip strength and mortality was limited and contrasting, and therefore inconclusive, and no consensus was found on what cut-points define a weak grip strength for either males or females.

6.3 Comparison with Previous evidence

The findings of this review were in accordance with those of two previous systematic reviews in this area by den Ouden et al. (2011) and Vermeulen et al. (2011) who both found the gait speed and grip strength are indicators of disability. Additionally, the finding of the current review that gait speed appeared to a more powerful indicator of disability than grip strength was also in line with the conclusions drawn by Vermeulen et al. (2011).

6.3.1 Gait Speed

The findings of this review in terms of gait speed were in line with those of two previous systematic reviews conducted by Clegg et al. (2014) and an expert panel from the IANA task force (Abellan Van Kan et al. 2009) who both found significant associations with frailty/adverse outcomes. The IANA task force found that gait speed was an indicator of disability, mortality and falls (Abellan Van Kan et al. 2009), and Clegg et al. (2014) concluded that gait speed is an indicator of frailty, both of which agree with the findings of this review. The expert panel concluded that the associations were strong enough for gait speed to be implemented as a single-item screening tool in clinical settings (Abellan Van Kan et al. 2009). Whereas, the more recent review by Clegg et al. (2014) concluded that the associations between gait speed and frailty were not strong enough for gait speed to be used a single-item screening tool. In the current review, none of the included studies assessed gait speed’s efficacy as a single-item screening tool in clinical settings, and therefore this was not determined. The review by Abellan Van Kan et al. (2009) also concluded that the optimal cut-off speed for determining slow gait speed was 0.8 m/s for older adults, whereas the findings of the current review in relation to an optimal cut-point was inconclusive.

6.3.2 Handgrip Strength

The findings of this review were in line with those of another previous review by Bohannon (2008), which also found that grip strength is an indicator of disability. However, Bohannon (2008) also concluded that grip strength is an indicator of mortality, whereas the findings of the current review in relation to these associations were inconclusive. The findings of this review were also in accordance with those of a previous prospective cohort study by Huang et al. (2010), who also concluded that a weak grip strength was an indicator of disability. Conversely, the findings of another follow-up study by Legrand et al. (2014) disagreed with those of the current review by concluding that there were no significant associations between grip and disability. The fact that the majority of evidence from the included studies found that grip strength is an indicator of disability with some contrasting evidence is in line with previous evidence.

6.4 Limitations

It is important to acknowledge that there were a number of limitations of this systematic review. This review only considered studies written in the English language, which may have potentially excluded important relevant studies. Another limitation was that only one reviewer carried out the entire search of all databases and abstract screening in order to coincide with University regulations for the purpose of this dissertation, potentially bringing the reliability of the search into question. Furthermore, because the CASP checklists are non-scaled appraisal tools (CASP 2017a; CASP 2017b), there are no set guidelines on what distinguishes high, moderate and low quality evidence studies. Therefore, the author of this review interpreted the relative strength of the studies subjectively, and consequently the accuracy of the quality classifications made may potentially be questionable. Another limitation was that because there was no appropriate CASP tool for appraising a pooled analysis of cohort studies, the study by Perera et al. (2016) was not quality assessed. Lastly, no contact was made with authors of the included studies to clarify areas that lacked information. A number of studies lacked detail in their protocols and contacting authors would have helped to clarify whether or not correct measurement precautions were considered (e.g. checking calibration). Additionally, the author of the current review was unable to find evidence for validation of outcomes used in several of included studies, and clarification with the authors of the studies would have been beneficial.

7. IMPLICATIONS

7. IMPLICATIONS

7.1 Implications for Clinical Practice

There is the potential for both of these performance indicators to be used as routine screening measures in clinical settings. Although the findings of this review indicate that gait speed is a more powerful indicator of frailty/adverse outcomes than grip strength, both tools could potentially be used in conjunction with one another in clinical practice. These are both simple, quick, cheap and feasible tools (Lee et al. 2017), and could realistically be administered by healthcare assistants routinely on a wide scale if appropriate training was provided. Identifying elderly people at risk of frailty can potentially help to reduce the burden on healthcare systems and the associated costs by allowing targeted intervention programs to be implemented (Monteserin 2010; Buckinx et al. 2015). Frailty is a potentially reversible syndrome (Pialoux et al. 2012), and preventative interventions before the onset of frailty occurs could therefore potentially reduce the prevalence of disability, mobility limitation, hospitalisations, mortality and falls among older adults. Preventing frailty would not only be beneficial for healthcare systems, but also for the individual's quality of life and their families (Buckinx et al. 2015). Additionally, because falls are an adverse outcome of frailty (Thompson 2016), individuals identified as being either frail or at-risk of frailty/adverse outcomes could potentially be identified for further falls-risk assessment with more established tools such as the Tinetti Balance and Gait Assessment or the Berg Balance Scale (Mancini and Horak 2010). As highlighted in Section 1, falls costs the NHS £2.3 billion every year (NHS 2017). Identifying those at-risk at an early stage on a wide scale could potentially help to lower these costs by allowing early interventions to prevent falls before they occur, rather than only targeting individuals that have a history of falls.

7.2 Implications for Future Research

There are a number of gaps in the literature and areas identified in this review that should be addressed in future research. The current systematic review and the two previous reviews in this area have focused on the elderly population (den Ouden et al. 2011; Vermeulen et al. 2011). Den Ouden et al. (2011) recommended that future research should focus on younger populations. This is still an area that needs to be addressed. Future research should include middle-aged populations to investigate whether either of these performance indicators can be used to identify individuals at risk of frailty/adverse outcomes a number of years in advance. Future research should also analyse the associations for grip strength with hospitalisations, requirement for care and mortality. Although the review by Abellan Van Kan et al. (2009) concluded that the optimal cut-off point for defining slow usual gait speed was 0.8 m/s, more recent studies have still been using different cut-off speeds (Huang et al. 2010; Lopez-Teros et al. 2013). Additionally, no consensus was found in the current review for cut-off points for gait speed (either usual or fast) or grip strength. There is a need for universally accepted standardised optimal cut-off points to be established at a national or international level if gait speed and grip strength are to be used as screening tools on a large scale, and future research should address this. Furthermore, standardised protocols for measuring and calculating gait speed and grip strength also need to be established as a significant amount of variability existed between the protocols of the included studies in this review.

Additionally, Shinkai et al. (2000) found that usual gait speed had a higher sensitivity for predicting of ADL dependence than fast gait speed in those aged ≥75, and fast gait speed was the most sensitive measure in those aged 65-74. Future studies should examine these relationships further to confirm these findings, as this may have particularly important clinical implications. Furthermore, there is still some debate in the literature as to whether or not gait speed is a powerful enough indicator of frailty/adverse outcomes to be implemented as a single-item screening tool in clinical settings (Abellan Van Kan et al. 2009; Clegg et al. 2014). Future research should address this. Lastly, another recommendation by den Ouden et al. (2011) was that future studies should assess the effects of preventative interventions on elderly people that have been identified as at-risk of adverse outcomes. This is still an area that needs to be addressed. Future research should investigate what types of interventions are most effective and feasible.

8. CONCLUSION

8. CONCLUSION

Based on the findings of the current systematic review, both gait speed and grip strength appear to be indicators of frailty and its associated adverse health-related outcomes. Gait speed seems to be an indicator of future disability, mobility limitation, hospitalisations, mortality and falls, and grip strength appears to be an indicator of future disability. Gait speed appears to be a stronger indicator of future disability than grip strength. Integrating these physical performance tests into clinical settings on a large scale as routine screening measures could potentially allow for individuals at risk of frailty and its associated adverse outcomes to be identified so that preventative interventions can be implemented.

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10. APPENDICES

Appendix A

CASP Cohort Study Checklist (CASP 2017a)

(A) Validity	Did the trial address a clearly focused issue?
	Was the cohort recruited in an acceptable way?
	Was the exposure accurately measured to minimise bias?
	Was the outcome accurately measured to minimise bias?
	(a)Have the authors identified all important confounding factors?
	(b)Have they taken account of the confounding factors in the design and/or analysis?
	(a)Was the follow up of subjects complete enough?
	(b)Was the follow up of subjects long enough?
(B) Results	What are the results of this study?
	How precise are the results?
	Do you believe the results?
(C) Relevance	Can the results be applied to the local population?
	Do the results of this study fit with other available evidence?

Appendix B

CASP Systematic Review Checklist (CASP 2017b)

(A) Validity	Did the review address a clearly focused question?
	Did the authors look for the right type of papers?
	Do you think all the important, relevant studies were included?
	Did the review's authors do enough to assess quality of the included studies?
	If the results of the review have been combined, was it reasonable to do so?
(B) Results	What are the overall results of the review?
	How precise are the results?
(C) Relevance	Can the results be applied to the local population?
	Were all important outcomes considered?
	Are the benefits worth the harms and costs?

Word Count: 13,711