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Analysis of Gait Speed and its Correlates in Middle-Aged and Older Adults: Findings from the Canadian Longitudinal Study on Aging

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Abstract

Gait speed is a marker of health and independence in older adults. Mitigation of gait speed impairments through intervention on modifiable risk factors is key to preventing adverse health declines. Using cross-sectional data from adults aged 45 to 85 years in the Canadian Longitudinal Study on Aging, this thesis estimated population gait speed norms and 'slow gait' prevalence and assessed the potentially modifiable and non-modifiable correlates of gait speed. Significantly slower average gait speeds and greater proportions of gait speeds below 1.0 m/s were seen in older age groups. While gait speed variability was largely explained by non-modifiable factors, statistically significant associations were found for several clinical and lifestyle factors that are modifiable through intervention and education. These findings were corroborated by our systematic review on the modifiable risk factors for slow gait speed in older community-dwellers. Future longitudinal research is required to explore the clinical relevance of these findings.

Keywords

gait speed; older adults; community-dwellers; risk factors; Canadian Longitudinal Study on Aging

Summary for Lay Audience

Gait (walking) speed is a marker of health and independence in older adults. Slow gait has been linked to a greater risk of falls, dependence in everyday activities, multimorbidity, cognitive decline, and mortality. To prevent and delay gait speed slowing and these negative outcomes, it is important to target risk factors that can be changed through clinical intervention and lifestyle modification. Using the cross-sectional data of adults aged 45 to 85 years in the Canadian Longitudinal Study on Aging, this thesis estimated population gait speed norms and the proportion of individuals with 'slow gait' and assessed the potentially modifiable and non-modifiable factors associated with gait speed. Significantly slower average gait speeds and greater proportions of gait speeds below 1.0 m/s were seen in older age groups. While gait speed variability was largely explained by non-modifiable factors, statistically significant associations were found for several potentially modifiable clinical and lifestyle factors. These findings were corroborated by our systematic review on the modifiable risk factors for slow gait speed in older community-dwellers. Future longitudinal research is required to explore the clinical relevance of these findings.

Co-Authorship Statement

This thesis follows an integrated format and includes three articles that have been or will be submitted for publication in peer-reviewed journals. Chapter 2 appears in the same format as when it was submitted for publication. Chapter 4 appears as an extended manuscript that will be re-formatted for future publication. Chapter 5 appears in an extended format as when it was submitted for publication. Co-authorship for each of these articles is described below.

Chapter 2: Figgins, E., Pieruccini-Faria, F., Speechley, M., Montero-Odasso, M. Modifiable Risk Factors for Slow Gait in Community-Dwelling Older Adults: A Systematic Review

Chapter 2 was written by Erica Figgins, with Dr. Speechley, Dr. Montero-Odasso, and Dr. Pieruccini-Faria as co-authors. Erica Figgins is the primary author of this paper. She performed all literature searches and article screening, extracted data from the included studies, and completed all draft writing. Dr. Montero-Odasso and Dr. Speechley are credited with conceptualizing the topic for this review and revising all drafts pre- and post-submission. Dr. Pieruccini-Faria is credited with assisting with article appraisal and draft revisions. This paper was submitted for publication to *Ageing Research Reviews* on May 9, 2020 (currently under review).

Chapter 4: Figgins, E., Montero-Odasso, M., Speechley, M. Normative Values of Gait Speed among Middle and Older-Aged Adults: Analysis of Data from the Canadian Longitudinal Study on Aging

Chapter 4 was written by Erica Figgins, with Dr. Speechley and Dr. Montero-Odasso as co-authors. Erica Figgins is the primary author of this paper and performed all analyses and writing. Dr. Speechley and Dr. Montero-Odasso are credited with providing methodological support for the analyses and draft revisions.

Chapter 5: Figgins, E., Choi, Y-H., Speechley, M., Montero-Odasso, M. Associations between Reversible Risk Factors and Gait Speed in Middle and Older-Aged Community-Dwelling Adults: Results from the Canadian Longitudinal Study on Aging

Chapter 5 was written by Erica Figgins, with Dr. Speechley, Dr. Montero-Odasso, and Dr. Yun-Hee Choi as co-authors. Erica Figgins is the primary author of this paper and performed all analyses and writing. Dr. Speechley, Dr. Montero-Odasso, and Dr. Choi are credited with providing methodological support for the analyses and draft revisions. This paper was submitted for publication to the *Journal of Gerontology: Medical Sciences* on August 12, 2020.

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List of Abbreviations

AFT	Animal Fluency Test
BMI	Body Mass Index
CESD-10	Center for Epidemiologic Studies Short Depression Scale (10-item)
CLSA	Canadian Longitudinal Study on Aging
COPD	Chronic Obstructive Pulmonary Disease
DSST	Digit Symbol Substitution Test
FCS	Fully Conditional Specification
HDL	High Density Lipoprotein
hsCRP	High Sensitivity C-Reactive Protein
MAR	Missing at Random
MCAR	Missing Completely at Random
MAT	Mental Alternation Test
NIH	National Heart Lung and Blood Institute
PASE	Physical Activity Scale for the Elderly
RAVLT	Rey Auditory Verbal Learning Test
TMT	Trail Making Test

Chapter 1

1 Introduction

1.1 Overview

The purpose of this chapter is to provide background information about the main topics of this thesis. The objectives and hypotheses of the studies as well as an overview of subsequent chapters will also be provided.

1.2 Biology of Gait

Gait is an essential function for humans that allows for movement through ever-changing environments with variable terrains. The production, maintenance, and adaptability of gait involves a complex interplay among multiple physiological and anatomical systems associated with locomotion. These pathways are typically influenced by additional factors outside of the locomotor system including neuropsychological factors and age-related declines in health and physical function.[1,2]

Early descriptions of the production of rhythmic gait movements suggested that it was an automatic motor task regulated solely by neural inputs from structures such as central pattern generators.[3,4] This belief, however, was challenged by the discovery that higher-order structures in the central nervous system significantly influence gait production as well. Under this revised mechanism, aspects of automaticity in gait production are acknowledged, but the ability to maintain and adapt one's gait in response to the perception of environmental stimuli is explained to be the result of coordinated communication among multiple brain regions associated with cognitive functions such as executive function, attention, and memory.[5–8] Greater demands are placed on these functions in response to multitasking conditions that involve performing additional tasks while simultaneously walking.[9] If the control of these complex cognitive functions becomes impaired, the allocation of necessary resources to effectively adjust one's motor behaviours in response to multiple tasks and stimuli is limited and abnormalities in gait performance can arise.[10]

1.3 Gait Speed Analysis

The act of walking can be described through the measurement of several spatiotemporal and biomechanical parameters including stride length, cadence, support time, and gait speed.[11,12] The analysis of these parameters in real-time has not only contributed to the understanding of usual gait but has also advanced efforts aimed at exploring the nature of gait impairments and their association with morbidity over the lifespan. Gait speed specifically has been recognized as an important measure of physical function as well as an indicator of health status and future well-being.[13] Methods of measuring gait speed include both manual and electronic techniques. For example, many gait speed tests involve individuals walking a prespecified distance while their time to cover this distance is measured using a stopwatch. Other more sophisticated methods can include the use of electronic walkways that record gait speed digitally.[14] Currently, a variety of different distances are employed for walking tests, with shorter distances between 4 meters and 10 meters most commonly used.[15] While a consensus on a standard protocol for walking test distance has not yet been adopted, tests with variable distances are thought to produce comparable results after being standardized to meters per second (m/s).[15,16]

1.4 Adverse Outcomes Associated with Slow Gait Speed

Analyses of gait in healthy individuals using the assessment tools described above have demonstrated that gait speed typically remains constant over early and middle adulthood.[17,18] Average usual gait speeds among healthy adults aged 20 to 60 years generally range between approximately 1.30 m/s to 1.45 m/s for men and 1.20 m/s to 1.40 m/s for women.[17] While declines in gait speed due to the biological effects of aging are expected once individuals reach older adulthood, the development of slower gait speed below the normal threshold, regardless of age, is indicative of possible underlying health problems.[19]

The association between slow gait and adverse outcomes is well documented. For example, adults who walk at slower paces face a greater risk of falls and musculoskeletal injuries,[20,21] morbidity,[22–24] and premature mortality.[25,26] Current guidelines have detailed general gait speed ranges and rates of clinically meaningful decline in gait speed that are

commonly associated with aspects of functional independence and health. In general, individuals with gait speeds of 1.0 m/s or faster have the highest functional independence and the lowest risk of experiencing adverse outcomes, however as gait speed declines below 1.0 m/s, issues are more likely to arise.[27] Namely, adults with gait speeds slower than 0.8 m/s, and especially slower than 0.6 m/s, frequently face mobility impairments and are more likely to fall, be hospitalized, and even be discharged to nursing care facilities.[27,28] In terms of quantifying declines in speed over time, annual declines ranging between 0.05 m/s and 0.1 m/s are also used as clinically meaningful indicators of health status.[29]

1.5 Risk Factors of Slow Gait Speed

As slow gait is quite prevalent among older adults and can have drastic impacts on wellbeing,[30] there is a pressing need to better understand its etiology so that effective intervention strategies can be developed and implemented in at-risk populations. Current understanding from the literature is that gait speed is influenced by a complex set of factors, which may vary between different populations of adults. These factors can be classified generally as non-modifiable and potentially modifiable. Risk factors that are non-modifiable include individual characteristics that cannot be intervened upon such as age, sex, and height. Conversely, risk factors that are considered potentially modifiable can be altered, managed, and/or prevented through clinical intervention and lifestyle changes. While gait speed can be significantly influenced by both types of factors, the factors that can be modified or prevented are especially important to efforts to mitigate slow gait and its negative effects in clinical and public health practice.

1.6 Thesis Overview

This thesis is presented in an integrated article format. The content of each chapter is listed below. Because of this format, some repetition of information is inevitable.

Chapter 2 includes a systematic review with the objective to summarize the potentially modifiable risk factors that are associated with ‘slow’ and ‘slowing’ gait speed in community-dwelling adults aged 60 years and older.

Chapter 3 provides in-depth details on the Canadian Longitudinal Study on Aging (CLSA) and thorough explanations of the methods employed in the analyses presented in Chapters 4 and 5.

Chapter 4 examines and compares the gait speed norms of men and women in four 10-year age groups as well as the prevalence of slow gait within these strata using baseline data from the Canadian Longitudinal Study on Aging (CLSA) Comprehensive cohort.

Chapter 5 explores the cross-sectional associations between demographic, clinical, anthropometric, and lifestyle factors and gait speed among participants in the CLSA baseline Comprehensive cohort to determine the influence of non-modifiable and potentially modifiable factors.

Chapter 6 provides a summary and final discussion of the findings presented in the studies within this thesis. It includes a description of research contributions, study limitations, and directions for future research.

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Chapter 2

2 Modifiable Risk-Factors for Slow Gait in Community-Dwelling Older Adults: A Systematic Review

A version of this chapter has been submitted for publication.

2.1 Abstract

Purpose: Slow gait speed in older adults is associated with increased risk for falls and fractures, functional dependence, multimorbidity, and even mortality. The risk of these adverse outcomes can be reduced by intervening on potentially modifiable risk factors. The purpose of this systematic review was to identify potentially modifiable risk factors associated with slow gait speed and clinically meaningful gait speed decline in older community-dwelling adults.

Methods: Literature searches were conducted in MEDLINE, EMBASE, CINAHL, Google Scholar, and in the bibliographies of retrieved articles.

Results: Forty studies met the inclusion criteria for qualitative review. Study designs were cross-sectional and longitudinal. Operational definitions of 'slow gait' and 'meaningful gait speed decline' were variable and based on sample distributions (e.g. quartiles), external criteria (e.g. < 0.8 m/s), and dynamic changes over time (e.g. ≥ 0.05 m/s decline per year). Twenty-six potentially modifiable risk factors were assessed in at least two studies. The risk factors most commonly investigated and that showed significant associations with slow gait and/or meaningful gait speed decline include physical activity, education, body mass index, pain, and depression/depressive symptoms.

Conclusion: Among older community-dwellers, potentially modifiable factors such as physical activity, education, body mass index, pain, and depression/depressive symptoms have been associated with slow or declining gait speed. Methods used to operationalize these outcomes must be considered when assessing risk factor effects. Our results suggest that there are modifiable targets to maintain gait speed that should be examined further in future investigations.

Keywords: gait speed, aging, systematic review, epidemiology

2.2 Introduction

Impairments in mobility are prevalent among older adults.[1] In particular, slow gait speed has garnered much attention due to its association with negative health outcomes including falls, musculoskeletal injuries, comorbidities, and mortality.[2–6] Slow gait is also a marker of general functionality and is linked with overall well-being and the ability to participate independently in daily activities.[7]

The causes of slowing gait speed with aging are understood to be multi-factorial.[8] Analyses of gait function across the adult lifespan have shown associations between several non-modifiable risk factors and declines in gait speed, with aging being one of the strongest predictors of such decline.[9,10] Due to the impact of slow gait on individuals' health and quality of life and its ability to predict future deterioration of health, research interest is shifting towards identifying potentially modifiable causes of gait speed decline and slow gait speed. In contrast to non-modifiable factors that are unalterable such as age and sex at birth, modifiable risk factors can potentially be altered and/or managed through various methods including clinical treatment and lifestyle changes. By identifying and intervening on these factors, diagnosis and treatment strategies can be improved to mitigate further morbidity and disability associated with gait speed impairment in at-risk populations.[11]

Previous systematic reviews have explored the influence of cognitive function on gait speed in aging populations.[12,13] However no systematic review has yet provided a comprehensive review of non-cognitive related factors associated with slow gait speed or clinically meaningful gait speed decline that could potentially be modified to prevent progressive declines in this motor function. Therefore, the aim of this systematic review was to identify potentially modifiable clinical and lifestyle factors associated with slow gait speed and clinically meaningful gait speed decline in older community-dwelling adults.

2.3 Methods

2.3.1 Inclusion and Exclusion Criteria

Studies were included if they met the following inclusion criteria: 1) sample of community-dwelling adults in any country, 2) subjects aged 60 years and older on average, 3) assessment of usual, or self-selected, gait speed as an independent physical function through face-to-face assessment using any measured time and distance walk test, 4) clearly stated operational definition (criteria or cutoff) of slow gait or clinically meaningful decline in gait speed, 5) investigation of at least one potentially modifiable risk factor for slow gait or clinically meaningful decline in gait speed, and 6) observational study design (cohort, cross-sectional, case-control).

Studies were excluded under the following conditions: 1) mean age of subjects under 60 years, 2) subjects were hospitalized, institutionalized, or sampled because of diagnosis of specific clinical conditions (e.g. Parkinson's disease or stroke), 3) assessment of risk factors using only composite outcome measures of physical function (e.g. frailty), 4) measurement of gait speed from treadmill walking, walking on non-flat surfaces, or other tests of ambulation (e.g. Dual-Task tests, Timed Up and Go test), or 5) intervention studies to improve physical functioning. Non-peer reviewed articles, systematic reviews, meta-analyses, randomized trials of interventions, case report and series, ideas, editorials, opinions, and animal research studies identified in the bibliographic search were also excluded.

2.3.2 Search Strategy

Article searches were performed in June 2019 in MEDLINE, EMBASE, and CINAHL. The search strategy was developed through consultation with a research librarian at Western University (Marisa Tippett) using MeSH and keyword terms that are related to the main elements of the research question. Key terms included walking speed, slow gait, aged, and community-dwelling (see Appendix 1 for full search strategy and results). No publication date or language restrictions were applied, and no comparison group was identified due to the exploratory nature of the review. Furthermore, searches in Google

Scholar using key terms and searches through the reference lists of the relevant articles were performed.

2.3.3 Study Screening and Selection

Articles retrieved from the online searches were exported into the Mendeley citation manager. After removing duplicates, level 1 screening of titles and abstracts of the potentially eligible articles was completed by one independent reviewer (EF). For level 2 screening, the full texts of articles selected from level 1 were retrieved and independently assessed for eligibility by two co-authors (EF and FF). Disagreements about study eligibility were discussed and resolved between EF and FF. Disagreement about study eligibility not resolved between EF and FF were taken to senior authors of this study (MS and MMO) for final decision.

2.3.4 Data Extraction

Data extraction was completed by one reviewer (EF). The information extracted included author, year of publication, study design and location, participant characteristics, method of gait speed measurement, criteria used to define slow gait or clinically meaningful decline in gait speed, and main statistical findings including identified risk factors. If any information was not provided, "NR" (Not Reported) was inputted into the corresponding section.

2.3.5 Risk of Bias Assessment

The methodological quality of the included studies was assessed by two independent reviewers (EF and FF) using the "Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies" developed by the National Heart, Lung, and Blood Institute (NIH).[14] This tool comprises 14 items to evaluate aspects of internal validity of observational studies including selection bias, information and measurement bias, and confounding. Each item could be given one of the following ratings: Yes, No, Not Applicable, Not Reported, or Cannot Determine. Studies were given a quality rating based on the number of items met using the NIH guidelines and then categorized as "good" [met 10-14 criteria], "fair" [met 5-9 criteria], or "poor" [met 0-4 criteria].[15]

Disagreements about scoring for each item were discussed and resolved between the reviewers. A summary of overall study ratings is provided in Table 2-1.

2.3.6 Synthesis of Results

In this quantitative systematic review, the data extracted from the selected articles were tabulated to allow for a synthesis of the findings that included summaries and comparisons of participant characteristics, outcome assessments, and overall trends of main findings. Meta-analyses of risk factor effects were not conducted due to heterogeneity in outcome cut-offs and lack of evidence for many factors.

2.4 Results

2.4.1 Study Quality and Characteristics

Forty articles published between 2006 and 2019 were included in this review; 21 were cross-sectional while 19 were longitudinal, with reported follow-ups ranging from 1 to 12 years. Most studies were performed in North American (14/40) and Asian (11/40) countries, with the remaining studies from Europe, South America, the Middle East, and Australia. The overall quality of each article is summarized in Table 2-1. Briefly, 15 studies were rated as ‘Good’ and 25 were rated as ‘Fair’. The cross-sectional studies generally achieved lower scores as their design inherently prohibited the assessment of a temporal relationship between the exposures and outcome. All studies reported the use of valid measurement tools to assess the variables of interest and most accounted for important covariates in their analyses. Sample size or power justification and blinding of study assessors was reported in less than a quarter of the studies. The full quality assessment for all articles is provided in Appendix B.

Sample sizes ranged from 108 to 7025 and the proportion of female participants ranged from 0% to 100%. Usual (i.e. self-selected) gait speed was measured in all studies, with walking test distances ranging from 2.4 meters to 20 meters. The most common walk test distances employed were 6 meters (9/40), 4 meters (7/40), 4.6 or 5 meters (7/40), 3 meters (6/40), and 20 meters (4/40). Distances less than 3 meters were reported in three studies, while those between 7 and 20 meters were reported in the remaining studies.

Criteria to define individuals as having slow gait or clinically meaningful decline in gait speed were reported in all studies but were noticeably inconsistent. The studies used a mix of relative (e.g. sample distribution-based, such as lowest quartile) and absolute (e.g. external criterion, such as less than 0.8 meters per second) cutoffs, as well as measures of changing gait speed (e.g. decline of 0.05 meters per second per year). Relative and absolute cutoffs were seen in both cross-sectional and longitudinal analyses while measures of changing gait speed could only be used in studies that assessed gait speed on multiple occasions over time. The most commonly used sample distribution-based criteria for slow gait were lowest quintile (8/40) and lowest quartile of gait speed (6/40) with various adjustments for factors such as age, sex, and height, and ≥ 1 standard deviation below age and sex gait speed means (3/40). The most common external criterion cutoffs for slow gait were < 0.8 m/s (7/40) and < 1.0 m/s (6/40). In the longitudinal studies, the most common definitions of significant declines in gait speed were ≥ 0.05 m/s decline per year (3/40) and ≥ 0.1 m/s decline per year (2/40). These heterogeneous measures resulted in a wide range of prevalence of slow gait in the 17 cross-sectional studies, with the frequency ranging between 1.56% to 65.8%. Among the longitudinal studies, 17 reported the frequency of participants who experienced a clinically meaningful decline in gait speed at follow-up. A full summary of study characteristics and findings can be found in Appendix C (Tables C-1 and C-2).

Table 2-1. Quality of studies included in review.

Author	**Year**	**Quality***
Kyrdalen et al.[16]	2019	Fair
Montero-Odasso et al.[17]	2019	Good
Nasimi et al.[18]	2019	Fair
Toyama et al.[19]	2019	Good
Laclaustra et al.[20]	2019	Good
Kwan et al.[21]	2019	Fair
Lassale et al.[22]	2019	Good
Xu et al.[23]	2019	Fair
Umegaki et al.[24]	2018	Fair

Adachi et al.[25]	2018	Fair
Simonsick, Aronson et al.[26]	2018	Good
Taylor et al.[27]	2018	Fair
Simonsick, Schrack et al.[28]	2018	Good
Ayers et al.[29]	2017	Good
Shafie et al.[30]	2017	Fair
Veronese et al.[31]	2017	Fair
Yokoyama et al.[32]	2017	Fair
Gill et al.[33]	2016	Good
Garcia-Esquinas et al.[34]	2016	Fair
Naples et al.[35]	2016	Good
Zeng et al.[36]	2016	Fair
Verghese et al.[37]	2016	Good
Plouvier et al.[38]	2016	Fair
Rosano et al.[39]	2016	Fair
Frison et al.[40]	2015	Fair
Tchalla et al.[41]	2015	Fair
Kirkness et al.[42]	2015	Fair
Lo-Ciganic et al.[43]	2015	Good
Busch et al.[44]	2015	Fair
Kim et al.[45]	2015	Good
Lana et al.[46]	2015	Fair
Leon-Munoz et al.[47]	2014	Good
Wu et al.[48]	2013	Fair
Ruggero et al.[49]	2013	Fair
Hirani et al.[50]	2013	Fair
Thorpe et al.[51]	2011	Good
Eggermont et al.[52]	2010	Fair
Yoshida et al.[53]	2010	Fair
Shardell et al.[54]	2009	Fair

Chu et al.[55]	2006	Good

*NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

2.4.2 Factors Assessed for Association with Gait Speed

A total of 85 potentially modifiable risk factors were studied. Refer to Appendix C (Tables C-1 and C-2). Of the 85 factors, 26 were found in at least two studies. As summarized in Table 1-2, the most commonly assessed factors include physical activity (10/40), body mass index (10/40), education level (7/40), pain (6/40), heart conditions (6/40), and depression/depressive symptoms (5/40). Each study tested associations at the five percent level of significance and the proportion of studies that reported statistically significant findings for each factor ranged from zero to 100 percent. All studies that examined education level, polypharmacy, calf circumference, digit symbol substitution test, and Mediterranean diet reported statistically significant effects. Other factors with statistically significant effects reported in less than 100 but at least 50 percent of studies included pain, depression/depressive symptoms, falls, fear of falling, arthritis, grip strength, impaired vision, physical activity, body mass index, bone mineral density, high sensitivity C-Reactive protein, and albumin. Results should be interpreted with caution because statistical significance can be influenced by sample size and statistically significant effects may not necessarily be clinically meaningful.

Table 2-2. Summary of risk factors assessed in at least two studies.

Factor Classification	Factors assessed in ≥ 2 studies	No. Studies that included the factor	No. (%) Studies reporting significant factor effects
Sociodemographic	Education Level	7/40	7/7 (100%)
Clinical	Pain	6/40	5/6 (83.3%)
	Heart Conditions	6/40	2/6 (33.3%)
	Depression/Depressive symptoms	5/40	4/5 (80%)
	Multimorbidity	4/40	1/4 (25%)
	Hypertension	4/40	1/4 (25%)
	Stroke	4/40	1/4 (25%)
	Falls	4/40	3/4 (75%)
	Arthritis	4/40	2/4 (50%)
	Grip Strength	3/40	2/3 (66.7%)
	Diabetes	3/40	0/3 (0%)

	Polypharmacy	2/40	2/2 (100%)
	Fear of Falling	2/40	1/2 (50%)
	Impaired Vision	3/40	2/3 (66.7%)
Lifestyle	Physical Activity	10/40	9/10 (90%)
	Smoking	3/40	0/3 (0%)
	Alcohol Consumption	3/40	1/3 (33.3%)
Body Composition	Body Mass Index	10/40	8/10 (80%)
	Calf Circumference	2/40	2/2 (100%)
	Bone Mineral Density	2/40	1/2 (50%)
Serum	Vitamin D	3/40	1/3 (33.3%)
	High Sensitivity C-Reactive Protein	2/40	1/2 (50%)
	Albumin	2/40	1/2 (50%)
Cognition	Digit Symbol Substitution	2/40	2/2 (100%)
	Trail Making Test	2/40	0/2 (0%)
Dietary	Mediterranean Diet	2/40	2/2 (100%)

2.4.2.1 Sociodemographic Factors

Education Level: Seven studies examined education as a contributor to slow gait speed or clinically meaningful decline in speed.[16,23,27,30,42,44,51] Xu et al. and Taylor et al. reported significantly reduced odds of slow gait for individuals with more than a high school education (OR=0.85, 95% CI=0.78; 0.93 and OR=0.49, 95% CI=0.36; 0.66 respectively). Taylor et al. further found a non-significant result for individuals with high school education only. In terms of being less educated, significantly increased odds of slow gait or clinically meaningful speed decline for individuals with 10 or fewer years of education were reported by Kyrdalen et al., Shafie et al., and Busch et al. with ORs ranging from 2.69 to 3.58. Additionally, Kirkness et al. reported significantly greater odds of slow gait for those with high school education or less, while Thorpe et al. reported a significantly greater odds of meaningful speed decline among women with less than 9th grade reading level abilities. Finally, Busch et al. and Shafie et al. reported significantly higher odds of slow gait among adults who were illiterate or who had no formal education (OR=3.20, 95% CI=NR and OR=5.11, 95% CI=2.04; 12.79 respectively).

Other Factors: Other sociodemographic risk factors for slow gait or clinically meaningful speed decline that were only identified in single studies were occupation,[38] not owning a home,[51] and low annual income.[42] Protective factors identified in single studies were access to medical care and being an urban resident.[36,42]

2.4.2.2 Clinical Factors

Depression and Depressive Symptoms: The association between slow gait and depression or depressive symptoms was estimated in five studies.[16,25,29,37,42] Using scores on modified versions of the Center for Epidemiologic Studies Depression Scale or Geriatric Depression Scale to categorize individuals as having depression or not, Kirkness et al. and Adachi et al. reported significantly higher odds of slow gait for individuals with depression (OR=1.97, 95% CI=1.35; 2.87 and OR=2.73, 95% CI=1.12; 6.68 respectively), while Verghese et al. reported a non-significant association for those with depression (RR=1.19, 95% CI=0.84; 1.69). Furthermore, Kyrdalen et al. found significantly greater odds of slow gait for individuals with more depressive symptoms and Ayers et al. reported greater risk of developing slow gait among individuals with symptoms of apathy.

Pain: Six studies examined the relationship between slow gait speed or clinically meaningful speed decline and pain.[26,27,37,42,45,52] Taylor et al. and Verghese et al. found that recent or frequent experience of pain in general was significantly associated with slow gait (OR= 1.38, 95% CI=1.11; 1.73 and RR=1.45, 95% CI=1.11; 1.89), however Kim et al. reported a non-significant association for pain (OR=0.76, 95% CI=0.45; 1.31). In addition, Eggermont et al. reported significantly greater odds of slow gait for individuals with higher tender point counts but did not find a significant association for single, multi-site, or widespread pain. In terms of specific pain sites, Kirkness et al. and Kim et al. found that knee pain significantly increased the odds of slow gait (OR=1.43, 95% CI=1.02; 2.01 and OR= 1.73, 95% CI=1.08; 2.76 respectively). Kirkness et al. additionally reported a significant effect for back pain on slow gait (OR=1.45, 95% CI=1.05; 2.01), however Simonsick et al. reported non-significant associations for lower limb and joint pain.

Multimorbidity: Measures of multimorbidity were included as potential predictors of slow gait speed or clinically meaningful speed decline in four studies.[16,27,36,51] Only Taylor et al. reported significant results for increased odds of slow gait in people with two comorbidities (OR=1.54, 95% CI=1.12; 2.11) and in those with three or more comorbidities (OR=2.18, 95% CI=1.48; 3.20). Contrarily, Zeng et al. found that having two or more comorbidities was not a significant predictor in their stepwise regression model for slow gait, and Kyrdalen et al. reported non-significant associations between slow gait and having three to four comorbidities or having five to eleven comorbidities (OR=1.32, 95% CI=0.51; 3.22 and OR=1.41, 95% CI=0.52; 3.43 respectively). Thorpe et al. also did not find a significant association between having two or more comorbidities and experiencing clinically meaningful gait speed decline over time in neither men (OR=1.31, 95% CI=0.97; 1.76) nor women (OR=1.22, 95% CI=0.89; 1.68).

Hypertension: Four studies assessed the association between hypertension and slow gait.[23,37,41,42] Both Kirkness et al. and Verghese et al. reported non-significant effects for hypertension (OR=1.41, 95% CI=0.96; 2.09 and RR= 0.98, 95% CI=0.70; 1.38 respectively). Xu et al. also did not find a significant effect (values not reported). However, in their assessment of the relationship between circulating vascular cell adhesion molecule-1 and slow gait, Tchalla et al. found a significant interaction effect between this vascular-related molecule and hypertension on slow gait as compared to normotensive individuals (OR= 3.01, 95% CI=1.56; 5.83).

Heart conditions: The association between slow gait and various heart conditions was examined in six studies.[23,37,38,42,44,45] Two of these studies created composite variables for cardiovascular conditions. First, using a composite variable that included angina, myocardial infarction, and cardiac failure, Verghese et al. found that having a heart condition did not significantly predict developing slow gait in the future (RR=1.01, 95% CI=0.74; 1.39). Second, using a different composite variable for cardiovascular disorder that included diagnosis of hypertension, arteritis, coronary heart disease, and stroke, Plouvier et al. found that having a cardiovascular disorder was not significantly associated with slow gait in women, but was among men (OR= 2.09, 95% CI=1.22; 3.58). Using single heart condition variables, Busch et al. reported that individuals with

cardiovascular disease were approximately twice as likely to have slow gait, while Kim et al. did not find a significant association between heart disease and slow gait (OR=1.30, 95% CI=0.74; 2.30). Xu et al. also did not find a significant effect for heart disease. Finally, Kirkness et al. reported no significant effect for heart failure alone on having slow gait.

Stroke: Four studies assessed the association between history of stroke and slow gait.[23,37,42,49] Using a cross-sectional design, Ruggero et al. reported significantly greater odds of slow gait for those who have experienced a stroke (OR= 3.41, 95% CI=1.31; 8.86), however no significant relationships between history of stroke and slow gait were found by Kirkness et al. or Xu et al. Verghese et al. also reported a non-significant effect for stroke history using a longitudinal analysis.

Polypharmacy: The relationship between polypharmacy and slow gait or clinically meaningful speed decline was measured in two studies.[16,17] Montero-Odasso et al. reported significantly increased odds of slow gait for more medications taken both cross-sectionally and longitudinally (OR=1.27, 95% CI=1.13; 1.42 and OR= 1.21, 95% CI=1.10; 1.32 respectively) and found that the risk of developing slow gait over time was more than three times higher for individuals with polypharmacy. Additionally, Kyrdalen et al. found significantly greater odds of slow gait for those taking 6 to 17 medications (OR= 4.28, 95% CI=1.63; 11.2) but not for those taking less than six medications.

Falls and Fear of Falling: Four studies examined falls and two studies examined fear of falling as potential predictors of slow gait or meaningful decline in gait speed.[16,37,45,49,55] Both Verghese et al. and Chu et al. reported significant associations between recent fall history and incidence of slow gait or meaningful speed decline (RR= 1.32, 95% CI=1.04; 1.66 and RR= 2.42, 95% CI=1.53; 3.83 respectively). Contrarily, Kim et al. did not find a significant association between experience of any falls and slow gait (OR=1.78, 95% CI=0.82; 1.86). Furthermore, Kyrdalen et al. found that recent history of multiple falls was linked to significantly greater odds of slow gait (OR= 3.70, 95% CI=1.18; 11.65), however no effect was seen for previous experience of a single fall. Lastly, Kyrdalen et al. did not find a significant association between fear of falling and slow gait (OR= 1.84,

95% CI=0.84; 4.02), however Ruggero et al. showed significantly greater odds of slow gait for individuals who reported being fearful of falling (OR= 2.27, 95% CI=1.21; 4.24).

Grip Strength: The association between grip strength and slow gait was examined in three studies.[25,37,44] Using grip strength values one or more standard deviations below age and sex means to categorize individuals as having muscle weakness, Verghese et al. reported a significantly greater incidence of slow gait for individuals classified as weak compared to non-weak (RR=1.48, 95% CI=1.07; 2.05). Using grip strength as a continuous measure, Adachi et al. found grip strength to be inversely associated with slow gait (OR=0.82, 95% CI=0.73; 0.93), however a significant relationship was not found by Busch et al.

Arthritis: Measures of arthritis were assessed as potential predictors of slow gait speed or clinically meaningful speed decline in four studies.[37,42,45,51] Kirkness et al. reported significantly greater odds of slow gait for individuals with clinically diagnosed knee osteoarthritis (OR=2.06, 95% CI=1.47; 2.89), while Thorpe only found a significant association for self-reported knee osteoarthritis among women (OR= 1.78, 95% CI=1.18; 2.69). Kim et al. reported a non-significant effect for self-reported knee osteoarthritis on slow gait (OR=1.19, 95% CI=0.67; 2.10). Lastly, Thorpe et al. reported a non-significant effect for hip osteoarthritis and Verghese et al. did not find a significant association between self-report of any type of arthritis and incidence of slow gait (RR=1.05, 95% CI=0.71; 1.53).

Diabetes: All three studies that examined the relationship between diabetes and slow gait reported non-significant associations.[23,37,42]

Impaired Vision: Three studies assessed the relationship between vision impairment and slow gait.[16,37,55] While Kyrdalen et al. did not find a significant association (OR=1.54, 95% CI=0.70; 3.40), Verghese et al. reported significantly greater risk of incident slow gait for those with poor vision (RR= 1.36, 95% CI=1.02; 1.89). Chu et al. also found poor visual acuity to be significantly associated with meaningful gait speed declines (RR=2.41, 95% CI=1.22; 4.78).

Other Clinical Factors: Other clinical risk factors for slow gait or clinically meaningful speed decline only identified in single studies were metabolic syndrome,[23] musculoskeletal disorders,[38] lung disease,[42] cancer,[42] disability,[30] hyperuricemia,[31] urinary incontinence,[49] and fatigability.[28] Other singularly identified clinical factors that did not have a significant association with slow gait or meaningful decline were statin use,[43] drug interactions,[35] hyperlipidemia,[45] COPD,[44] asthma,[42] tumor,[23] dyslipidemia,[23] renal function,[19] self-rated health,[36] ulcer,[42] tiredness and energy level,[28] and osteoporosis.[45]

2.4.2.3 Lifestyle Factors

Physical Activity: The relationship between level of physical activity and slow gait was examined in ten studies.[19,23,25,30,36–38,44,45,49] Seven of these studies found significantly lower odds of slow gait among those who reported being physically active in some way, with ORs ranging from 0.27 to 0.94. Plouvier et al. reported significantly lower odds only for individuals who engaged in recreational activities for more than two hours per week and Kim et al. did not find a significant association between regular exercise and slow gait (OR= 0.79, 95% CI=0.50; 1.26). In terms of physical inactivity, both Verghese et al. and Ruggero et al. reported significantly greater likelihood of slow gait for individuals who were not physically active (RR= 1.94, 95% CI=1.20; 3.12 and OR=2.24, 95% CI=1.18; 4.25 respectively).

Smoking: Three studies included smoking as a potential predictor of slow gait.[23,36,38] None of these studies found smoking to significantly influence the odds of having slow gait.

Alcohol Consumption: Three studies included alcohol consumption as a potential correlate of slow gait.[23,36,37] While Xu et al. reported significantly lower odds of slow gait for those who consumed alcohol (OR= 0.71, 95% CI=0.54; 0.95), Zeng et al. and Verghese et al. found no significant association between alcohol consumption and likelihood of slow gait.

Other Lifestyle Factors: Other lifestyle factors that were associated with slow gait but were only identified in single studies were unstructured daily routine and impaired activities of daily living.[36,44] Other singularly identified clinical factors that did not have a significant association with slow gait were hours of sleep and poor sleep quality.[23,37] Finally, factors identified in single studies that showed a protective effect were hobby engagement,[36] social networking,[30] social participation,[21] and life-space.[21]

2.4.2.4 Body Composition Factors

Body Mass Index (BMI): The association between BMI and slow gait or clinically meaningful speed decline was examined in ten studies.[16,18,23,33,36–38,42,45,51] Using BMI as a continuous measure, Zeng et al. reported a significant positive association between BMI and slow gait speed (OR=1.25, 95% CI=1.09; 1.43), while Xu et al. and Kyrdalen et al. did not find a significant association. Using normal BMI as a reference, both Nasimi et al. and Kim et al. reported significant associations between underweight BMI and greater odds of slow gait (OR= 5.22, 95% CI=1.35; 20.12 and OR=1.25, 95% CI=1.11; 1.40 respectively). Using non-obese BMI as the reference, Verghese et al. and Plouvier et al. found a significantly greater likelihood of slow gait among those who were obese (RR=1.35, 95% CI=1.07; 1.69, OR=2.34, 95% CI=1.14; 4.81 [men], and OR=3.31, 95% CI=1.35; 8.13 [women] respectively), while Thorpe et al. found a significant effect for obesity only among women (OR=1.36, 95% CI=1.01; 1.83). Plouvier et al. further reported no significant effect for overweight BMI as compared to normal BMI in neither men nor women. Next, using normal weight as the reference, Gill et al. found that individuals with overweight BMI and those with obese BMI were at significantly greater risk of having slow gait (RR=1.3, 95% CI=1.0; 1.7 and RR=2.1, 95% CI=1.6; 2.7 respectively), and when also incorporating waist circumference into their analyses, they reported that only those who were overweight or obese in the largest waist circumference category had a significantly increased the risk of slow gait as compared to those in the smaller waist categories. Lastly, Kirkness et al. found significantly lower odds of slow gait for those considered healthy, underweight, or overweight as compared to those considered obese (OR= 0.55, 95% CI=0.36; 0.85 and OR= 0.48, 95% CI=0.34; 0.69 respectively).

Calf Circumference: Two studies measured the association between calf circumference and slow gait.[18,45] Both Nasimi et al. and Kim et al. reported significantly reduced odds of slow gait with increased calf circumference (OR= 0.82, 95% CI=0.72; 0.92 and OR= 0.81, 95% CI=0.72; 0.92 respectively).

Bone Mineral Density: Two studies included bone mineral density as a potential predictor of slow gait.[23,45] Kim et al. found that greater bone mineral density was significantly associated with lower odds of slow gait (OR=0.51, 95% CI=0.32; 0.79), while Xu et al. did not find bone mineral density to be a significant predictor of slow gait (values not reported).

Other Body Composition Factors: Another body composition factor that was identified to impart risk on experiencing slow gait but was only identified in a single study was body fat.[18] Other factors examined in single studies that did not have a significant association with slow gait were visceral fat area,[18] fat-free mass,[18] muscle protein,[18] bone mineral content,[18] and central adiposity.[23]

2.4.2.5 Serum Factors

Vitamin D: The association between vitamin D and slow gait was examined in three studies.[45,50,54] Shardell et al. reported significantly greater odds of slow gait for men with low vitamin D (OR=2.20, 95% CI=1.17; 4.11) but this effect was not seen in women (OR=1.12, 95% CI=0.59; 2.14). Neither Hirani et al. nor Kim et al. found significant effects for 25-hydroxyvitamin D on slow gait, however Hirani et al. reported significantly greater odds of slow gait for individuals in the lowest quartile of 1,25-dihydroxyvitamin D (OR=1.65, 95% CI=1.05; 2.63).

High Sensitivity C-Reactive Protein (CRP): Two studies assessed the relationship between CRP and slow gait.[22,53] While Yoshida et al. did not find a significant effect for elevated CRP (OR=1.82, 95% CI=0.94; 3.51), Lassale et al. reported significantly greater odds of slow gait for individuals with elevated CRP cross sectionally (OR=1.43, 95% CI=1.03; 1.98) as well as for individuals whose CRP levels increased from medium to high over follow-up (OR=1.61, 95% CI=1.15; 2.24).

Albumin: Two studies included albumin as a potential predictor of slow gait.[18,45] Kim et al. reported significantly lower odds of slow gait for higher albumin level while Nasimi et al. did not find a significant effect (OR=0.17, 95% CI=0.06; 0.46 and OR=1.48, 95% CI=0.88; 2.46 respectively).

Other Serum Factors: Other serum factors that were identified to impart risk on experiencing slow gait but were only identified in single studies were plasma fatty acids,[40] high density lipoprotein,[45] and cystatin C.[45] Other factors examined in single studies that did not have a significant association with slow gait were triglycerides,[18] B2-microglobulin,[45] hemoglobin A1c,[45] and parathyroid hormone.[54]

2.4.2.6 Cognitive Factors

Digit Symbol Substitution Test (DSST): Two studies assessed the relationship between scores on the digit symbol substitution test and slow gait.[24,39] Both Umegaki et al. and Rosano et al. found that higher DSST scores were linked to lower odds of slow gait cross-sectionally (OR= 0.71, 95% CI=0.54; 0.94, OR=0.97, 95% CI=0.97; 0.98 [subclinical gait speed group], and OR= 0.93, 95% CI=0.93; 0.95 [clinical gait speed group]). Rosano et al. did not find similar significant associations longitudinally.

Trail Making Test (TMT): Performance on the trail making test was assessed for an association with slow gait in two studies.[16,25] Kyrdalen et al. reported a non-significant association for performance on part B of the TMT with slow gait (OR=1.56, 95% CI=0.64; 3.83), and Adachi et al. found a non-significant effect for the difference in time spent between part B and A (OR=1.00, 95% CI=1.00; 1.01).

Other Cognitive Factors: Other cognitive factors that were identified to impart risk on experiencing slow gait but were only identified in single studies were cognitive impairment and white matter hyperintensities.[37,39] Factors examined in single studies that did not have a significant association with slow gait were logical memory performance and Mini Mental State Examination performance.[24,25] Lastly, a factor identified in a single study that showed a protective effect on slow gait was absence of dementia.[27]

2.4.2.7 Dietary Factors

Mediterranean Diet: The association between adherence to a Mediterranean diet and slow gait was examined in two studies.[21,47] Kwan et al. reported that individuals whose Mediterranean diet scores were in the upper two tertiles had significantly lower odds of slow gait (OR= 0.38, 95% CI=0.17; 0.84 [T2] and OR= 0.17, 95% CI=0.06; 0.44 [T3]). Leon-Munoz et al. additionally reported that only individuals whose scores on the Mediterranean Diet Adherence Screener were in the highest tertile had significantly lower odds of slow gait (OR= 0.53, 95% CI=0.35; 0.79). Leon-Munoz et al. found no significant effect for Mediterranean Diet Score.

Other Dietary Factors: Other dietary factors that were identified to impart risk on experiencing slow gait but were only identified in single studies were low fiber intake and dietary inflammatory index.[20,48] Factors examined in single studies that did not have a significant association with slow gait were energy intake,[23] protein intake,[23] fruit and vegetable consumption,[34] and meals per day.[36] Finally, factors identified in single studies that showed a protective effect on slow gait were dietary variety and dairy consumption.[32,46]

2.5 Discussion

To our knowledge, this is the first systematic review to comprehensively examine a broad range of potentially modifiable risk factors for slow gait speed and clinically meaningful decline in gait speed among community-dwelling older adults. Across the 40 studies included in this review, 85 potentially modifiable risk factors were assessed for an association with slow gait or clinically meaningful gait speed decline. Of these factors, 26 were examined in two or more studies.

The included studies used cross-sectional and longitudinal designs. More than half of the studies were given a ‘fair’ quality rating which was mainly influenced by the simultaneous assessment of exposures and outcomes during the same time periods. The size of the odds/risk ratios were generally small to moderate and tended to be heterogeneous. Sources of heterogeneity include differences in exposure measurements, cutoffs, and the design used. Another major probable reason for the heterogeneity of

effects is the use of different operational definitions of slow gait and meaningful decline. The approaches used included relative cutoffs based on the observed distributions of gait speed in the study samples (e.g. quartiles/quintiles), external criteria (e.g. < 0.8 m/s), and dynamic measures of change in gait speed over time (e.g. ≥ 0.05 m/s decline per year). The use of relative cutoffs based on sample distributions has advantages. It is a transparent and simple use of descriptive statistics to create strata of approximately equal size. This guarantees a sufficient number of people with the slowest gait speed for statistical comparisons. This is not assured if an external criterion is used, particularly with a small sample that was recruited from a group with above-average gait speed. However, the gait speed cutoff of the slowest quartile will likely differ among samples recruited from populations with different average gait speeds, which will cause heterogeneity in odds ratios across studies even if all other variables in all studies are measured identically. Another problem is that there is no reason to expect an internally derived lowest quartile cutoff to be close to an external criterion, which will be another source of heterogeneous findings across studies. Ultimately, while this review is informative, definitive conclusions should not be made from the evidence currently presented as the effects for the risk factors were summarized through qualitative observation only, and insufficient evidence for many factors is present to ensure that the effect measures are truly reflective of populations beyond the studies.

The three risk factors most commonly investigated among the studies in this review were physical activity, BMI, and education level. Overall, the effect estimates reported for each of these factors were mostly consistent and suggested that the likelihood of experiencing slow gait or clinically meaningful speed decline was decreased for those who were physically active and increased for those who were obese, underweight, and less educated. The benefits of regular physical activity on multiple aspects of health including chronic illnesses, functional capacity, and longevity have been well-documented.[56] In older adults especially, engagement in moderate to high levels of physical activity has clear benefits for delaying or preventing incident functional impairments and disability such as slow gait that can reduce independence in everyday life.[57] Conversely, a notably high or low BMI has been associated with a greater risk of functional declines and incident disability.[58] Obesity is associated with the development

of comorbidities that contribute to these declines including musculoskeletal conditions, cardiovascular conditions, and diabetes.[59] Being underweight also has potential negative effects on aspects of physical function in older adults such as muscle strength and may be linked with nutritional deficiencies that further promote health declines.[60,61] Being less educated may also increase the risk of gait speed impairment in complex ways. Low socioeconomic status, which includes one's education level, is a known contributor to the experience of various health disparities. Low education level specifically has been linked to a greater risk of adverse outcomes including disability, development of chronic conditions, and overall poor health.[62–65] Individuals with fewer years of education are also more likely to engage in sedentary lifestyles and unhealthy behaviours.[66,67] Additionally, as those with low socioeconomic status frequently face barriers to accessing healthcare resources,[68] their likelihood of receiving care for health declines and associated physical impairments including slow gait is reduced.

Other factors that also appeared more commonly across the included studies were pain, depression/depressive symptoms, and heart conditions. Among the results for pain, which included effect estimates for both general and site-specific measures, an overall trend for greater likelihood of slow gait was exhibited for those with some type of pain. Experience of frequent or chronic pain is known to negatively impact multiple domains of quality of life such as physical function, independence, and psychological well-being.[69] Pain severity and its association with mobility impairments can additionally be exacerbated by chronic conditions including musculoskeletal disorders and obesity, and by other unhealthy behaviours.[70] Incidence of disability in functional parameters including gait can also be magnified by the ways in which individuals think about their pain, which may involve pain catastrophizing and pain-related fear.[71,72] The results for depression-related effect measures were also fairly consistent in that having depression or more depressive symptoms increased the likelihood of slow gait. Longitudinal associations between depression and incident disability have been observed.[73,74] While depression can directly influence physical functioning through biological pathways, this relationship may also be influenced by other factors that co-occur in those with depression including multimorbidity and unhealthy lifestyle behaviours.[75,76] Conversely, many of the studies examining heart conditions found a non-significant effect of these

measures on the likelihood of slow gait speed. As presented in current literature, components of frailty including slow gait share similar causal pathways with cardiovascular disease and many studies have identified slow gait as a predictor of adverse cardiovascular outcomes.[77–79] While impairments in motor function may be independently influenced by the diagnosis of various heart conditions,[80,81] other vascular factors associated with the development of these conditions (e.g. hypertension, inflammation) could account for the effect that heart conditions appear to have on gait speed.[82] Existence of a potential link between heart conditions and gait speed impairment does however merit further investigation.

It is important to note that other clinical, behavioural, serological, and cognitive risk factors were assessed in addition to the factors described above. Many of these factors may play important roles in the development of slow gait or significant gait speed decline however our synthesis shows that the evidence available for these factors remains limited. In order to gain a better understanding of the relationships between these factors and gait speed, gaps such as those highlighted in this review must be addressed with additional research.

Overall, it is clear that in older populations, gait speed is influenced by a complex network of biological, mechanical, and psychological factors. Past research on several of the factors identified in this review has shown that many do play a role in aspects of physical functioning including gait speed. While reviews on the effects of other specific factors such as cognitive functioning and dual-tasking have provided evidence that these individual traits significantly influence gait speed, they only provide information about a limited number of contributors to the causal pie for gait speed decline. Thus, the current review is a step towards identifying a more complete series of potential risk factors that influence the likelihood of gait speed decline as well as some factors unlikely to be fruitful avenues for subsequent research.

This systematic review is not without limitations. First, it includes many cross-sectional studies which hinders the ability to draw conclusions about the causal relationship between the identified risk factors and gait speed impairment. As mentioned above, there

is noticeable heterogeneity in the classification of slow gait or meaningful speed decline across the studies, inconsistency in walking test distance, inconsistency in the types of covariates adjusted for, and differences in the operational definitions and comparison-reference categories of these risk factors. While the inclusion of populations of older adults residing in community settings was not limited by geographic location, generalizing the findings of this review to older community-dwelling adults in any country or geographic area is cautioned strongly not only due to possible differences in demographic, socioeconomic, lifestyle, and clinical characteristics between populations in developed and developing countries, but also due to the other issues listed above.

We provide systematic evidence to suggest that the risk of experiencing slow gait speed or clinically meaningful gait speed decline can be influenced by a variety of potentially modifiable factors such as physical activity, education, body mass index, pain, and depression/depressive symptoms. With a better understanding of the multifactorial causes of gait speed impairments, enhancement of current methods to diagnose older adults at risk for slow gait is possible, and individual clinical and lifestyle intervention strategies can be tailored to target factors that contribute the highest amount of risk. Public health interventions that target older populations can also be refined to provide education about the risk factors associated with gait speed decline and how preventing slow gait can, in turn, reduce the risk of associated illness and injury in the future. Due to the inconsistencies and limitations that still exist in the current evidence base, additional longitudinal studies on aging populations are needed to explore the causal relationships between the factors that have been suggested to be associated with slow gait or meaningful gait speed decline. When conducting these studies, investigators should consider the use of one “best” walking test protocol and should consider implementing consistent cutoff values to mark the development of slow gait speed or experience of meaningful gait speed decline. Additionally, when investigators operationalize slow gait with sample-based distributional cutoffs, they should also conduct parallel analyses using uniform external cutoffs (e.g. < 0.8 m/s) to increase the comparability of their analyses to those from other studies.

2.6 Conclusion

There are several potentially modifiable risk factors that may impact the risk of slow gait or meaningful declines in gait speed among community-dwelling older adults. This preliminary synthesis of sociodemographic, clinical, lifestyle, anthropometric, serum, cognitive, and dietary risk factors presents avenues for further investigations of the complex etiology of this mobility impairment. Rather than using only statistical significance as the basis for future research, investigators should ensure their studies have adequate power to detect clinically meaningful associations between slow gait and the factors of interest. The methods used to operationalize slow gait and meaningful gait speed decline should also be considered when interpreting and comparing results among studies as they can contribute to heterogeneity in risk factor effects.

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Chapter 3

3 Detailed Methods for Chapters 4 and 5

3.1 Overview

This chapter provides information on the Canadian Longitudinal Study on Aging (CLSA) from which data was obtained for the analyses presented in Chapters 4 and 5. Section 3.2 provides a description of the data source, including the sampling design and data collection and management procedures. The measurement instruments used to collect data on the main outcome and all independent variables are detailed in Section 3.3. Information on the statistical analyses performed and other considerations in subsequent chapters are listed in Section 3.4.

3.2 Data Source

The data used in this thesis came from the CLSA. Specifically, Chapters 4 and 5 involved analyses of baseline data from the CLSA Comprehensive cohort collected from May 2012 to May 2015. The CLSA is a national longitudinal study aimed at evaluating health trajectories across the adult lifespan and characterizing determinants of aging processes in a representative sample of community-dwelling Canadian adults.[1] The CLSA was developed by the Institute of Aging in partnership with Statistics Canada, the Government of Canada, the Public Health Agency of Canada, provincial ministries, and multiple university research institutions.

3.2.1 Sampling Design and Recruitment

Community-dwelling Canadian adults who were aged 45 to 85 years at the time of baseline data collection were the target population for the CLSA. In total, the CLSA recruited approximately 50,000 subjects at baseline, with about 20,000 of those individuals in the Tracking cohort who provided information via computer-assisted telephone interviews, and another 30,000 in the Comprehensive cohort who underwent face-to-face interviews, performed physical assessments, and provided biological samples during assessments in-home or at the data collection site nearest to them.[2] Individuals

were excluded from the CLSA if they were living in one of the territories, certain remote areas, or in a First Nations reserve or settlement, or if they were full time members of the Canadian Armed Forces, institutionalized, unable to communicate in English or French, or were cognitively impaired.[2] The studies in this thesis focused solely on data from the Comprehensive cohort as only the people in this cohort underwent gait speed assessments.

Several sampling frames were used in the creation of the CLSA Comprehensive cohort to ensure it was nationally representative, including provincial healthcare registration databases and random digit dialing.[2,3] Due to the requirement of attending in-person assessments, only individuals living within 25 to 50 kilometers of the data collection sites were recruited for the Comprehensive cohort. Across 7 provinces, there was a total of 11 data collection sites to represent the Pacific Coast, the Prairies, Central Canada, and the Atlantic Region.[2]

Sample size targets in each province were as follows: n = 3,000 for Alberta, Manitoba, Newfoundland and Labrador, and n = 6,000 for British Columbia, Ontario, and Quebec.[3] Strata were created within each province based on biological sex and 10-year age group (i.e. 45-54, 55-64, 65-74, 75-85) resulting in a total of 56 strata for the Comprehensive cohort.[3] These strata were further crossed with education level (i.e. low education vs. not low education). To obtain samples from provincial health registries, provincial government departments were asked to mail CLSA information packages with returnable consent forms to eligible individuals within that respective province. Provinces that granted access to their registries for sampling were Ontario, Manitoba, British Columbia, Newfoundland and Labrador, and Nova Scotia. Information packages were first mailed to a stratified random sample of all eligible individuals in the province, and then to specific low-education areas that were underrepresented in the initial round of sampling.[3] To meet the sampling quotas unfulfilled from sampling the provincial health registries alone, additional participants were recruited through random digit dialing, whereby a random sample of landline phone numbers of residences within 25 to 50 kilometers of each data collection site was generated.[3] Calls were made to these households to determine if any people living there met the inclusion criteria and if they were willing to participate in the

study. Finally, adults in the Quebec NuAge cohort study aged 75 to 85 years were contacted to obtain permission to use their data in the CLSA. NuAge participants who consented to providing their information were included in the Comprehensive cohort as random digit dialing participants.[3]

3.2.2 Data Collection Procedures

After agreeing to participate in the CLSA Comprehensive cohort, eligible individuals underwent in-home baseline interviews administered by trained CLSA staff. During these interviews, participants provided informed consent and then completed the Comprehensive Main-wave In-home Questionnaire to gather information on sociodemographic characteristics, health status, lifestyle behaviours, and cognitive function.[2] Following completion of an in-home interview, participants underwent further assessment at the data collection site nearest to them to measure their physical function and complete a Comprehensive Main-wave Disease Symptoms Questionnaire and neuropsychological battery.[2] Blood and urine samples were also obtained from participants who consented to providing biological specimens.

To date, the CLSA employs both a manual and electronic data storage system with safeguards to ensure the maintenance of security and privacy of all data collected.[2] Data collected from all sites across Canada are sent to a centralized server at the CLSA National Coordinating Centre at McMaster University. Using the Opal program, data cleaning and management is performed by staff at the Statistical Analysis Center. Applications for access to CLSA data are reviewed by the Data and Sample Access Committee, and once access is granted, Opal is used to send de-identified data to researchers.

3.3 Measurement Instruments

In the following section, details on the measurement instruments used to collect data on the variables of interest for the analyses in subsequent chapters are given.

3.3.1 Main Outcome

Gait speed is the main outcome variable in both Chapters 4 and 5 and was used as a continuous variable. A four-meter walk test with a static start was used to measure usual gait speed.[4] Participants were asked to stand with their toes behind a line marked on the floor and were told to walk straight at their usual pace until they walked a few steps past another line 4-meters away. Timing began immediately after the assessor said, "Ready, set, go," and stopped once the participant completely crossed the 4-meter finish line. Participants could use assistive devices such as canes and walkers to complete the test if needed. Time to complete the walk once was recorded in seconds using a stopwatch and was converted into meters per second (m/s).

3.3.2 Independent Variables

Descriptions of the independent variables used in Chapters 4 and 5 are provided below. To note, responses for categorical and binary variables recorded as 'Don't Know' or 'Refused' in the CLSA dataset were treated as missing values.

3.3.2.1 Sociodemographic Characteristics

Age, Sex & Province: CLSA leaders recommend that age, sex, and province be included as the minimum set of covariates for adjustment in analyses using this data.[3] Participants' ages were determined by asking for their date of birth and their sex was coded as either 'female' or 'male'. The CLSA Comprehensive cohort had representation from seven provinces: Alberta, British Columbia, Manitoba, Newfoundland and Labrador, Nova Scotia, Ontario, and Quebec. Sex and age categorized into four 10-year groups (45-54, 55-64, 65-74, 75+) were used in Chapter 4 while sex, age (continuous), and province were included in Chapter 5. Both age and sex have been associated with variations and declines in gait speed over the adult lifespan. The association between older age and slower gait speed has been well documented.[5] This age-related decline in mobility is broadly understood to be the result of physiological, compositional, and structural changes that occur within the body which influence systems that are essential for physical function (e.g. musculoskeletal system).[6,7] Studies have also observed that men tend to

walk faster than women on average, however anthropometric characteristics, such as leg length, likely account for these apparent sex differences in gait speed.[8]

Race: To capture racial diversity, participants were asked if they identified with the following individual groups: White, Chinese, South Asian, Black, Filipino, Latin American, Southeast Asian, Arab, West Asian, Japanese, Korean, North American Indian, Inuit, Métis, or Other. Since most Canadians identify as white,[9] the white race variable coded as 'white' and 'not white' was used in Chapters 4 and 5. Current evidence suggests that the burden of physical disability is unequal across different racial communities. Namely, racial minorities often face a greater risk of mobility and other functional impairments, likely as a result of the effects of socioeconomic disparities such as poverty, low education, and restricted access to healthcare.[10,11]

Level of Education: The highest level of education attained was recorded using four levels coded as (1) 'Less than secondary school graduation', (2) 'Secondary school graduation, no post-secondary education', (3) 'Some post-secondary education', and (4) 'Post-secondary degree/diploma'. This categorical variable was used in Chapters 4 and 5. Research has demonstrated that education level is significantly associated with health-related outcomes and physical functioning across the adult lifespan. Individuals who are less educated are more likely to engage in unhealthy behaviours and often have poorer health which increases the risk of functional declines in older age.[12] Those with fewer years of education may also lack adequate health literacy skills to navigate healthcare services and proactively manage their health when issues such as mobility difficulties arise.[13]

3.3.2.2 Anthropometric & Clinical Characteristics

Height & Weight: Participants' standing heights without shoes were measured using a Seca 213 stadiometer and their weights were measured using the 140-10 Healthweigh digital physician scale. Height was included in both Chapter 4 and 5 while weight was included in Chapter 5. Both continuous variables were included as covariates to account for their potential influence on gait speed. Namely, taller height may lead to faster walking speeds and heavier weight may contribute to slower walking speeds.[14,15]

Grip Strength: Grip strength was measured using a Tracker Freedom® Wireless Grip Dynamometer. While sitting in a chair with their feet flat on the floor and arms unsupported, participants held the dynamometer in their dominant hand and kept their elbow bent at a 90-degree angle.[16] They were then instructed to squeeze the dynamometer as hard as possible. This was performed three times and their average grip strength in kilograms was calculated. Average grip strength was used as a continuous variable in Chapter 5. Grip strength is frequently used as a measure of overall muscle strength in clinical settings, with lower grip strength values indicating potential muscle weakness.[17] Muscle weakening is a common issue in older adulthood that, if not managed effectively, can increase the risk of functional declines and mobility impairments.[18]

Chronic Pain: Experience of chronic pain was assessed by asking participants, "Are you usually free of pain or discomfort?" Responses were recorded as either 'Yes' or 'No', with 'No' indicating presence of chronic pain. This binary variable was used in Chapter 5. Pain is a complex phenomenon that influences multiple aspects of everyday function; for example, cognition, social involvement, emotional wellbeing, and physical ability.[19] In older adults especially, pain and its associated morbidity are prevalent and can contribute to and worsen mobility impairments, which has been demonstrated in previous investigations.[20,21]

Incontinence: Experience of any kind of incontinence was assessed by asking, "Do you ever have trouble getting to the bathroom in time?" Responses were recorded as either 'Yes' or 'No', with 'Yes' indicating experience of incontinence. This binary variable was used in Chapter 5. Incontinence is a geriatric syndrome that can have debilitating effects on functional ability and independence. Links between incontinence and slower walking have previously been demonstrated in older adults, with the potential for a bidirectional relationship proposed.[22,23]

Depressive Symptoms: Depressive symptoms were assessed using the Center for Epidemiologic Studies Short Depression Scale (CESD-10). This screening tool contained ten questions related to the frequency of feeling depressed and lonely, the ability to 'get going', and restless sleep, to which participants could select one of four responses (i.e. all

of the time, occasionally, some of the time, rarely or never).[2] Overall scores ranging from 0 to 30 were derived from the ten items in the CESD-10 questionnaire to create a count variable and this was used in Chapter 5. Depression is a prevalent neuropsychiatric disorder that has been linked to a greater risk of multimorbidity, disability, and poor health behaviours.[24] Investigations of the causes of depression have highlighted that this condition likely shares similar pathophysiological pathways with impairments related to mobility and fraily.[25] As a result, studies have found depression or higher number of depressive symptoms to increase the risk of slower gait speed and vice versa.[26,27]

Sleep Disturbance: To operationalize sleep disturbance in Chapter 5, a variable measuring the frequency of waking up and having trouble falling asleep was chosen. Participants were asked, "Over the last month, how often did you wake in the middle of the night or too early in the morning and found it difficult to fall asleep again?" Their responses were categorized into one of five options: (1) 'Never', (2) '< Once per week', (3) 'Once or Twice per week', (4) '3-5 times per week', and (5) '6-7 times per week'. The 'Never' and '< Once per week' categories were combined, resulting in four categories overall. Although research on the association between gait speed and sleep quality is limited, some studies have found that poorer sleep, operationalized using a variety of methods, may be associated worse physical function including slower gait speed.[28–30] Conclusions, however, are still mixed lending to the need for further investigation on the potential of sleep issues to influence gait.

Serum Biomarkers: Non-fasting blood samples were taken from consenting participants during their data collection site visits. Basic analyses of the samples were performed at the data collection sites while more complex analyses were performed at other sites including Biorepository and Bioanalysis Centre at McMaster University and the Genetic and Epigenetic Centre in Vancouver.[2] The following serum components were used as continuous variables in Chapter 5: vitamin D in mmol/L, high sensitivity C-reactive protein (hsCRP) in mg/L, and high-density lipoprotein cholesterol (HDL) in mmol/L. The values for vitamin D and hsCRP were transformed using the square-root and natural logarithm transformations respectively to reduce skewness. Current literature suggests that impairments in mobility may be associated with Vitamin D deficiencies,[31–33] chronic

inflammation indicated by elevated hsCRP levels,[34] and lower HDL cholesterol levels which are linked to an increased risk of multiple chronic diseases.[35,36]

3.3.2.3 Cognitive Function

Multiple domains of cognition play a crucial role in the production of gait. As such, the incidence and progression of cognitive deficits often leads to gait abnormalities including slower gait speed.[37] Investigations of the role of executive functioning in gait performance have shown that it significantly influences the control and execution of gaiting behaviours as individuals navigate through their environment, and that impaired executive functioning can lead to gait speed declines.[37,38] In addition to this, performance in other domains such as memory and verbal fluency have also been correlated with gait speed,[39–41] demonstrating the complex relationship between cognition and mobility.

Executive Function: The Mental Alternation Test (MAT) and the Stroop Test were used as measures of executive function in Chapter 5.[2] For the MAT, participants were asked to alternate as many numbers and letters as they could out loud (i.e. 1-A, 2-B, 3-C, etc.) in 30 seconds. The number of correct alternations, which could range from 0 to 51, was used as a count variable. The Stroop Test involved three trials. First, as a baseline measure, participants were asked to say the colour of solid circles. In the next trial, participants were asked to say the ink colour of printed words. Finally, the third trial required participants to say the ink colour of printed colour names. The times to complete each trial were recorded in seconds. For the Chapter 5 analysis, a Stroop Interference variable was created by subtracting participants' Trial 1 (least difficult) time from their Trial 3 (most difficult) time.[42] Extreme outliers ± 3 standard deviations were excluded from the analyses (i.e. three individuals excluded with the highest scores deemed abnormal).

Memory & Verbal Fluency: Memory was assessed using the Rey Auditory Verbal Learning Test (RAVLT).[2] For this test, participants were read a list of 15 words. Trial one (REY I) involved immediate recall where participants were asked to recall as many words as possible in 90 seconds immediately after the list was read to them. The second trial of the test (REY II) involved delayed recall where participants were asked to recall

words from the same list in 90 seconds after a 30-minute delay. Verbal fluency was assessed using the Animal Fluency Test (AFT).[2] For this test, participants were asked to name as many different animals as possible in 60 seconds. The REY I, REY II, and AFT scores were used as count variables in Chapter 5.

3.3.2.4 Lifestyle Behaviours

Smoking Status: Participants were asked if they were either (1) current smokers, (2) non-smokers who have never smoked, or (3) former smokers who currently do not smoke but have in the past. Smoking is a known risk factor for several key cardiovascular conditions that can influence physical health and is associated with unhealthy behaviours that can also contribute to the progression of functional declines.[43,44]

Alcohol Consumption: Participants' alcohol consumption was assessed by asking if they were either (1) regular drinkers (i.e. at least one drink per month), (2) occasional drinkers, or (3) non-drinkers (i.e. no alcohol consumed in the last 12 months). Prior research has suggested that alcohol consumption may impart health benefits in older age. For example, one study demonstrated that consumption of moderate amounts of alcohol may be linked to better physical performance, including faster gait speed, as compared to those who drink excessively or not at all.[45]

Physical Activity: Participants' level of physical activity was measured using the Physical Activity Scale for the Elderly (PASE) questionnaire.[2] Using a set of standardized questions, participants were asked about their engagement in walking, sports and recreational activities, household activities, and work/volunteer activities over the past 7 days. The frequency and time spent participating in each activity was recorded to generate a weighted score for each item. Scores for each questionnaire item were summed to produce an overall score, which was used as a continuous variable in Chapter 5. Physical activity is important throughout life to maintain health and mobility and is especially beneficial in older age to counteract age-related declines. For example, previous studies have shown that older adults who are physically active are more likely to have greater muscle strength and are at a lower risk of physical impairments .[46]

3.3.2.5 Chronic Conditions

Chronic conditions can have complex negative effects on health and mobility, especially in older adulthood.[47–49] Diagnosis of chronic conditions was assessed in the CLSA through self-report by asking participants, "Has your doctor ever told you that you have…" to which they answered 'Yes' or 'No' to each item. These binary variables were used in Chapter 5 either individually or were combined to create new binary composite variables and were classified as either non-modifiable or potentially modifiable.

Non-Modifiable Chronic Conditions: Three non-modifiable conditions were included in the analyses: (1) Neurodegenerative disease (Dementia/Alzheimer's disease, Parkinson's disease/ Parkinsonism, and/or multiple sclerosis), (2) memory problem, and (3) macular degeneration.

Potentially Modifiable Chronic Conditions: Nine potentially modifiable conditions were included in the analyses: (1) cardiovascular condition (heart disease, peripheral vascular disease, angina, and/or heart attack), (2) stroke (stroke and/or transient ischemic attack), (3) diabetes, (4) hypertension, (5) cancer, (6) osteoarthritis (knee and/or hip osteoarthritis), (7) sensory impairment (fair/poor self-rated hearing and/or fair/poor self-rated vision), (8) neuropsychiatric condition (anxiety disorder, mood disorder, epilepsy, and/or migraine headaches), and (9) respiratory condition (asthma and/or emphysema/ chronic bronchitis/ COPD/ other chronic lung issues).

3.4 Statistical Analysis

Methods for application of the complex survey analysis in Chapters 4 and 5 are described in section 3.4.1. Analyses for Chapters 4 and 5 are detailed in sections 3.4.2 and 3.4.3 respectively. Other considerations regarding missing data for the analyses in Chapter 5 are explained in subsequent sections.

3.4.1 Statistical Software and Complex Survey Analysis

The analyses in Chapters 4 and 5 were performed using IBM SPSS Statistics for Windows Version 25.0 and SAS Version 9.4. To account for the sampling procedures used to create the CLSA cohort, complex survey analysis was performed.[3] In general,

(trimmed) inflation weights were applied in descriptive analyses and analytic weights rescaled to sum the actual sample size of the Comprehensive cohort were applied in regression analyses. Geographic strata specific to the Comprehensive cohort and cluster, given as each participant's identification number, were specified in the software as well.

3.4.2 Preliminary Descriptive Analyses

Prior to conducting the analyses in Chapters 4 and 5, descriptive statistics were generated for the overall CLSA Comprehensive cohort baseline sample (n=30,097) using the mean ± standard error (SE) or median and interquartile range for continuous variables and frequency and percentage for categorical variables. These descriptive statistics, along with the proportion of missing data for each variable, are presented in Appendix D (Table D-1). The distributions of each continuous variable were visually inspected using histograms to assess normality. Multicollinearity was assessed with a correlation matrix, with a correlation coefficient of 0.8 used as the cutoff to indicate collinearity. The linearity of the relationships between gait speed and the independent variables was further inspected using scatterplots. Continuous variables were transformed if their values were greatly skewed (Chapter 5: variables transformed were vitamin D and hsCRP due to large positive skew), and extreme outliers were excluded if values were 3 or more standard deviations from the mean (Chapter 5: outliers excluded in Stroop interference variable).

3.4.3 Analyses for Chapter 4

A total of 30,097 participants in the CLSA Comprehensive cohort completed baseline assessments. Participants were included in the Chapter 4 analyses if they had data on age, sex, gait speed, and height. After listwise exclusion, 29,700 (98.7%) of participants had complete data on the variables of interest. Comparisons of the characteristics of individuals included in the analysis with those who were excluded (n=397) were conducted using two-tailed t-tests and chi-square tests for continuous and categorical variables respectively. The distribution of gait speed for the analytic sample was also visually inspected using a histogram.

The primary objective of Chapter 4 was to generate normative statistics (i.e. population norms) for gait speed in the analytic sample by sex and age. Eight strata were created by crossing sex (male, female) with 10-year age group (45-54, 55-64, 65-74, 75+). The mean gait speed, standard deviation, and 95% confidence interval was tabulated for each stratum. Since leg length can influence the pace at which individuals normally walk,[50,51] gait speed values standardized by height were also tabulated by dividing gait speed by average height in meters.

The second objective of Chapter 4 was to measure the prevalence of slow gait in each sex and age stratum. As 'slow gait' can be defined in different ways (Figgins et al. 2020, *under review*), three criteria were employed: 1) gait speed less than 1.0 m/s but greater than or equal to 0.8 m/s, 2) gait speed less than 0.8 m/s but greater than or equal to 0.6 m/s, and 3) gait speed less than 0.6 m/s. These cutoffs were chosen as they have been associated with increased risks of adverse outcomes including falls and hospitalization, level of functional independence, and mobility in adults.[52–54] A fourth gait speed category for individuals with gait speeds greater than 1.0 m/s was also included as gait speeds faster than 1.0 m/s are considered normal for adults.

3.4.3.1 Variance Estimation

In studies with complex sampling designs, individuals from different population subgroups have variable probabilities of being sampled. Thus, to calculate accurate measures of variance, departures from simple random sampling in the complex sampling design must be accounted for.[55] Current complex survey analysis programs do not directly produce standard deviations for variables. As such, the Taylor series linearization method was used in SAS with PROC SURVEYMEANS to estimate the standard deviations for the gait speed estimates in each sex and age stratum while incorporating the complex sampling design.[56] Briefly, Taylor linearization is a method used to obtain finite population variance estimators for parameters in samples with complex survey designs.[55] It involves using the sample mean of a variable of interest and the sum of the sampling weights to first estimate the total population size ($\widehat{N}$) and population mean of

the variable ($\hat{\bar{y}}$). Using these, a variable (z) can be generated with a value for each observation in the sample equal to:

$$z_k = \frac{1}{\hat{N} - 1}\left(y_k - \hat{\bar{y}}\right)^2 \qquad k = 1, \ldots, n$$

The weighted total of this new variable is then estimated, and the square root is taken to obtain the finite population standard deviation for the variable of interest.[56]

3.4.4 Analyses for Chapter 5

The analyses in Chapter 5 also used baseline data from the CLSA Comprehensive cohort. Participants were included if they had complete data on gait speed as well as the following independent variables: age, sex, province, education level, race, height, weight, all twelve chronic condition variables, all five cognitive score variables, vitamin D, hsCRP, HDL, CESD-10 score, grip strength, pain, incontinence, sleep disturbance, PASE score, smoking status, and alcohol consumption. Of the 30,097 participants in the CLSA Comprehensive cohort who completed the baseline assessment, 20,201 (67.1%) individuals had complete data for gait speed along with all other variables of interest.

Descriptive statistics for the analytic sample (n=20,201) were generated, with mean and standard error reported for continuous variables and frequency and percent reported for categorical variables. T-tests and chi-square tests were conducted to determine if any characteristics of the sample differed significantly from those excluded (n=9,896) as a result of selection bias.

The first objective was to assess the bivariate associations between gait speed and the independent factors that are non-modifiable and potentially modifiable. This was done using the Complex Samples General Linear Model (CSGLM) procedure in SPSS (from menu: *Analyze* > *Complex Samples* > *General Linear Model*). The second objective was to construct a regression model with the non-modifiable and potentially modifiable factors to measure the amount of variation in gait speed explained by these factors and to further investigate the associations of the potentially modifiable factors with gait speed. Hierarchical multivariable linear regression modelling was performed using CSGLM in

SPSS as well with gait speed as the continuous dependent variable. Hierarchical multivariable linear regression modelling is used to examine the amount of variance in a dependent variable that is explained by multiple predictors that are entered sequentially in pre-specified sets. The independent variables for this analysis were grouped prior to running the regression resulting in five hierarchical models as listed in Table 3-1. The rationale for the order of the variable sets was to adjust the model first for fundamental sociodemographic and design-based variables, followed by non-modifiable factors, then by potentially modifiable cognitive factors, then modifiable chronic diseases, and finally by clinical and lifestyle factors. Regression coefficients with 95% confidence intervals and statistical significance were reported for each model. The R^2 value for each model was also given to show the amount of variance in gait speed that was explained by the addition of each set of variables.

Table 3-1. Hierarchical models.

Model 1	Sociodemographic factors (age, sex, province, race, education)
Model 2	Model 1 + Non-Modifiable Chronic Conditions (Neurodegenerative disease, memory problem, macular degeneration) + Anthropometric factors (height, weight)
Model 3	Model 2 + Cognition (REY I, REY II, AFT, MAT, Stroop Interference)
Model 4	Model 3 + Modifiable Chronic Conditions (cardiovascular condition, stroke, diabetes, hypertension, cancer, osteoarthritis, sensory impairment, neuropsychiatric condition, respiratory condition)
Model 5	Model 4 + Other Modifiable Clinical/Lifestyle Factors (vitamin D, hsCRP, HDL, depressive symptoms (CESD-10), grip strength, chronic pain, incontinence, sleep disturbance, physical activity (PASE), smoking status, alcohol consumption)

3.4.4.1 Missing Data

Patterns among missing values for all variables of interest were examined prior to conducting the analyses. When selecting only cases with complete data for all variables, approximately 67% of individuals had valid responses. Vitamin D, hsCRP, and HDL had the largest percentages of missing cases (10.3% each). The data were assumed to be missing at random (MAR), meaning that other variables in the dataset may predict the missingness in certain variables but the variables themselves do not predict their own

missingness.[57] Listwise deletion of cases was used first to manage missing values across all the variables of interest which resulted in a sample size of 20,201.

Missing value analysis was also performed on the sets of chronic condition variables used to create each composite variable to determine if it would be appropriate to exclude cases with missing responses to any of the individual variables being considered in a set. Both the proportion of missingness as well as patterns of missingness were evaluated. Overall, the proportion of cases excluded for having any missing values was low, with 0.4%, 2.1%, 0.9%, 2.0%, 0.7%, 0.7%, and 0.1% of cases excluded for the neurodegenerative disease, cardiovascular condition, stroke, osteoarthritis, neuropsychiatric condition, respiratory condition, and sensory impairment composite variables respectively. Additionally, no appreciable associations were seen between missing responses and age, sex, and other variables in each composite set. This justified the use of cases only with valid 'Yes' or 'No' responses to the entire set of individual conditions being considered for each composite variable.[57]

Since the data were assumed to be MAR but not missing completely at random (MCAR), analyzing only complete cases may introduce bias in the estimates.[58] As such, multiple imputation of missing values was performed, and the hierarchical regression analysis was conducted again as a sensitivity analysis to determine if the missingness introduced any bias into the results. The fully conditional specification (FCS) method for arbitrary missing data patterns was chosen for multiple imputation. This method allows for imputation of both continuous and categorical variables as it uses a separate conditional distribution for each variable in the model.[58] Binary and categorical variables were imputed using the discriminant function and continuous variables were imputed using predictive mean matching.[59] To account for the complex survey design, the sampling weight variable was also included as a covariate in the model.[60] Following guidelines proposed by White et al. that the number of imputed data sets should be equal to the proportion of missing cases,[59] 30 imputed datasets were created. Imputation diagnostics were then run in SAS by inspecting trace plots and comparing summary statistics for the imputed and original data (Appendix D, Table D-1).[58] SPSS Version 25.0 software does not currently include tools to analyze complex survey data that has had missing data

imputed through multiple imputation. Thus, to perform a sensitivity analysis with missing values imputed, the CLSA dataset was imported into SAS Version 9.4 to run multiple imputation and perform the regression analysis using the PROC SURVEYREG and PROC MIANALYZE functions.

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Chapter 4

4 Normative Values of Gait Speed among Middle and Older-Aged Adults: An Analysis of Data from the Canadian Longitudinal Study on Aging

4.1 Introduction

Gait speed is a parameter of mobility that is the product of multiple biomechanical, physiological, and sensory processes.[1–5] Due to their complex interactions, impairments in these underlying processes can disrupt the production and maintenance of normal gait speed, especially in older adults. Given that gait speed can be measured easily and objectively during clinical assessments, this behaviour is commonly used as an indicator of health quality and functional independence.[6] It is also used to predict older individuals' risks of experiencing adverse outcomes including falls, hospitalizations, and mortality.[7,8]

Many methods currently exist to measure gait speed, however shorter distance timed walk tests between 4 and 10 meters in length are most frequently employed.[9] While timed walk tests are widely implemented in clinical settings, the results of these tests are not easily interpretable without normative values for reference. Population norms have long been used in clinical areas like pediatrics to identify children whose height or weight is substantially below average for their age (e.g. below the fifth or tenth percentile). Norms are based on large representative samples and can be reported separately by sex or other sociodemographic variables. In the context of gait speed, clinical assessors can use norms, which are commonly separated by covariates such as sex and height, to determine if an individual patient is performing within the range of function that is expected based on their demographics. Additionally, an individual's gait speed can be expressed in percentile terms both at one point in time as well as to measure relative change over time. This comparative information can be used as a screening tool to further identify those who may have underlying impairments that have yet to be diagnosed or who are at an increased risk for developing additional health issues in the future.[10]

Normative statistics such as percentile equivalents reflect the composition of the population from which the sample was drawn. Several studies have previously generated normative values for gait speed in older adults from various populations.[11–14] While informative, there is noticeable heterogeneity in the values obtained, and due to the variability in the source and size of the samples used, these values may not be truly representative of the gait speed norms of other specific populations with different characteristics. To address these gaps, the present study analyzed baseline data from the Canadian Longitudinal Study on Aging (CLSA), a large nationally representative sample of Canadians aged 45-85 years of age, with the following three objectives:

i) To estimate the normative values of gait speed for Canadian men and women in four age groups (45-54, 55-64, 65-74, 75+ years)

ii) To estimate the prevalence of 'slow gait' using three common cut-point ranges: ≥ 0.80 to < 1.00 m/s, ≥ 0.60 to < 0.80 m/s, and < 0.60 m/s

iii) To demonstrate the transformation of an individual's gait speed into a population percentile

4.2 Methods

4.2.1 Source Population

This study involved cross-sectional analysis of baseline data from the CLSA Comprehensive cohort collected between May 2012 and May 2015. The CLSA is a national longitudinal study aimed at evaluating health trajectories across the adult lifespan and characterizing determinants of aging processes in a representative sample of community-dwelling Canadians adults.[15] In total, the CLSA recruited approximately 50,000 subjects aged 45 to 85 years at baseline, with about 20,000 of those individuals in the Tracking cohort who provided information via computer-assisted telephone interviews, and another 30,000 in the Comprehensive cohort who underwent face-to-face interviews, performed physical assessments, and provided biological samples during assessments in-home or at the data collection site nearest to them.[16] The present study focused solely on data from participants in the Comprehensive cohort as only the people in this cohort underwent gait speed assessments.

Several sampling frames were used in the creation of the CLSA Comprehensive cohort to ensure it was nationally representative including provincial healthcare registration databases and random digit dialing.[16,17] Strata were created within each province based on sex and age group (45-54, 55-64, 65-74, and 75-85) resulting in a total of 56 strata for the Comprehensive cohort.[17] These strata were further crossed with education level. Individuals were excluded if they were living in one of the territories, certain remote areas, or in a First Nations reserve or settlement, or if they were full time members of the Canadian Armed Forces, institutionalized, unable to communicate in English or French, or were cognitively impaired.[16] Due to the requirement of attending in-person assessments, only individuals who were living within 25 to 50 kilometers of the data collection sites were recruited for the Comprehensive cohort.

4.2.2 Study Sample

Upon sampling completion, the CLSA had enrolled 30,097 individuals in the Comprehensive cohort at baseline. For the present study, only individuals who had valid data on age, sex, gait speed, and height were included in the analyses. Overall, 397 participants were excluded as they were missing data on the variables of interest, resulting in a final sample size of 29,700.

4.2.3 Data Collection

Participants in the CLSA Comprehensive cohort underwent baseline interviews between May 2012 and May 2015 both in-home and at the data collection centers. Participants' ages were determined by asking for their date of birth and their sex was coded as either 'female' or 'male'. The standing height of participants without shoes was measured using a Seca 213 stadiometer and recorded in meters.[16]

A four-meter walk test with a static start was used to measure usual gait speed.[18] Participants were asked to stand with their toes behind a line marked on the floor and were told to walk straight at their usual pace until they walked a few steps past another line 4-meters away. Timing began immediately after the assessor said, "Ready, set, go," and was stopped once the participant completely crossed the 4-meter finish line. Participants could use assistive devices such as canes and walkers to complete the test if

needed. Time to complete the walk once was recorded in seconds using a stopwatch and was converted into meters per second (m/s).

4.2.4 Statistical Analysis

Comparisons of the characteristics of the 29,700 subjects included in the analysis with the 397 individuals who were excluded due to missing data were conducted using two-tailed t-tests and chi-square tests for continuous and categorical variables respectively. The distribution of 4-meter usual gait speed for the entire analytic sample was visually inspected using a histogram.

To generate normative statistics on 4-meter usual gait speed, strata were formed in the analytic sample by creating four 10-year age groups (45-54, 55-64, 65-74, 75+). The mean gait speed, standard deviation, and 95% confidence interval were tabulated for males and females in each of the four age groups. Since leg length can influence the pace at which individuals normally walk, gait speed values standardized by height were also tabulated by dividing gait speed by average height in meters.[14,19,20] The mean height-standardized usual gait speed, standard deviation, and 95% confidence interval were tabulated for each stratum as well.

Prevalence of slow gait was reported as a count and percentage. As ‘slow gait’ can be defined in different ways, the following three criteria were employed to generate prevalence values: 1) gait speed less than 1.00 m/s but greater than or equal to 0.80 m/s, 2) gait speed less than 0.80 m/s but greater than or equal to 0.60 m/s, and 3) gait speed less than 0.60 m/s. These cutoffs were chosen as they have been associated with increased risks of adverse outcomes including falls and hospitalization, varying levels of functional independence, and mobility declines in adults.[6,7,21,22] A fourth gait speed category for individuals with gait speeds equal to or greater than 1.00 m/s was also included as gait speeds at or above this cutoff are generally considered normal for adults.

Analyses were performed using SAS Version 9.4 and Excel Version 16.16.8. Since the CLSA is a complex sample survey, sampling weights were used in all the analyses to obtain results that are representative of the Canadian population as per CLSA

guidelines.[17] Taylor series linearization method was used to estimate the complex sample standard deviations as this measure is not automatically produced by complex survey software.[23]

4.3 Results

Of the 30,097 individuals in the CLSA Comprehensive cohort who completed a baseline assessment, 29,700 (98.7%) had complete data for the variables of interest. Compared to those who were included in the analytic sample, individuals who were excluded tended to be older and had less education (Table 4-1).

Table 4-1. Characteristics of included and excluded groups.

Variable	**Analytic Sample with Complete Data (n=29,700)**	**Excluded Group with Missing Data (n=397)**	***p***
Age, mean ± SE[a]	59.44 ± 0.07	63.32 ± 0.70	< .001
Sex, n (%)			.439
Female	15116 (50.3)	204 (52.8)	
Male	14584 (49.7)	193 (47.2)	
Race, n (%)			.753
White	28396 (94.7)	375 (94.3)	
Non-white	1304 (5.3)	22 (5.7)	
Education, n (%)			< .001
Less than secondary school graduation	1606 (4.8)	37 (8.9)	
Secondary school graduation only	2792 (8.9)	46 (13.5)	
Some post-secondary education	2195 (6.7)	41 (9.7)	
Post-secondary degree/diploma	23050 (79.6)	272 (67.9)	

[a] Means, standard errors, and percentages estimated using (trimmed) inflation weights.

4.3.1 Distribution of Gait Speed in the Analytic Sample

As shown in Figure 4-1, 4-meter usual gait speed in the sample appears normally distributed. The overall mean (SD) usual gait speed of the sample was 0.999 (0.198) m/s. The fastest gait speed in the sample was 2.564 m/s while the slowest gait speed was 0.106 m/s.

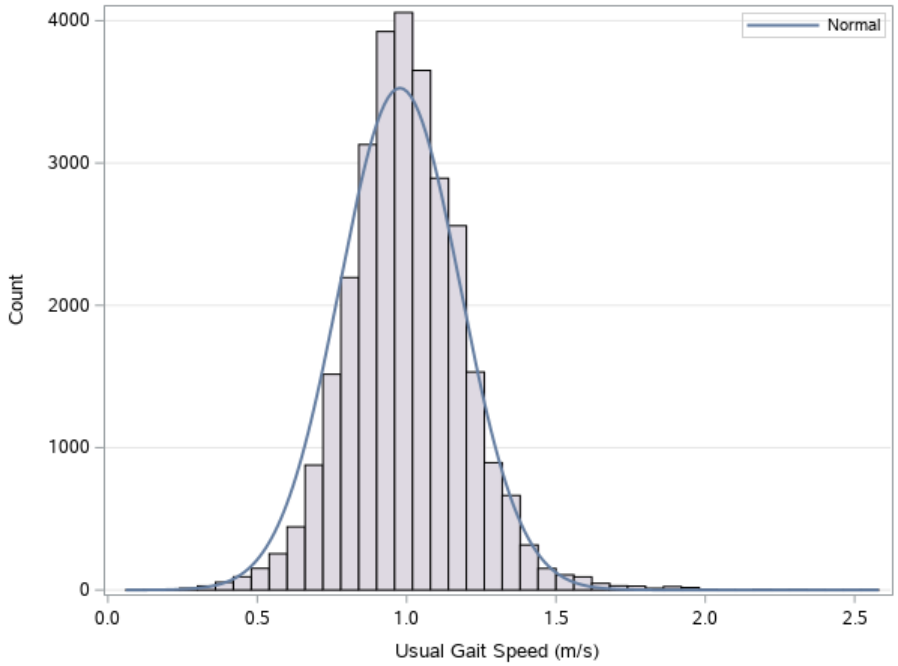

Figure 4-1. Distribution of usual gait speed (m/s) for the analytic sample.

4.3.2 Normative Values for Gait Speed by Sex and Age

The normative values for gait speed in each sex and age group are presented in Table 4-2. Declining trends in gait speed norms were evident across increasing age group, with steeper decreases noticeable among females compared to males. Mean usual gait speeds for males and females in the 45-54 and 55-64-year age groups were similar, with values at or above 1.00 m/s. However, for individuals in the two oldest age groups, mean gait speeds were below 1.00 m/s, especially in the 75+ year age groups where the means for males and females were 0.884 m/s and 0.832 m/s respectively.

As seen with unstandardized gait speed, mean height-standardized gait speed values also appeared slower with older age among males and females. However, in contrast to males having faster average unstandardized gait speeds, women appeared to have faster mean height-standardized gait speeds regardless of age.

Table 4-2. Normative values of usual gait speed and height-standardized usual gait speed by sex and age.

Males					
Variable	**45-54** (n=3644)	**55-64** (n=4706)	**65-74** (n=3609)	**75+** (n=2625)	**Total** (n= 14584)
Gait Speed, mean (SD)[a]	1.042 (0.173)	1.023 (0.194)	0.974 (0.189)	0.884 (0.189)	1.009 (0.190)
Gait Speed, 95% CI	1.036-1.048	1.017-1.029	0.968-0.981	0.877-0.892	1.006-1.013
Height-Standardized Gait Speed, mean (SD)[b]	0.588 (0.098)	0.581 (0.110)	0.559 (0.108)	0.512 (0.110)	0.574 (0.107)
Height-Standardized Gait Speed, 95% CI	0.585-0.592	0.578-0.584	0.555-0.563	0.508-0.517	0.572-0.576
Females					
Variable	**45-54** (n=3898)	**55-64** (n=5023)	**65-74** (n=3634)	**75+** (n=2561)	**Total** (n=15116)
Gait Speed, mean (SD)	1.045 (0.190)	1.001 (0.195)	0.940 (0.195)	0.832 (0.187)	0.988 (0.203)
Gait Speed, 95% CI	1.039-1.051	0.995-1.007	0.933-0.947	0.825-0.841	0.985-0.992
Height-Standardized Gait Speed, mean (SD)	0.637 (0.115)	0.618 (0.120)	0.586 (0.121)	0.525 (0.117)	0.609 (0.123)
Height-Standardized Gait Speed, 95% CI	0.634-0.641	0.615-0.622	0.582-0.590	0.520-0.530	0.607-0.612

[a] Means, standard deviations, and confidence intervals estimated using analytic sampling weights.
[b] Height-standardized usual gait speed = gait speed (m/s)/height (m)
Notes: CI=confidence interval; SD=standard deviation

4.3.3 Prevalence of Slow Gait Speed

Table 4-3 shows the prevalence of individuals within each gait speed group. The 45-54 and 55-64-year age groups had the greatest proportions of males and females with 'normal' gait speeds at or above 1.00 m/s. However, a shift in the distributions of individuals across the gait speed categories was apparent within the two oldest age groups such that a larger proportion had gait speeds that were slower than 1.00 m/s. Notably, among men and women aged 65-74 and 75+ years, those with gait speeds ≥ 0.80 to <1.00 m/s made up the largest proportion within each stratum. Further, the proportion of males and females within the ≥0.60 to <0.80 m/s gait speed group was nearly double between the 55-64-year and 65-74-year groups as well as between the 65-74-year and 75+ year groups (Males: 7.9%, 13.4%, 25.1%; Females: 10.0%, 18.3%, 31.9%). Additionally, the proportion of men and women aged 75+ years whose gait speeds were slower than 0.60 m/s was more than three times that seen for men and women in the 65-74-year age group.

Table 4-3. Prevalence of gait speeds by sex and age.

Males					
Gait Speed Cut-off	**45-54** (n=3644)	**55-64** (n=4706)	**65-74** (n=3609)	**75+** (n=2625)	**Total** (n= 14584)
≥1.00 m/s, n (%)[a]	2153 (59.1)	2463 (53.0)	1535 (43.9)	658 (24.5)	6809 (51.4)
≥ 0.80 to <1.00, n (%)	1279 (35.1)	1795 (38.0)	1477 (41.1)	1119 (45.1)	5670 (37.9)
≥0.60 to <0.80, n (%)	190 (5.2)	394 (7.9)	529 (13.4)	688 (25.1)	1801 (9.4)
< 0.60 m/s, n (%)	22 (0.5)	54 (1.0)	68 (1.5)	160 (5.3)	304 (1.3)
Females					
Gait Speed Cut-off	**45-54** (n=3898)	**55-64** (n=5023)	**65-74** (n=3634)	**75+** (n=2561)	**Total** (n=15116)
≥1.00 m/s, n (%)	2270 (59.6)	2403 (49.7)	1277 (36.3)	458 (17.6)	6408 (47.4)
≥ 0.80 to <1.00, n (%)	1348 (33.9)	1960 (38.8)	1539 (42.5)	1000 (40.4)	5847 (37.7)
≥0.60 to <0.80, n (%)	248 (5.7)	564 (10.0)	700 (18.3)	832 (31.9)	2344 (12.4)
< 0.60 m/s, n (%)	32 (0.7)	96 (1.5)	118 (2.9)	271 (10.1)	517 (2.5)

[a] Percentages estimated using (trimmed) inflation sampling weights.

4.3.4 Expressing Individual Gait Speed as a Percentile

An individual's gait speed is first converted to a Z score using the Excel STANDARDIZE function. Then, because gait speed is approximately normally distributed (Fig. 4-1), the Z score is expressed as a percentile using the NORM.S.DIST function:

1. Z score for individual = STANDARDIZE (X, mean, sd)

   where:

   X = individual's measured gait speed in m/s

   mean = stratum-specific mean gait speed from Table 4-2

   sd = stratum-specific standard deviation from Table 4-2
2. Percentile for individual = NORM.S.DIST (Z, TRUE)

   where:

   Z = Z score from STANDARDIZE function

   TRUE = a statement to produce cumulative percentiles.

Example 1 (ignoring height): Ms. A is a 75-year-old woman with a measured gait speed of 0.85 m/s. The STANDARDIZE (0.85, 0.832, 0.187) function in Excel yields Z = 0.35719722. The NORM.S.DIST (0.35719722, TRUE) function returns the value 0.63952792. Ms. A's gait speed is approximately equivalent to the 64^{th} percentile for her age and gender group.

Example 2 (incorporating height): Ms. A is 170 cm tall. Her height-normalized gait speed = [gait speed (m/s)/height(m)] = 0.85 / 1.7 = 0.5. The STANDARDIZE (0.5, 0.525, 0.117) function returns Z = -0.2136752. The NORM.S.DIST (-0.2136752, TRUE) function returns the value 0.58459982. When Ms. A's height is taken into account, her height-adjusted gait speed is approximately equivalent to the 58^{th} percentile for her age-gender group.

4.4 Discussion

This study provides normative values of 4-meter usual gait speed and height-standardized usual gait speed. A description of slow gait prevalence was also tabulated. These values were obtained using a large, nationally representative sample of community-dwelling middle and older-aged adults living in Canada.

The usual gait speed values obtained in this analysis were comparable to but generally slower than those for similar-aged subjects in previous reports. Specifically, the mean usual gait speeds among the two oldest CLSA age groups (65-74 and 75+) was below 0.90 m/s. Contrarily, using a 4-meter static start walk test like that employed in the present study, Bohannon and colleagues reported average gait speeds ranging from 0.95 m/s to 1.07 m/s for men and women aged 70-79-years and 80-85-years.[24] Hollman and colleagues also reported mean gait speeds ranging from 0.98 m/s to 1.22 m/s for men and women aged 70 years and older using 5.6-meter electronic GAITRite walkway with acceleration and deceleration zones.[11]

The discrepancies in normative values may be the result of several factors. First, other investigations of gait speed across the adult lifespan have relied on smaller and less representative samples of community-dwelling adults to estimate population parameters. Researchers have noted that subjects who are healthier and better functioning may be more likely to participate in health research.[25,26] In comparison, individuals were not specifically excluded from the CLSA cohort at baseline based on walking ability or common health conditions but rather if they had serious impairments that would impede them from completing any of the study assessments or if they were institutionalized. Furthermore, adults residing in seniors' residences where minimal care is provided were included in the baseline sample. As a result, the CLSA baseline cohort likely contained some individuals with mild or moderate mobility impairments or other health issues that may have influenced their gait speed. Individuals were also not excluded from the current analysis for having gait speeds below a certain threshold. However, only a small proportion of individuals had gait speeds slower than 0.60 m/s and their effect on the normative values obtained would have been negligible.

Another potential explanation for the discrepancy in mean usual gait speeds between this study and others reporting normative values may be the type of walk test protocol used. CLSA participants could use assistive devices such as canes and walkers if needed to complete the walk test. Use of assistive devices during walk tests has been associated with slower gait speeds, which may be explained not only by the devices themselves but also by the underlying impairments that these individuals have that necessitated them having to use an assistive device.[27] Additionally, while a 4-meter test with a static start was used to measure gait speed in this study, other studies reporting normative gait speed values have used both shorter and longer walking distances with either static starts or dynamic starts that include acceleration and deceleration zones. Reviews of performance on various walking tests have suggested that compared to longer distance tests with either a static or dynamic start, the gait speeds obtained from short distance tests with a static start tend to be the slowest.[27–29] Although the influence of these protocol elements have been challenged,[30] they must still be considered when determining if the gait speed values obtained using a specific type of walk test are truly representative of the population they are seeking to describe.

As a consensus on one best definition of slow gait has not yet been reached, we additionally reported prevalence values across ranges of gait speeds below 1.00 m/s. Previous studies investigating slow gait in samples of older adults have used a variety of single cut-off definitions, which has led to heterogeneous prevalence estimates.[31–33] By exploring gait speed and slowness more thoroughly across the adult lifespan using multiple cut-off points, we gain a better picture of the individuals among which this impairment is more common, and the demographic groups that contain individuals who have more severely impaired gait speeds.

Finally, percentile figures express the position of an individual's performance relative to a reference population. The age-gender-specific height-adjusted percentile ranks calculable from our values should provide a more accurate reflection of individuals' gait speed performance, for example, to determine eligibility for an exercise intervention to improve mobility.

Due to the cross-sectional design of this analysis, measurement of changes in gait speed over time across the demographic strata were not possible. Additionally, since this study sample focused only on community-dwelling Canadian residents, the normative gait speed statistics obtained may not be generalizable to other adult populations. Nonetheless, the normative values for usual gait speed presented have the potential to be used as a reference to aid in the interpretation of patients' walking test results during clinical assessments, especially in Canadian contexts.

4.5 References

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Chapter 5

5 Associations between Reversible Risk Factors and Gait Speed in Middle and Older-Aged Community-Dwelling Adults: Results from the Canadian Longitudinal Study on Aging

A version of this chapter has been submitted for publication.

5.1 Abstract

Importance: Gait speed is an important marker of morbidity and mortality in older adults. Investigations of the non-modifiable and potentially modifiable correlates of gait speed in nationally representative samples are lacking. **Objective:** To assess the potentially modifiable and non-modifiable factors associated with gait speed in community-dwelling middle and older-aged adults. **Design:** Cross-sectional analysis of baseline data (May 2012 to May 2015) from the Canadian Longitudinal Study on Aging (CLSA) Comprehensive cohort. **Setting and Participants:** The CLSA is a cohort study comprising a nationally representative sample of community-dwelling Canadian adults aged 45 to 85 years at the time of baseline assessment. **Exposures**: Non-modifiable factors (i.e. socio-demographics, anthropometric factors, non-modifiable chronic conditions) and potentially modifiable factors (i.e. potentially modifiable chronic conditions, cognitive, clinical and lifestyle factors). **Main Outcome and Measure:** Usual gait speed (m/s) measured using a 4-meter walk test. **Results:** Of the 30,097 participants who completed a baseline assessment, 29,705 (98.7%) had gait speed measured. Of this, 20,201 (9971 [48.6%] female; 19479 [95.7%] white) had valid data on all study variables. The coefficient of determination, R^2, of the final hierarchical regression model was 19.7%, with the non-modifiable and potentially modifiable factor blocks explaining 15.6% and 4.1% of gait speed variability respectively. Potentially modifiable factors significantly associated with gait speed include cardiovascular condition (unstandardized regression coefficient, B= -.018, 95% CI= -.026; -.010; *P*<.001), stroke (B= -.025, 95% CI= -.041; -.009; *P*=.003), osteoarthritis (B= -.012, 95% CI= -.019; -.005; *P*=.001), serum Vitamin D (B= .003; 95% CI= .002; .005; *P*<.001), C-Reactive protein (B= -.003; 95%

CI= -.007; -.0002; *P*=.039), depressive symptoms (B= -.003, 95% CI= -.003; -.002; *P*<.001), physical activity (B=.0001; 95% CI= .00005; .0001; *P*<.001), grip strength (B=.003; 95% CI= .002; .003; *P*<.001), smoking (B= -.027; 95% CI= -.038; -.017; *P*<.001), chronic pain (B= -.011; 95% CI= -.017; -.005; *P*<.001), and trouble getting to the bathroom on time (B= -.031; 95% CI= -.040; -.022; *P*<.001). **Conclusions and Relevance:** The correlates of gait speed in adulthood are multifactorial, with many being potentially modifiable through intervention, education, and lifestyle changes.

5.2 Introduction

Gait impairments are prevalent among older adults and can severely affect health and physical function.[1,2] Slow gait speed specifically is associated with severe medical outcomes including falls and musculoskeletal injuries, multimorbidity, and mortality.[3–5] Recently, it has been shown that even gait speed changes and slowing in mid-life are associated with future adverse events and cognitive impairment.[6] Due to this prognostic value, the measurement of gait speed and its determinants in clinical settings is key to identify and treat older individuals at risk of facing future declines.[7]

Maintenance of normal gait speed is complex and reflects the interplay of many factors during adulthood that can be classified as non-modifiable and potentially modifiable. In contrast to non-modifiable factors which are unalterable (e.g. age, sex at birth), modifiable risk factors can potentially be altered/managed through various methods including clinical treatment and lifestyle changes. While studies have examined a wide range of non-modifiable and potentially modifiable factors affecting gait speed in older adults,[8–11] none have been done in large nationally representative samples including those of middle age. To address this gap, we identified correlates of gait speed using population-based data from the Canadian Longitudinal Study on Aging (CLSA). The specific objectives were to assess the bivariate associations between gait speed and non-modifiable and potentially modifiable factors and use multivariable regression to explain maximal variability in usual gait speed. Interest was on potentially modifiable factors to help focus intervention and education strategies in at-risk subgroups.

5.3 Methods

5.3.1 Study Design & Source Population

This was a cross-sectional analysis of baseline data (May 2012-May 2015) from the CLSA Comprehensive cohort. The CLSA is a Canada-wide longitudinal study of aging in a representative sample of ≈50,000 community-dwelling adults aged 45 to 85 years at recruitment.[12] About 20,000 people in the Tracking cohort provided information via computer-assisted telephone interviews, and another 30,000 in the Comprehensive cohort underwent face-to-face interviews, performed physical assessments, and provided biological samples in-home or at a data collection site.[13]

Several sampling frames were used in the creation of the CLSA Comprehensive cohort to ensure it was nationally representative including provincial healthcare registration databases and random digit dialing.[13,14] Strata were created within each province based on sex and age group (45-54, 55-64, 65-74, and 75-85) resulting in a total of 56 strata for the Comprehensive cohort. These strata were further crossed with education level. Individuals were excluded if they were living in one of the territories, certain remote areas, or in a First Nations reserve or settlement, or if they were full time members of the Canadian Armed Forces, institutionalized, unable to communicate in English or French, or were cognitively impaired.[13] Due to the requirement of attending in-person assessments, only individuals living within 25 to 50 kilometers of the data collection sites were recruited for the Comprehensive cohort.

5.3.2 Data Collection

Data collection procedures have been described elsewhere.[13] Briefly, the Comprehensive cohort baseline assessments evaluated sociodemographic characteristics, health status, lifestyle behaviours, cognitive and physical function, and drawn blood and urine samples. Written informed consent was obtained from CLSA participants and study protocols were approved by the ethical review boards of participating institutions.

5.3.2.1 Gait Speed

Usual gait speed, the primary outcome, was measured using a four-meter walk test with static start.[15] Participants stood with their toes behind a marked line and were told to walk straight at their usual pace until they walked a few steps past another line 4-meters away. Timing began immediately after the assessor said, "Ready, set, go," and stopped once the participant completely crossed the 4-meter finish line. Participants could use assistive devices such as canes and walkers if needed. Time to complete the walk once was recorded in seconds using a stopwatch and was converted into meters per second (m/s).

5.3.2.1 Independent Variables

Age, sex, province of residence, race, and highest level of education attained were included as sociodemographic covariates. Standing height (meters) and weight (kilograms) were included as anthropometric covariates.

The clinical factors included were grip strength,[16,17] chronic pain evaluated with the question, "Are you usually free of pain or discomfort?",[18] incontinence evaluated with the question, "Do you ever have trouble getting to the bathroom in time?",[19] depressive symptoms measured using the Center for Epidemiologic Studies Short Depression Scale (CESD-10),[20] and sleep disturbance operationalized using the question, "Over the last month, how often did you wake in the middle of the night or too early in the morning and found it difficult to fall asleep again?"[21] The clinical serum markers included were Vitamin D (mmol/L),[22] High Sensitivity C-Reactive Protein (hsCRP; mg/L),[23] and High-Density Lipoprotein (HDL; mmol/L).[24] The values for Vitamin D and hsCRP were transformed using the square-root and natural logarithm transformations respectively because of skewness.

Measures of cognitive function were included using the following cognitive domains: memory (Rey Auditory Verbal Learning Test [REY I, REY II]),[25] verbal fluency (Animal Fluency Test [AFT]),[26] and executive function (Mental Alternation Test [MAT]; Stroop Test).[27,28] A continuous Stroop (Interference) variable was created by subtracting participants' Stroop trial 1 (least difficult) time from their Stroop trial 3 (most difficult) time, and extreme outliers ±3 standard deviations from the mean were excluded.[29]

Lifestyle factors included smoking status, alcohol consumption, and physical activity measured using the Physical Activity Scale for the Elderly (PASE).[30] Self-reported non-modifiable chronic conditions included neurodegenerative disease (Dementia/ Alzheimer's disease, Parkinson's disease, and/or Multiple Sclerosis); memory problems; and macular degeneration. Self-reported potentially modifiable chronic conditions included cardiovascular (heart disease, peripheral vascular disease, angina, and/or heart attack); stroke (stroke and/or transient ischemic attack); diabetes; hypertension; cancer; osteoarthritis (knee and/or hip osteoarthritis); sensory impairment (fair/poor self-rated hearing and/or fair/poor self-rated vision); neuropsychiatric condition (anxiety disorder, mood disorder, epilepsy, and/or migraine headaches); and respiratory condition (asthma and/or emphysema/chronic bronchitis/COPD/other chronic lung issues).

5.3.3 Statistical Analysis

Descriptive statistics were generated using the mean ± standard error (SE) or median [IQR] for continuous variables and frequency (percentage) for categorical variables. A comparison of characteristics of the subjects included in the analysis with the group excluded due to missing data were conducted using two-tailed t-tests and chi-square tests for continuous and categorical variables respectively.

Bivariate linear associations between gait speed and each of the independent variables were assessed using the Complex Samples General Linear Model (CSGLM) procedure in SPSS (from menu: *Analyze* > *Complex Samples* > *General Linear Model*). Hierarchical multivariable linear regression modelling was performed using the CSGLM procedure as well to examine the correlates of gait speed. The independent variables of interest were grouped a priori into five hierarchical model blocks (Table 5-1). The rationale for the order the blocks were fitted was to adjust first for fundamental sociodemographic and design-based variables, followed by non-modifiable factors, then by potentially modifiable cognitive factors, then modifiable chronic diseases, and finally by modifiable clinical and lifestyle factors. Regression coefficients, denoted by B, with 95% confidence intervals and statistical significance were reported for each model. The coefficient of determination, R^2, for each model was examined to show the amount of variance in gait speed that was explained by the addition of each block.

To assess the potential for bias due to missing values, the hierarchical regression was repeated after imputing missing data using the fully conditional specification (FCS) method for arbitrary missing data patterns. To account for the complex survey design, the sampling weight variable was included as a covariate in the imputation model.[31] Following guidelines proposed by White et al. that the number of imputed data sets should be equal to the proportion of missing cases,[32] 30 imputed datasets were created.

All main analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Due to limitations of SPSS in analyzing complex sample data sets that have had missing values imputed through multiple imputation, SAS Version 9.4 was used to perform multiple imputation and re-run the hierarchical regression with the imputed data. Since the CLSA is a complex sample survey, analytic and (trimmed) inflation sampling weights were used in the analyses to obtain results that are representative of the Canadian population as per CLSA guidelines.[14]

Table 5-1. Hierarchical models used to measure correlates of gait speed.

Model 1	Sociodemographic factors (age, sex, province, race, education)
Model 2	Model 1 + Non-Modifiable Chronic Conditions (Neurodegenerative disease, memory problem, macular degeneration) + Anthropometric factors (height, weight)
Model 3	Model 2 + Cognition (REY I, REY II, AFT, MAT, Stroop Interference)
Model 4	Model 3 + Modifiable Chronic Conditions (cardiovascular condition, stroke, diabetes, hypertension, cancer, osteoarthritis, sensory impairment, neuropsychiatric condition, respiratory condition)
Model 5	Model 4 + Other Modifiable Clinical/Lifestyle Factors (vitamin D, hsCRP, HDL, depressive symptoms (CESD-10), grip strength, chronic pain, trouble getting to bathroom on time, sleep disturbance, physical activity (PASE), smoking status, alcohol consumption)

5.4 Results

5.4.1 Sample Characteristics

Of the 30,097 participants in the Comprehensive cohort baseline, 29,705 (98.7%) had values for gait speed. Overall, 20,201 (67.1%) participants had valid data for gait speed and all other variables of interest. Compared to those with complete data, individuals

excluded due to missing data (n= 9896) tended to be older, female, and non-white, with less education, and slower gait speeds (Appendix E, Table E-1).

Table 5-2 shows the characteristics of the analytic sample. The mean age was 58.8 years (SE=0.08) and 48.6% were female. Most participants were white (95.7%) and had a post-secondary degree or diploma (81%). The most common chronic conditions were hypertension (30.3%), neuropsychiatric condition (29.6%), and osteoarthritis (15.7%). The mean usual gait speed was 1.01 m/s (SE=0.002).

Table 5-2. Baseline descriptive statistics for analytic sample (n=20,201).

Variable	Population Estimate[a]
Age, mean ± SE, years	58.84 ± 0.08
Height, mean ± SE, m	1.69 ± 0.0009
Weight, mean ± SE, kg	79.57 ± 0.15
Vitamin D, mean ± SE, mmol/L	82.73 [46.3]
hsCRP, mean ± SE, mg/L	1.04 [1.82]
HDL, mean ± SE, mmol/L	1.51 ± 0.004
Gait Speed, mean ± SE, m/s	1.01 ± 0.002
Grip Strength, mean ± SE, kg	35.54 ± 0.11
REY I (Immediate Recall), mean ± SE	6.11 ± 0.02
REY II (Delayed Recall), mean ± SE	4.37 ± 0.02
AFT, mean ± SE	20.70 ± 0.05
MAT, mean ± SE	27.91 ± 0.08
Stroop (Interference), mean ± SE	12.79 ± 0.06
Depressive Symptoms (CESD-10), mean ± SE	4.98 ± 0.04
Physical Activity (PASE), mean ± SE	154.38 ± 0.73
Sex, No. (%)	
Female	9971 (48.6)
Male	10230 (51.4)
Province, No. (%)	
Alberta	1871 (11.5)
British Columbia	4237 (29.9)
Manitoba	2286 (8.8)
Newfoundland and Labrador	1446 (2.1)
Nova Scotia	2004 (3.4)
Ontario	4279 (12.9)
Quebec	4078 (31.4)
Race, No. (%)	
White	19479 (95.7)
Non-white	722 (4.3)
Highest Education Level, No. (%)	
Less than secondary school graduation	910 (4.0)
Secondary school graduation only	1795 (8.6)

Some post-secondary education	1439 (6.4)
Post-secondary degree or diploma	16057 (81.0)
Trouble to get to bathroom on time, No. (%)	
Yes	2382 (10.7)
No	17819 (89.3)
Chronic Pain, No. (%)	
Yes	6859 (33.3)
No	13342 (66.7)
Sleep disturbance, No. (%)	
6-7 times/week	2272 (10.9)
3-5 times/week	2458 (12.5)
1-2 times/week	3263 (16.6)
Never or less than once/week	12208 (60.0)
Smoking Status, No. (%)	
Current smoker	1721 (8.8)
Former smoker	8783 (41.0)
Never smoker	9697 (50.2)
Alcohol Consumption, No. (%)	
Regular Drinker	15725 (79.3)
Occasional Drinker	2347 (10.4)
Non-Drinker	2129 (10.3)
Neurodegenerative Disease, No. (%)	213 (1.0)
Memory Problem, No. (%)	257 (1.2)
Macular Degeneration, No. (%)	757 (2.8)
Cardiovascular Condition, No. (%)	3020 (12.5)
Stroke, No. (%)	735 (2.7)
Diabetes, No. (%)	3311 (14.2)
Hypertension, No. (%)	7121 (30.3)
Cancer, No. (%)	2934 (11.5)
Osteoarthritis, No. (%)	3770 (15.7)
Sensory Impairment, No. (%)	3126 (14.6)
Neuropsychiatric Condition, No. (%)	5814 (29.6)
Respiratory Condition, No. (%)	3253 (15.6)

[a] Means, standard errors, medians, IQRs, and percentages estimated using (trimmed) inflation weights.
Notes: AFT=Animal Fluency Test; CESD-10=Center for Epidemiologic Studies Depression Scale; HDL= High Density Lipoprotein; hsCRP=high sensitivity C-Reactive protein; IQR=interquartile range; MAT= Mental Alternation Test; PASE=Physical Activity Scale for the Elderly; SE=standard error.

5.4.2 Correlates of Gait Speed: Bivariate Associations

The bivariate relationships between gait speed and its potential correlates are presented in Table 5-3. Additional details are provided below.

5.4.2.1 Sociodemographic Correlates

Age was significantly negatively associated with gait speed. Next, being female was associated with slower gait speed, with men and women walking at average speeds of 1.02 m/s (95% CI=1.01; 1.02) and 1.00 m/s (95% CI=0.99; 1.01) respectively. Identifying as non-White was also associated with slower gait speed compared to those who identified as White, with the White and non-White racial groups walking at average speeds of 1.01 m/s (95% CI=1.01; 1.02) and 0.97 m/s (95% CI=0.96; 0.99) respectively. Finally, compared to the post-secondary degree/diploma education group, lower levels of education were associated with slower gait speeds. The mean gait speed for those with a post-secondary degree/diploma was 1.02 m/s (95% CI=1.02; 1.02) while those with some post-secondary education and those who only graduated secondary school had mean gait speeds of 0.99 m/s (95% CI=0.98; 1.00) and 0.98 m/s (95% CI=0.97; 0.99) respectively. The mean gait speed for individuals with less than a secondary school graduation was 0.90 m/s (95% CI=0.89; 0.92).

5.4.2.2 Anthropometric & Clinical Correlates

Height was positively associated with gait speed whereas weight was negatively associated. Both Vitamin D (square root transformed) and HDL were positively associated with gait speed while hsCRP (natural log transformed) was negatively associated.

Depressive symptoms (CESD-10) were negatively associated with gait speed, while grip strength was positively associated. Chronic pain was associated with slower gait speed compared to those who reported being free of chronic pain, with mean gait speeds of 1.03 m/s (95% CI=1.02; 1.03) for those usually free of pain and 0.98 m/s (95% CI=0.98; 0.99) for those with chronic pain. Trouble getting to the bathroom on time was also associated with slower gait speed compared to those who reported no trouble, with an average

walking speed of 0.94 m/s (95% CI=0.93; 0.95) for the group who reported trouble and 1.02 m/s (95% CI=1.02; 1.02) for the group who reported having no trouble. For sleep disturbance, only reporting waking up and having difficulty falling back asleep 6 or 7 times per week was significantly associated with slower gait speed compared to those who reported sleep disturbance occurring less than once per week or never, with mean gait speeds of 1.00 m/s (95% CI=0.99; 1.01) for the 6-7 times per week group and 1.01 m/s (95% CI=1.01; 1.02) for the reference group.

5.4.2.3 Cognitive Correlates

High performance in immediate and delayed recall, verbal fluency, and attention were significantly associated with faster gait speed. Stroop (interference) scores were negatively associated with gait speed showing that a larger difference between the time taken to complete the first (easiest) and third (hardest) trials of the Stroop test was associated with slower gait speeds.

5.4.2.4 Lifestyle Behaviour Correlates

Higher physical activity (PASE) was positively associated with gait speed. Compared to never smoking, being a current or former smoker was associated with slower gait speeds. Never-smokers, current smokers, and former smokers walked at average speeds of 1.03 m/s (95% CI=1.02; 1.03), 0.98 m/s (95% CI=0.97; 0.99), and 1.00 m/s (95% CI=0.99; 1.00) respectively. Finally, report of regularly or occasionally drinking alcohol in the last 12 months was associated with faster gait average speeds compared to never drinking, with the mean gait speeds of regular drinkers, occasional, and non-drinkers being 1.02 m/s (95% CI=1.02; 1.02), 0.98 m/s (95% CI=0.97; 0.99), and 0.97 m/s (95% CI=0.96; 0.98) respectively.

5.4.2.5 Chronic Condition Correlates

All non-modifiable and potentially modifiable chronic conditions were each significantly negatively associated with gait speed. Those who reported that they had a neurodegenerative disease, memory problem, or macular degeneration had average gait speeds of 0.92 m/s (95% CI=0.88; 0.96), 0.93 m/s (95% CI=0.90; 0.96), and 0.95 m/s

(95% CI=0.93; 0.96) respectively while the groups who reported not having these conditions all had average gait speeds of 1.01 m/s (all 95% CIs=1.01; 1.02). Participants who reported a history of stroke had a mean gait speed of 0.91 m/s (95% CI=0.89; 0.93), while those without a stroke history had a mean gait speed of 1.01 m/s (95% CI=1.01; 1.02). Participants who reported having hypertension had a mean gait speed of 0.97 m/s (95% CI=0.96; 0.97), while those who reported no hypertension walked at an average speed of 1.03 m/s (95% CI=1.03; 1.03)

Those who reported that they had cancer, any neuropsychiatric condition, or any respiratory condition had average gait speeds of 0.98 m/s (95% CI=0.97; 0.99), 1.00 m/s (95% CI=0.99; 1.01), and 1.00 m/s (95% CI=0.99; 1.01) respectively. The groups who reported not having cancer, any neuropsychiatric condition, or any respiratory condition all had average gait speeds of 1.02 m/s (all 95% CIs=1.01; 1.02). Finally, participants who reported any cardiovascular condition, osteoarthritis, diabetes, or any sensory impairment had mean gait speeds of 0.94 m/s (95% CI=0.94; 0.95), 0.96 m/s (95% CI=0.95; 0.96), 0.96 m/s (95% CI=0.96; 0.97), and 0.98 m/s (95% CI=0.97; 0.99) respectively. The groups who did not report a cardiovascular condition, osteoarthritis, diabetes, or a sensory impairment all had mean gait speeds of 1.02 m/s (95% CIs=1.02; 1.02/ 1.02; 1.03/ 1.02; 1.02/ 1.01; 1.02 respectively).

Table 5-3. Bivariate associations between gait speed and selected factors.

Variable	B (95% CI)[a]	*p*
Sociodemographic Factors		
Age, years	-.005 (-.006; -.005)	<.001
Province, ON (Ref)		<.001
AB	-.020 (-.031; -.006)	
BC	.035 (.026; .043)	
MB	-.036 (-.047; -.026)	
NL	-.052 (-.064; -.041)	
NS	.081 (.068; .093)	
QC	.007 (-.002; .016)	
Sex, Male (Ref)		
Female	-.015 (-.021; -.010)	
Race, White (Ref)		<.001
Non-white	-.039 (-.057; -.022)	
Highest Education Level, Post-secondary degree or diploma (Ref)		<.001
Some post-secondary	-.034 (-.045; -.023)	
Secondary only	-.037 (-.046; -.027)	
Less than secondary	-.116 (-.130; -.103)	
Anthropometric Factors		
Height, m	.285 (.254; .315)	<.001
Weight, kg	-.001 (-.001; -.001)	<.001
Chronic Conditions		
Neurodegenerative Disease	-.092 (-.128; -.056)	<.001
Memory Problem	-.085 (-.113; -.056)	<.001
Macular Degeneration	-.065 (-.082; -.048)	<.001
Cardiovascular Condition	-.076 (-.085; -.068)	<.001
Stroke	-.103 (-.121; -.085)	<.001
Diabetes	-.056 (-.064; -.048)	<.001
Hypertension	-.062 (-.068; -.056)	<.001
Cancer	-.034 (-.043; -.026)	<.001
Osteoarthritis	-.064 (-.071; -.056)	<.001
Respiratory Condition	-.015 (-.022; -.009)	<.001
Sensory Impairment	-.037 (-.045; -.028)	<.001
Neuropsychiatric Condition	-.015 (-.022; -.009)	<.001
Cognitive Factors		
REY I (Immediate Recall)	.014 (.012; .015)	<.001
REY II (Delayed Recall)	.010 (.009; .011)	<.001
AFT	.006 (.006; .007)	<.001
MAT	.004 (.003; .004)	<.001
Stroop (Interference), sec	-.005 (-.005; -.004)	<.001
Clinical Factors		
HDL, mmol/L	.028 (.022; .034)	<.001
Vitamin D (square root), mmol/L	.003 (.001; .004)	.001
hsCRP (natural log), mg/L	-.030 (-.033; -.027)	<.001
Depressive symptoms (CESD-10)	-.005 (-.006; -.005)	<.001

Trouble getting to bathroom on time	-.085 (-.095; -.075)	<.001
Chronic Pain	-.045 (-.051; -.038)	<.001
Grip Strength, kg	.003 (.003; .003)	<.001
Sleep disturbance, Never or less than once/week (Ref)		.011
6-7 times/week	-.011 (-.021; -.001)	
3-5 times/week	.007 (-.002; .016)	
1-2 times/week	.007 (-.001; .015)	
Lifestyle Factors		
Physical Activity (PASE)	.0004 (.0003; .0004)	<.001
Smoking Status, Never (Ref)		
Current Smoker	-.043 (-.054; -.032)	<.001
Former Smoker	-.031 (-.037; -.024)	
Alcohol Consumption, Never (Ref)		
Regular Drinker	.046 (.036; .057)	<.001
Occasional Drinker	.004 (-.009; .018)	

[a] Bivariate parameter estimates (B) for each independent factor obtained using complex samples general linear model analysis (with analytic sampling weights) with gait speed (m/s) as the dependent variable.
Notes: HDL=High Density Lipoprotein; hsCRP=high sensitivity C-Reactive protein; AFT=Animal Fluency Test; MAT=Mental Alternation Test; CESD-10=Center for Epidemiologic Studies Depression Scale; PASE=Physical Activity Scale for the Elderly.

5.4.3 Potentially Modifiable and Non-Modifiable Correlates of Gait Speed: Hierarchical Regression

The relationships between gait speed and the non-modifiable and potentially modifiable factors in the five hierarchical regression models are presented in Table 5-4. Inclusion of the two sets of non-modifiable factors alone explained 15.6% of gait speed variability. Cognitive factors, potentially modifiable chronic conditions, and other potentially modifiable clinical and lifestyle factors explained an additional 0.8%, 0.7%, and 2.6% of variability respectively. The R^2 for the final model was 19.7%.

Several potentially modifiable factors were statistically significantly associated with gait speed in the final regression model. The chronic conditions that were significantly negatively associated with gait speed were cardiovascular condition (B= -.018, 95% CI= -.026; -.010), stroke (B= -.025, 95% CI= -.041; -.009), and osteoarthritis (B= -.012, 95% CI= -.019; -.005). In terms of serum factors, (sqrt) Vitamin D concentration was positively associated with gait speed (B= .003; 95% CI= .002; .005), and (log) hsCRP concentration was negatively associated (B= -.003; 95% CI= -.007; -.0002).

Having less than secondary school graduation was also significantly associated with slower gait speed (B= -.030, 95% CI= -.043; -.017) as was being a current smoker (B= -.027; 95% CI= -.038; -.017). Contrarily, physical activity (PASE score) was positively associated with gait speed (B=.0001; 95% CI= .00005; .0001). Several potentially modifiable clinical factors were also significantly associated with gait speed. Depressive symptoms (CESD-10 score) were negatively associated with gait speed (B= -.003, 95% CI= -.003; -.002), while grip strength was positively associated (B=.003; 95% CI= .002; .003). Reporting chronic pain (B= -.011; 95% CI= -.017; -.005) or trouble getting to the bathroom on time (B= -.031; 95% CI= -.040; -.022) were both negatively associated with gait speed.

Cognitive tests for memory, executive function, and verbal fluency were significantly associated with gait speed as well. Better performance on immediate recall (REY I) was positively associated with gait speed (B=.003; 95% CI=.001; .005) along with performance on tests of verbal fluency [AFT] (B=.002; 95% CI= .001; .002) and executive function [MAT] (B= .0009; 95% CI= .0005; .001).

5.4.3.1 Sensitivity Analysis

To account for potential selection bias as a result of listwise exclusion of missing cases, the models were re-run with missing cases imputed (Appendix F, Table F-1). Overall, the imputed parameter estimates were of similar magnitude and direction. The only notable change was that two potentially modifiable chronic conditions that were not initially statistically significant (diabetes and sensory impairment) became so in the imputed sample.

Table 5-4. Hierarchical regression analysis of non-modifiable and potentially modifiable correlates of gait speed.

Model 1[a] [R^2 (%) =11.8%]		
Variable	**B (95% CI)**	***P***
Constant	1.323 (1.305; 1.342)	<.001
Age, years	-.005 (-.005; -.005)	<.001
Sex, female	-.014 (-.020; -.009)	<.001
Province, ON (Ref)		
AB	-.028 (-.040; -.016)	<.001
BC	.034 (.026; .043)	<.001
MB	-.031 (-.041; -.021)	<.001
NL	-.059 (-.070; -.047)	<.001
NS	.077 (.065; .089)	<.001
QC	.010 (.002; .019)	.020
Race, White (Ref)		
Non-White	-.058 (-.075; -.041)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary	-.020 (-.031; -.010)	<.001
Secondary education only	-.025 (-.034; -.016)	<.001
Less than secondary school graduation	-.078 (-.091; -.064)	<.001
Model 2 [R^2 (%) =15.6%; R^2 change = 3.8%]		
Variable	**B (95% CI)**	***P***
Constant	.728 (.644; .812)	<.001
Age, per year	-.005 (-.005; -.005)	<.001
Sex, female	.012 (.004; .021)	.003
Province, ON (Ref)		
AB	-.031 (-.043; -.019)	<.001
BC	.026 (.018; .035)	<.001
MB	-.025 (-.035; -.015)	<.001
NL	-.051 (-.062; -.040)	<.001
NS	.081 (.069; .093)	<.001
QC	.013 (.004; .022)	.003
Race, White (Ref)		
Non-White	-.051 (-.068; -.035)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.014 (-.024; -.004)	.009
Secondary education only	-.017 (-.026; -.008)	<.001
Less than secondary school graduation	-.059 (-.073; -.046)	<.001
Height, m	.432 (.386; .478)	<.001
Weight, kg	-.002 (-.002; -.002)	<.001
Neurodegenerative Disease	-.073 (-.107; -.040)	<.001
Memory Problem	-.067 (-.093; -.041)	<.001
Macular Degeneration	-.007 (-.022; .009)	.390
Model 3 [R^2 (%) = 16.4%; R^2 change = 0.8%]		
Variable	**B (95% CI)**	***P***
Constant	.655 (.570; .741)	<.001
Age, years	-.004 (-.004; -.004)	<.001
Sex, female	.009 (.001; .018)	.024
Province, ON (Ref)		

AB	-.031 (-.043; -.019)	<.001
BC	.024 (.016; .032)	<.001
MB	-.023 (-.033; -.013)	<.001
NL	-.048 (-.059; -.036)	<.001
NS	.085 (.073; .097)	<.001
QC	.019 (.010; .028)	<.001
Race, White (Ref)		
Non-White	-.039 (-.043; -.019)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.010 (-.021; .0002)	.054
Secondary education only	-.010 (-.019; -.002)	.022
Less than secondary school graduation	-.044 (-.057; -.031)	<.001
Height, m	.402 (.355; .448)	<.001
Weight, kg	-.002 (-.002; -.002)	<.001
Neurodegenerative Disease	-.070 (-.104; -.037)	<.001
Memory Problem	-.058 (-.084; -.032)	<.001
Macular Degeneration	-.007 (-.022; .008)	.366
REY I (Immediate Recall)	.004 (.002; .006)	<.001
REY II (Delayed Recall)	-.002 (-.004; -.0002)	.026
AFT	.002 (.001; .003)	<.001
MAT	.001 (.001; .001)	<.001
Stroop (Interference), sec	-.001 (-.001; -.0001)	.014
Model 4 [R^2 (%) = 17.1%; R^2 change = 0.7%]		
Variable	**B (95% CI)**	***P***
Constant	.671 (.585; .756)	<.001
Age, years	-.004 (-.004; -.003)	<.001
Sex, female	.010 (.002; .019)	.015
Province, ON (Ref)		
AB	-.031 (-.043; -.019)	<.001
BC	.024 (.016; .032)	<.001
MB	-.023 (-.033; -.013)	<.001
NL	-.049 (-.060; -.038)	<.001
NS	.084 (.072; .096)	<.001
QC	.020 (.011; .028)	<.001
Race, White (Ref)		
Non-White	-.038 (-.055; -.022)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.009 (-.020; .001)	.076
Secondary education only	-.010 (-.019; -.002)	.021
Less than secondary school graduation	-.039 (-.053; -.026)	<.001
Height, m	.374 (.328; .420)	<.001
Weight, kg	-.002 (-.002; -.002)	<.001
Neurodegenerative Disease	-.064 (-.098; -.031)	<.001
Memory Problem	-.046 (-.072; -.020)	.001
Macular Degeneration	-.003 (-.018; .013)	.739
REY I (Immediate Recall)	.004 (.002; .006)	<.001
REY II (Delayed Recall)	-.002 (-.004; -.0001)	.036
AFT	.002 (.001; .003)	<.001
MAT	.001 (.001; .001)	<.001
Stroop (Interference), sec	-.0004 (-.001; -.000004)	.048
Cardiovascular Condition	-.024 (-.031; -.016)	<.001
Stroke	-.032 (-.049; -.015)	<.001
Diabetes	-.011 (-.019; -.003)	.004

Hypertension	-.007 (-.013; -.001)	.022
Cancer	.0003 (-.008; .008)	.945
Osteoarthritis	-.018 (-.025; -.011)	<.001
Sensory Impairment	-.014 (-.021; -.006)	.001
Neuropsychiatric Condition	-.013 (-.019; -.007)	<.001
Respiratory Condition	-.007 (-.014; .001)	.069
Model 5 [R^2 (%) = 19.7%; R^2 change = 2.6%]		
Variable	**B (95% CI)**	***P***
Constant	.668 (.581; .755)	<.001
Age, years	-.003 (-.003; -.002)	<.001
Sex, Female	.050 (.040; .061)	<.001
Province, ON (Ref)		
AB	-.034 (-.046; -.022)	<.001
BC	.024 (.016; .032)	<.001
MB	-.019 (-.028; -.009)	<.001
NL	-.051 (-.062; -.040)	<.001
NS	.086 (.074; .097)	<.001
QC	.019 (.011; .028)	<.001
Race, White (Ref)		
Non-White	-.026 (-.043; -.010)	.002
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.004 (-.014; .006)	.425
Secondary education only	-.006 (-.015; .002)	.161
Less than secondary school graduation	-.030 (-.043; -.017)	<.001
Height, m	.247 (.199; .295)	<.001
Weight, kg	-.002 (-.002; -.001)	<.001
Neurodegenerative Disease	-.049 (-.082; -.016)	.003
Memory Problem	-.031 (-.056; -.006)	.017
Macular Degeneration	.002 (-.013; .018)	.747
REY I (Immediate recall)	.003 (.001; .005)	.004
REY II (Delayed recall)	-.002 (-.004; -.0002)	.033
AFT	.002 (.001; .002)	<.001
MAT	.0009 (.0005; .001)	<.001
Stroop (Interference), sec	-.0002 (-.001; .0002)	.359
Cardiovascular Condition	-.018 (-.026; -.010)	<.001
Stroke	-.025 (-.041; -.009)	.003
Diabetes	-.003 (-.011; .004)	.411
Hypertension	-.006 (-.012; .0001)	.059
Cancer	.003 (-.005; .010)	.494
Osteoarthritis	-.012 (-.019; -.005)	.001
Sensory Impairment	-.006 (-.013; .002)	.164
Neuropsychiatric Condition	-.0008 (-.007; .005)	.803
Respiratory Condition	-.0006 (-.008; .007)	.870
HDL, mmol/L	.003 (-.004; .010)	.460
Vitamin D (square root), mmol/L	.003 (.002; .005)	<.001
hsCRP (natural log), mg/L	-.003 (-.007; -.0002)	.039
Depressive Symptoms (CESD-10)	-.003 (-.003; -.002)	<.001
Trouble getting to bathroom on time	-.031 (-.040; -.022)	<.001
Chronic Pain	-.011 (-.017; -.005)	<.001
Grip Strength, kg	.003 (.002; .003)	<.001
Sleep disturbance, Never or less than once/week (Ref)		
6-7 times/week	.007 (-.003; .016)	.153
3-5 times/week	.007 (-.001; .016)	.093

1-2 times/week	.004 (-.003; .012)	.244
Physical Activity (PASE)	.0001 (.00005; .0001)	<.001
Smoking Status, Never (Ref)		
Current Smoker	-.027 (-.038; -.017)	<.001
Former Smoker	-.008 (-.014; -.003)	.004
Alcohol Consumption, Never Drinker (Ref)		
Regular Drinker	.016 (.006; .025)	.001
Occasional Drinker	.009 (-.003; .020)	.158

[a] Analytic sampling weights applied in hierarchical regression analysis.
Notes: AFT=Animal Fluency Test; CESD-10=Center for Epidemiologic Studies Depression Scale; HDL= High Density Lipoprotein; hsCRP=high sensitivity C-Reactive protein; MAT=Mental Alternation Test; PASE=Physical Activity Scale for the Elderly.

5.5 Discussion

This study estimated the associations of non-modifiable and potentially modifiable risk factors with gait speed in a large representative sample of community-dwelling middle and older aged adults and estimated the amount of variation in gait speed that could be explained by potentially modifiable factors. To our knowledge, this is one of the first such studies.

5.5.1 Variation in Gait Speed is Largely Explained by Non-Modifiable Factors

Our study demonstrated that in community-dwelling adults, nearly 16 percent of variation in gait speed was explained solely by the blocks of non-modifiable factors (i.e. sociodemographic and anthropometric factors, non-modifiable chronic conditions). Potentially modifiable factors (i.e. cognitive measures, clinical factors, modifiable chronic conditions, lifestyle behaviours) also significantly explained about four percent of gait speed variability.

It is well understood that average gait speed is strongly influenced by multiple non-modifiable biological factors including age and height.[33–35] Recently, research has also shown that gait disturbances are a hallmark of progressive neurodegenerative diseases which involve the degeneration of neural structures directly involved in motor control along with brain regions associated with cognitive functions that are essential for maintaining normal gait.[36]

The variability in gait speed explained by potentially modifiable factors further provides evidence that gait speed is a complex motor function not solely determined by age and other unalterable characteristics. Rather, it can be thought of as the product of a multifactorial set of etiological factors acting through a network of pathophysiological pathways.[37] Following this paradigm, isolated factors may insufficiently explain variations in gait speed; however, when considered as part of an interactive system, their effects may be clearer and more substantial. Ultimately, applying this multidimensional approach is crucial to gain a more complete understanding of the correlates of gait speed, and to further mitigate abnormal declines in gait speed that indicate underlying morbidity not associated with natural biological processes.[38]

5.5.2 Gait Speed is Significantly Associated with Multiple Potentially Modifiable Factors

Several potentially modifiable factors were significantly associated with gait speed in the final regression model. The chronic conditions that were significantly negatively associated with gait speed in the final regression model including osteoarthritis, stroke, and any cardiovascular condition. Previous studies have found that older adults with osteoarthritis tend to walk slower and are more likely to experience gait speed declines as a result of the mobility-impairing symptoms.[39,40] However, with intervention, improvement of functionality and quality of life is possible.[41] Significant negative associations between history of stroke and gait speed in older adults have been previously reported,[9,42,43] although findings are not consistent.[10,44] The significant result we found for having any cardiovascular disease (i.e. heart disease, myocardial infarction, angina, peripheral vascular disease) also conflicts with many non-significant findings in the literature,[10,44,45] which may suggest that the directionality of this relationship is reversed, with slower gait speed predicting adverse cardiovascular events instead.[46] Regardless, prevention of strokes and cardiovascular conditions through clinical intervention, lifestyle modification, and education may partially mitigate detrimental mobility impairments and subsequent morbidity in at-risk individuals.[47,48]

Having below a secondary school education was also significantly negatively associated with gait speed. Analyses of socioeconomic disparities within communities have

demonstrated that individuals with fewer years of education are more likely to become disabled, engage in negative health behaviours, and face greater barriers to accessing essential health care services including lacking adequate health literacy skills.[49–51] While only 4% of CLSA participants had not completed high school, the significant association of low education level with gait speed in this cohort highlights the importance of improving graduation rates in socioeconomically disadvantaged groups.

The negative association we found for smoking is consistent with previous studies,[10,52,53] and supports arguments for the detrimental effects of smoking on physiological systems underlying mobility.[54] The positive association of alcohol consumption on gait speed in our sample is also in line with other investigations,[52,55] however a plausible explanation for this finding is that individuals who can tolerate alcohol may simply be healthier and more mobile than those who do not drink. It is also well understood that engaging in physical activity across the adult lifespan promotes cardiovascular health and improves muscle strength and our finding contributes to the growing body of literature demonstrating the benefits of active lifestyles on walking speed in older age.[56,57]

We additionally found a significant positive association for serum vitamin D and a significant negative association for C-reactive protein. This supports previous findings that lower vitamin D levels and higher C-reactive protein levels are linked to slower gait speed in older adults, [22,23,58–60] and ultimately highlights the importance of considering the roles of these and other biomarkers in the multifactorial causality of gait impairments.

Grip strength, depressive symptoms, chronic pain, and trouble getting to the bathroom on time were also significantly associated with gait speed. Weaker grip strength has been linked to mobility declines.[16,61] Although many older adults experience natural age-related muscle loss, this can be mitigated through various lifestyle changes including regular physical activity.[62] Next, while we found an inverse cross-sectional association between number of depressive symptoms and gait speed, longitudinal investigations have suggested potentially bidirectional and reversed relationships.[63,64] Models of the biological pathways shared by depression and gait impairments have been proposed,[65] and comorbid issues may further partially explain their relationship.[66]

Chronic pain interferes with physical function and participation in everyday activities. Although definitions of pain vary, studies generally report significant associations with slower gait speed in adults, reinforcing the importance of pain management in mobility decline mitigation efforts.[9,10,18,67–69] Likewise, research has suggested that incontinence – both bowel and urinary – can impose severe burdens on wellbeing. Evidence for the correlation between urinary incontinence specifically with gait speed is conflicting,[70,71] and this relationship may instead be reversed or bidirectional since slow walking can hinder one's ability to travel to the bathroom in a timely fashion and fear of incontinence can contribute to mobility limitations as affected individuals feel less comfortable engaging in regular daily activities.[72]

Finally, we found significant positive associations for most of the cognitive tests (i.e. REY, AFT, MAT). Researchers have argued that multiple cognitive domains play important roles in the motor control of initiation, maintenance, and adaptability of gait.[73] Thus, impairments in cognition can lead to the development of gait abnormalities.[74] Given the relationship between cognition and gait, implementing strategies to bolster cognitive performance throughout the adult lifespan may impart benefits on mobility well into older age.

It must be noted that many of the associations found for the potentially modifiable factors highlighted above appeared to be small to moderate in magnitude. Although the use of the large CLSA sample for this study offered the power to detect statistically significant associations, the clinical significance of these results remains unclear. Ultimately, consideration of the results in terms of their clinical meaningfulness in addition to their statistical associations is necessary should they be referenced in the future in efforts to define optimal targets for intervention to maintain healthy gait speed.

5.5.3 Limitations

This study has several limitations. Due to the cross-sectional design, we were not able assess the directionality of the associations between the selected correlates and gait speed or analyze gait speed changes prospectively. People were excluded from the CLSA based on several geographic factors as well (e.g. residence in the territories, First Nations

settlements/ reserves, or farther than 25-50 km from data collection sites), and the majority who were recruited into the study were community-dwelling, White, highly educated, and relatively healthy – all of which may limit the generalizability of the results to other adult populations.

Next, the measurement of chronic conditions was done by self-report. Although self-report has been shown to be a reliable and valid method to obtain information about chronic conditions, individuals may have had undiagnosed conditions that they were not aware of at the time of assessment, and self-report diagnoses do not incorporate severity or response to treatment. Several composite variables combining similar conditions were also created to simplify the analyses (e.g. cardiovascular conditions, neuropsychiatric conditions). By doing so, some detail on the associations of specific conditions with gait speed may have been lost.

Lastly, a non-exhaustive set of correlates was used for this analysis. We did not measure the effects of other clinical factors possibly associated with gait speed such as polypharmacy, falls, or musculoskeletal injuries. We also were unable to include other social determinants of health – including access to medical care or social support – that play major roles in healthy aging.

5.5.4 Conclusion

In this cross-sectional analysis of over 20,000 middle and older-aged Canadians, we found associations of non-modifiable and potentially modifiable factors with gait speed. We showed that while the variation in gait speed was largely explained by non-modifiable factors, multiple factors were potentially modifiable, including education, chronic pain, muscle strength, and cardiovascular conditions. We provide a framework for future longitudinal analyses of gait speed and its complex determinants and preliminary evidence to inform potential intervention strategies in at-risk adult populations.

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Chapter 6

6 Summary and Conclusion

6.1 Overview

The objective of this chapter is to summarize the research and results presented in this thesis and contextualize the findings within previous literature. Research and methodological contributions are discussed along with limitations of the studies conducted. Directions for future research and overall conclusions are also outlined.

6.2 Summary of Main Findings

The main goal of this thesis was to contribute to the growing body of literature seeking to understand gait speed variations across the adult lifespan and identify the demographic, clinical, and behavioural factors that may underlie these gait speed variations in older age. By systematically reviewing current available literature, evidence for the effects of multiple potentially modifiable risk factors on slow and declining gait speed was synthesized (Chapter 2), providing a framework for an additional analysis of gait speed correlates in a cohort of middle and older-aged community-dwelling Canadian adults (Chapter 5). To complement the analysis of gait speed correlates, normative gait speed data and the prevalence of slow gait were also estimated in this Canadian cohort to describe the differences that exist across age and biological sex (Chapter 4).

6.2.1 Modifiable Risk Factors for Slow Gait in Community-Dwelling Older Adults: A Systematic Review

The objective of the systematic review presented in Chapter 2 was to identify potentially modifiable factors associated with slow gait speed and clinically meaningful gait speed decline in older community-dwelling adults. In total, 40 studies met the inclusion criteria and were qualitatively synthesized. Across these cross-sectional and longitudinal studies, which were deemed fair or good quality, sample sizes ranged from 108 to 7025 participants and usual gait speed was measured using walk test distances ranging from 2.4 meters to 20 meters. Multiple different criteria were used to define slow gait and

meaningful gait speed decline, with cutoffs being based either on sample distributions (e.g. quartiles), external criteria (e.g. < 0.8 m/s), or dynamic changes over time (e.g. ≥ 0.05 m/s decline per year). Due to the heterogeneity in these criteria and other methodological factors, the slow gait prevalence estimates reported in the studies varied widely, with frequencies ranging from 1.56% to 65.8%. Overall, 85 potentially modifiable risk factors were assessed for an association with slow gait or meaningful gait speed decline. Of these, 26 factors were assessed in at least two studies. Factors were organized into the following groups for qualitative synthesis: sociodemographic, clinical, lifestyle, body composition, serum, cognitive, and dietary.

Among the sociodemographic factors, education level was the only factor assessed in multiple studies. Most studies that included education level in their analyses reported significantly greater odds of slow gait or meaningful decline for adults who attained lower levels of education (e.g. less than high school). Thirteen clinical factors were also identified in at least two studies including depression, pain, multimorbidity, hypertension, heart conditions, stroke, polypharmacy, falls, fear of falling, grip strength, arthritis, diabetes, impaired vision. Most studies that assessed depression, pain, and polypharmacy found that these conditions significantly increased the odds of slow gait while stronger grip strength was found to be protective against slow gait. In general, effects reported for multimorbidity, hypertension, heart conditions, and diabetes were non-significant, and the effects reported for history of stroke, falls, fear of falling, arthritis, and vision impairments were mixed.

Lifestyle factors that were assessed in multiple studies were physical activity, smoking, and alcohol consumption. Many studies found that engaging in physical activity was protective against slow gait. Non-significant effects were reported for smoking, and inconsistent findings were reported for alcohol consumption. Among the body composition variables, BMI, calf circumference, and bone mineral density were assessed in multiple studies. Many studies reported significant associations between obese BMI and greater odds of slow gait and some reported significant negative effects for underweight BMI as well. Greater calf circumference was found to be significantly

associated with lower odds of slow gait while effects for bone mineral density were mixed.

Three serum factors were also assessed in multiple studies: vitamin D, high sensitivity C-Reactive Protein, and albumin. Effects reported for these factors were inconsistent, however some studies found that lower vitamin D and elevated C-Reactive protein were significantly associated with greater odds of slow gait. Cognitive factors that were assessed in multiple studies were performance on the digit symbol substitution and trail making tests. Higher scores on the digit symbol substitution test were found to be associated with lower odds of slow gait cross-sectionally, however non-significant effects were reported for performance on the trail making test. Finally, among the dietary factors, Mediterranean diet was the only factor assessed in at least two studies. Both studies reported that greater adherence to a Mediterranean diet reduced the odds of slow gait, however different measurement tools were used to assess diet adherence.

Because of the heterogeneity in defining slow gait and meaningful gait speed decline and the small amount of studies examining many of the identified factors, definitive conclusions about factor effects could not be drawn. Despite this, the review was successful in showing that the causes of slow gait and meaningful gait speed decline are complex and multifactorial and provided valuable information for subsequent analyses.

6.2.2 Normative Values of Gait Speed among Middle and Older-Aged Adults: An Analysis of Data from the Canadian Longitudinal Study on Aging

Due to the complex processes underlying its production, gait speed is a marker of health and functional ability. In order for timed walking tests to be useful in determining whether older adults have or are at risk for developing impairments, normative values outlining expected ranges of performance must be available for reference. The primary objective of the Chapter 4 analysis was to estimate the normative values of usual (i.e. self-selected) gait speed by age and biological sex using nationally representative baseline data of 29,700 adults aged 45 to 85 years from the Canadian Longitudinal Study on Aging Comprehensive cohort. Using these values, an example demonstrating the

transformation of an individual's gait speed into a population percentile was presented to show the applicability of the normative data in a real-world clinical setting. The final objective of Chapter 4 was to estimate the prevalence of 'slow gait' using multiple cut-point ranges to describe the distribution of gait speed impairments across middle and older adulthood.

Calculation of descriptive gait speed data by sex and age revealed that for both men and women, average usual gait speeds were slower among the oldest age groups (i.e. 65-74 and 75+ years) compared to the younger age groups (i.e. 45-54 and 55-64 years). In general, men had faster average gait speeds compared to women regardless of age, however when standardized by height, the average gait speeds of women appeared faster. Prevalence estimates for slow gait also revealed age-related trends. Notably, a greater proportion of men and women in the two oldest age groups walked slower than a 'normal' speed (i.e. <1.0 m/s) compared to those aged 45-54 and 55-64 years. Among the two oldest age groups, the majority of adults had gait speeds greater or equal to 0.8 m/s but less than 1.0 m/s. Additionally, the proportions of men and women aged 75+ years with gait speeds below 0.6 m/s were more than triple that seen in the 65-74 year age groups.

Much of the discussion surrounding the normative values obtained in this study focused on potential reasons why the average gait speeds of the CLSA participants appeared slower than those of older adults from other studies presenting normative values. It was suggested that sampling eligibility criteria (e.g. inclusion of adults with mild/moderate physical impairments) and elements of the walk test protocol employed (e.g. allowed use of assistive devices) were likely contributors to these slower average walking speeds. Given that many other studies providing gait speed norms have employed stricter participant inclusion criteria (e.g. healthy, able to walk unassisted), their values may not be truly representative of the older adult populations they are seeking to describe. Thus, the values obtained from the CLSA may be more appropriate references.

6.2.3 Associations between Reversible Risk Factors and Gait Speed in Middle and Older-Aged Community-Dwelling Adults: Results from the Canadian Longitudinal Study on Aging

Using the baseline data from the CLSA Comprehensive cohort as well, Chapter 5 sought to examine the demographic, clinical, and lifestyle correlates of usual (i.e. self-selected) gait speed among middle and older adults. The amount of variation in gait speed explained by these factors, which were classified as either non-modifiable or potentially modifiable, was estimated, and the associations between individual potentially modifiable factors and gait speed were also examined.

In total, 20,201 adults aged 45 to 85 years were included in the analysis. Using hierarchical multivariable linear regression models, the sets of non-modifiable factors (i.e. demographics, anthropometric factors, and non-modifiable chronic conditions) were found to explain a greater proportion of gait speed variability than the potentially modifiable factors (i.e. cognitive factors, modifiable chronic conditions, other modifiable clinical and lifestyle factors), although all factor sets explained a significant proportion of variance regardless of the amount. Several potentially modifiable factors were found to be significantly associated with gait speed as well. These factors included low education level, smoking, physical activity, any cardiovascular condition, stroke, osteoarthritis, serum vitamin D, high sensitivity C-Reactive protein, depressive symptoms, grip strength, chronic pain, and having trouble getting to the bathroom on time.

Overall, this study confirmed previous findings that non-modifiable biological factors play a large role in gait speed. However, the results showed that these factors did not entirely explain gait speed variations, which supports the idea that gait speed is a multifactorial function that is also influenced by factors that can potentially be changed through clinical intervention and lifestyle modification. Ultimately, this study is a preliminary step toward developing models to longitudinally analyze gait speed and its determinants using prospective data such as those collected from future CLSA waves and improving current gait speed impairment mitigation strategies.

6.3 Research and Methodological Contributions

Gait speed a fundamental component of mobility that allows individuals to travel through variable environments and independently engage in daily activities. As gait speed is the product of many complex bodily processes, underlying illnesses and impairments affecting these processes can result in abnormal gait speed declines that can be detrimental in older age.[1] To effectively mitigate these harmful declines, it is important to identify and intervene on factors in earlier adulthood that can be changed through clinical treatment and lifestyle modification.[2] The research presented in this thesis adds new evidence confirming that although gait speed is inevitably influenced by age, it is also affected by a multifactorial set of factors including those that can be modified. Taken together, the findings presented in Chapters 2, 4 and 5 demonstrate the necessity of standardized methods to effectively assess gait speed and its determinants and highlight possible avenues for future prospective analyses of the etiology of gait speed declines that can inform current clinical practices.

Chapter 2 provides a synthesis of the potentially modifiable risk factors associated with slow and slowing gait speed among older adults. To our knowledge, the topic of this systematic review was novel and is relevant given that research on gait impairments in older adults has been expanding significantly with the recent growth of older populations. Although this was only a qualitative review, the findings provide valuable information about the roles that various types of risk factors may have in the incidence of slow gait speed. By examining the reported factor effects, this review suggests areas that may be worth investigating further in future prospective studies and intervention trials, and other areas that may not be as promising. Along with risk factor identification, this review also emphasized the heterogeneity in current methods used to operationalize slow and slowing gait. As slow and slowing gait were defined based on many different cutoff criteria (i.e. sample distribution, external criteria, dynamic change), the estimated prevalence of slow and slowing gait varied widely across the included studies and the effects reported for the risk factors were not directly comparable. This finding ultimately demonstrates the need for uniform cutoffs to obtain prevalence estimates that are more reflective of true

population characteristics and risk factor effect values that are comparable between studies.

Next, Chapter 4 contributes normative gait speed estimates and slow gait prevalence estimates among community-dwelling adults in a Canadian context. These descriptive analyses add informative evidence to existing literature seeking to explain gait speed trends across the adult lifespan, which currently lacks analyses of large, nationally representative samples of adults. The significant gait speed trends we observed between men and women across age groups were consistent with the findings of previous research; however, differences in the average gait speed values obtained were evident and most likely due to the implementation of varying methodologies between the CLSA and traditional studies on gait speed norms.[3–5] By using a more inclusive sample and less restrictive protocols, the normative gait speed values obtained from the CLSA may reflect the gait function of older adults more accurately and serve as a more realistic reference for clinicians and researchers administering walking tests to assess the functional ability of older adults, especially in Canadian contexts. Next, by estimating the prevalence of slow gait using multiple operational definitions, we were also able to examine the extent of impairment severity across the adult lifespan among Canadians. As demonstrated in Chapter 2, many studies employ single, heterogeneous cutoffs to dichotomize individuals as having ‘slow’ gait or ‘normal’ gait speed. This single cutoff method not only leads to inconsistent slow gait prevalence estimates across studies,[6–8] but also results in a loss of detail about the full spectrum of gait speed impairment. The application of several discrete ranges of gait speed for prevalence estimation in our study demonstrates the usefulness of this method not only for simply describing the degrees of gait speed function across sex and age groups but also for identifying meaningful trends across these groups which may require further investigation to elucidate underlying causes and indicate when interventions may be more appropriate to mitigate gait speed impairment.

Finally, Chapter 5 expands on previous studies that have investigated the associations between non-modifiable and potentially modifiable factors and gait speed. To our knowledge, this is the first study to conduct such an investigation using a large

representative sample of community-dwelling Canadian adults. Unlike previous studies which have mainly focused on the individual associations between risk factors and gait speed, our study also offers a wider picture of the varying contributions of non-modifiable and potentially modifiable factors together on gait speed variability. In doing so, this study was able to demonstrate the multifactorial nature of gait speed in real life and highlights the importance of considering the roles that different types of potentially modifiable factors may have in adult gait speed production beyond the effects of non-modifiable factors such as aging. Along with characterizing the explanatory nature of grouped factors on gait speed variability, using a hierarchical regression allowed us to examine the associations between individual potentially modifiable factors and gait speed after statistically adjusting for the effects of several non-modifiable factors. The associations found were generally in line with previous studies of older adults, supporting current understanding of prominent gait speed correlates that may be optimal targets for interventions to mitigate gait speed impairments. While this study only presents cross-sectional evidence like many others in the literature,[9–11] the results provide a basis for future longitudinal modelling of gait speed determinants using robust datasets such as the CLSA. This additional work is essential as researchers continue striving toward a better understanding of the multifactorial etiology of gait speed impairments.

6.4 Limitations

While informative, the research presented in this thesis has several limitations. First, only observational studies were included in our systematic review since this design is most practical for measuring the effects of modifiable risk factors on the risk of slow gait and meaningful gait speed decline. Observational designs are often associated with greater risks for biases that can be imposed during sampling and variable measurement, and when missing data is present. While most of the studies included in this review were deemed to be fair or good quality, these biases and other methodological issues could have impacted the validity and generalizability of their results. Another limitation of this review was that meta-analyses of the risk factors identified were not conducted. Along with generally lacking a sufficient number of studies to analyze for many of the risk factors, there was also a large amount of heterogeneity in methods used to measure slow

gait/meaningful gait speed decline across the studies (i.e. differing walk test protocols, differing cutoff values for outcome operationalization). This ultimately reduced the comparability of effects between the studies.

Next, limitations were imposed by the cross-sectional nature of the analyses in Chapters 4 and 5. In Chapter 4, the estimation of normative gait speed values was restricted to a single time point. While trends in the gait speed norms could be examined between men and women of differing ages at this time point, assessment and comparison of between and within-participant gait speed declines longitudinally was not possible, which would have provided greater detail regarding the nature of gait speed at the individual level over the adult lifespan. In Chapter 5, conclusions regarding the temporality of the relationships observed between the selected demographic, clinical, and lifestyle correlates and gait speed could not be drawn definitively. Although the cross-sectional relationships seen between the selected correlates and gait speed may hold true, the factors that had significant effects may contrarily have bidirectional or reversed relationships with gait speed in real life.

The type of walk test employed in the CLSA to measure gait speed may have also influenced the study findings, especially in Chapter 4 where the estimated gait speed norms appeared slower than those previously published. While different types of walk tests are generally reported to reliably produce similar walking speeds, variations in protocol can still impact the speeds at which adults appear to walk and lead to misrepresentation of their actual walking speeds outside of clinical research settings.[12] In the case of the CLSA, a shorter distance test with a static start was used; thus, acceleration and deceleration times at the start and end of the walking test were not fully accounted for. Participants were also allowed to use assistive devices to complete the walk test which may further correlate with slower walking speeds.

There are other limitations surrounding the analysis in Chapter 5. Measurement of several variables included as potential correlates of gait speed relied on some form of self-report (e.g. chronic conditions, physical activity). These methods have been validated for use in adult populations, however assessors must assume that participants have accurately and

truthfully recalled the required information and errors in reporting can potentially introduce bias. Also, while we attempted to include important, more commonly investigated variables in our models, we acknowledge that there are other factors that may also play a significant role in the gait speed of older adults that could not be included in the regression analysis.

A final noteworthy limitation linking both Chapters 4 and 5 involves the use of large sample sizes. Large samples inherently have more statistical power to detect statistically significant relationships compared to small samples at the same Type I error probability. While this allowed us to find significant associations in our analyses of gait speed norms and gait speed correlates, many of the effects appeared small or moderate. Ultimately, interpretation of these findings is cautioned as these statistically significant results may not translate into effects that are clinically meaningful.

6.5 Directions for Future Research

Together, the studies in this thesis provide a strong basis for future research on gait speed and its determinants in older adults. Although efforts to study modifiable gait speed determinants have continuously expanded over the last several decades, syntheses of the findings of this research remain scarce. By systematically reviewing a wide range of potentially modifiable risk factors associated with slow and declining gait speed, we have highlighted many factors that should be investigated further using robust prospective studies to better understand their true effects on gait speed impairment. Additionally, through our synthesis we showed that future studies on slow and declining gait speed should consider employing multiple cutoffs to operationalize these outcomes to ensure consistency and comparability of results.

The findings reported in Chapters 4 and 5 also present frameworks for future longitudinal modelling of gait speed in Canadian adults. Using the baseline gait speed norms of the CLSA participants as a reference, additional studies can further model the gait speed declines experienced by these participants at subsequent follow-up time points. Particularly, trajectories of decline can be characterized and potentially be applied to the development of clinical reference tools that can be used to identify patients experiencing

abnormal declines in gait speed that require further investigated. The model of gait speed correlates in Chapter 5 can also be used in the future to examine such correlates longitudinally to establish the causal relationships seen cross-sectionally. If possible, these longitudinal analyses can be adapted to include other factors that are emerging as potential influencers of mobility, such as social determinants of health and clinical factors like polypharmacy.

Many studies of gait speed and its associated factors were done outside of Canada and unfortunately, the characteristics of these samples often limit their generalizability to groups residing in other areas. Thus, our studies offer insights to the necessity of conducting future research in Canadian contexts to understand the unique characteristics of Canadians adults that influence their gait speed over their lifespan. Overall, future research endeavors should focus on examining the clinical relevance of gait speed trends and risk factor effects. In doing so, intervention and education tools can be enhanced to optimally mitigate gait speed impairments earlier in life and reduce the risk of additional adverse outcomes.

6.6 Conclusion

The main objective of this thesis was to examine the factors that influence gait speed and the risk of slow and slowing gait in older community-dwelling adults. By synthesizing the results of published studies that have investigated slow gait determinants, the systematic review showed that there are many potentially modifiable factors that may serve as useful targets for maintaining gait speed in older age. Furthermore, the two additional studies describing gait speed trends and correlates among older adults in the Canadian Longitudinal Study on Aging support previous findings that gait speed is variable across the adult lifespan and is significantly influenced by both non-modifiable and potentially modifiable factors. Ultimately, the results of all three studies shed light on the need for robust longitudinal studies on gait speed to better understand the ways in which it is influenced by these different factors. The findings can be used to inform clinicians and researchers seeking to mitigate gait speed declines in adults and its associated adverse outcomes. They can also be used to support the enhancement of

current practices and programs aimed at improving the health and independence of older adults.

6.7 References

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Appendices

Appendix A Systematic Review Search Strategy

Table A- 1. Search strategies by database.

Concept	MEDLINE	EMBASE	CINAHL	Keywords
Gait Speed	exp Walking Speed/	exp Walking Speed/	MH "Walking Speed"	"walking speed" OR "gait speed" OR "gait velocity" OR "slow gait" OR "walk speed" OR "walk velocity" OR "walking velocity" OR "slow walking" OR "gait decline" OR "gait impairment" OR "timed walk" OR "timed walks" OR "timed walking" OR "timed gait"
Aged	exp Aged/	exp Aged/	MH "Aged+"	aged OR elderly OR senior OR geriatric OR "older adults" OR "older people" OR "older persons" OR "older individuals"
Community-Dwelling		exp Normal Human/		"community dwelling" OR "community dwellers" OR healthy OR "normal human" OR "normal people" OR "normal persons" OR "normal individuals"
Total Citations	2525	3813	1361	7699 (4352 after removing duplicates)

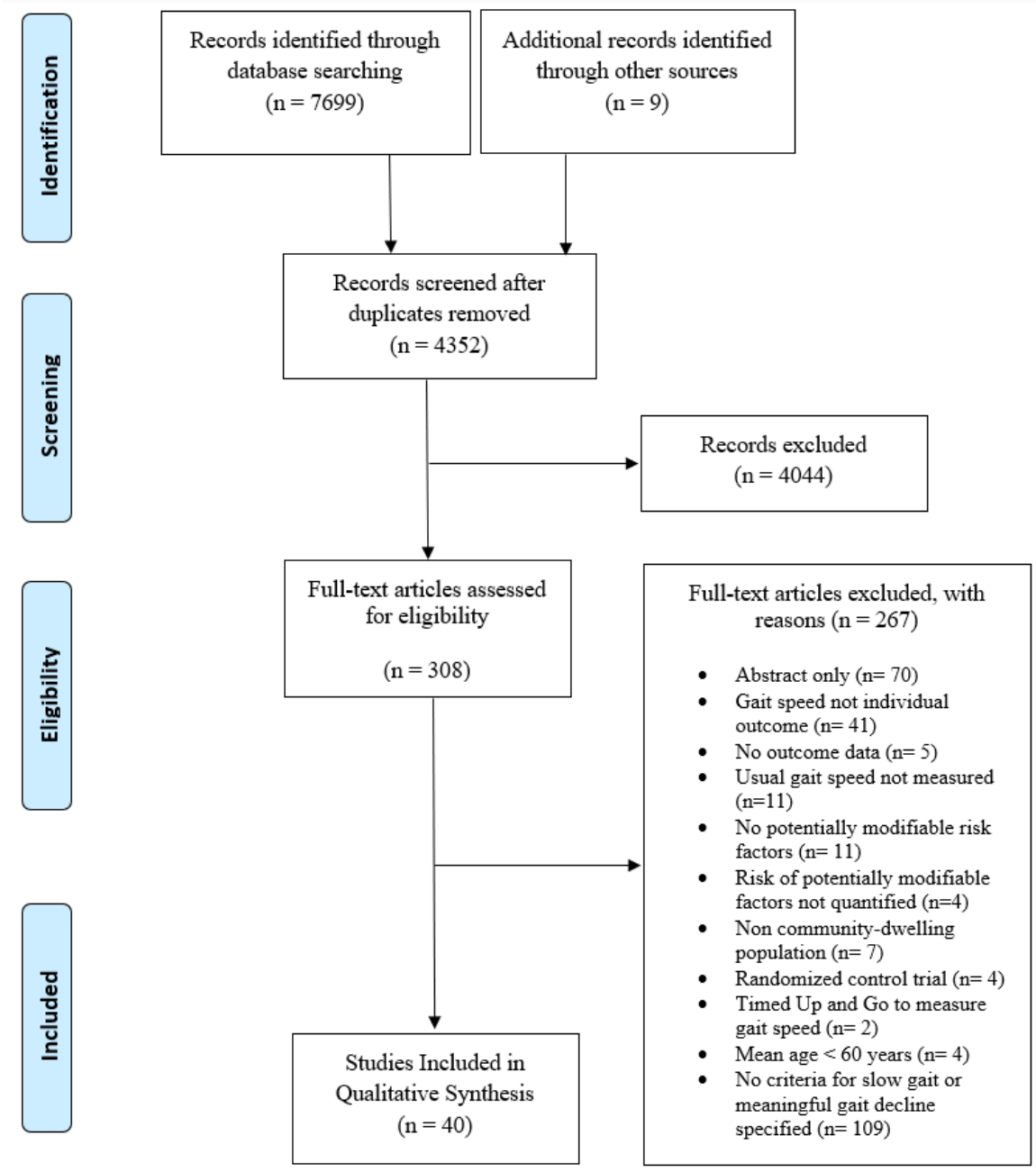

Figure A- 1. Flow chart of study selection.

Appendix B Quality of Included Studies

Table B- 1. Risk of bias assessment for included studies.

Study	Criteria*													
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Kyrdalen et al.	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	N
Montero-Odasso et al.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y
Nasimi et al.	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	NR	NA	Y
Toyama et al.	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Laclaustra et al.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NR	N	Y
Kwan et al.	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	NR	NA	Y
Lassale et al.	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Umegaki et al.	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Xu et al.	N	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Adachi et al.	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Simonsick, Aronson et al.	Y	Y	Y	Y	N	Y	Y	NA	Y	Y	Y	NR	Y	Y
Taylor et al.	Y	Y	Y	Y	N	N	N	NA	Y	NA	Y	NR	NA	Y
Simonsick, Schrack et al.	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Ayers et al.	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Frison et al.	Y	Y	N	Y	N	N	N	Y	Y	N	Y	Y	NA	Y
Shafie et al.	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Gill et al.	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y
Veronese et al.	Y	Y	Y	Y	N	Y	Y	N	Y	NA	Y	NR	N	Y
Yokoyama et al.	Y	Y	NR	N	N	Y	Y	Y	Y	Y	Y	NR	N	Y

Garcia-Esquinas et al.	Y	Y	NR	N	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Naples et al.	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y
Zeng et al.	Y	Y	NR	Y	N	N	N	N	Y	N	Y	NR	NA	Y
Verghese et al.	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	NR	Y	Y
Plouvier et al.	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Rosano et al.	Y	Y	NR	Y	N	Y	Y	Y	Y	N	Y	NR	N	Y
Tchalla et al.	Y	Y	NR	Y	Y	N	N	Y	Y	N	Y	NR	NA	Y
Kirkness et al.	Y	Y	Y	Y	N	N	N	N	Y	N	Y	NR	NA	Y
Lo-Ciganic et al.	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y
Busch et al.	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Kim et al.	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	NR	N	Y
Lana et al.	Y	Y	NR	Y	N	Y	Y	Y	Y	NR	Y	NR	N	Y
Leon-Munoz et al.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y
Wu et al.	Y	Y	N	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Ruggero et al.	Y	Y	Y	Y	N	N	N	N	Y	N	Y	NR	NA	Y
Hirani et al.	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Thorpe et al.	Y	Y	NA	Y	N	Y	Y	NA	Y	Y	Y	NR	Y	Y
Eggermont et al.	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Yoshida et al.	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y
Shardell et al.	Y	Y	Y	Y	Y	N	N	N	Y	N	Y	NR	NA	Y
Chu et al.	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	Y	NR	Y	Y

*Criteria are as follows:

[1] Was the research question or objective in this paper clearly stated?

[2] Was the study population clearly specified and defined?

[3] Was the participation rate of eligible persons at least 50%?

[4] Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?

[5] Was a sample size justification, power description, or variance and effect estimates provided?

[6] For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?

[7] Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?

[8] For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?

[9] Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?

[10] Was the exposure(s) assessed more than once over time?
[11] Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
[12] Were the outcome assessors blinded to the exposure status of participants?
[13] Was loss to follow-up after baseline 20% or less?
[14] Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?
NR=Not Reported; NA=Not Applicable

Appendix C Characteristics of Studies Included in Systematic Review

Table C- 1. Summary of characteristics for studies with cross-sectional design.

Study & Location	Sample Size	Age (mean ± SD or range)	% Female	Gait Speed Measurement	Criteria for slow gait/ decline in gait speed	Prevalence of slow gait/ decline in gait speed, N (%)	Modifiable Risk Factors Assessed
Nasimi et al. (Iran)	501	70.4 ± 4.6	49.3	4m walk test	< 0.8 m/s	218 (43.5)	Underweight Calf circumference Body fat Visceral fat area Fat-free mass Protein Bone mineral content Albumin Triglycerides
Toyama et al. (Australia)	789	72-75	0	6m walk test, fastest of two trials	< 0.8 m/s	Baseline: 77 (10.0)	Renal function Physical activity
Xu et al. (China)	2633 (group ≥60yr)	females ≥60: 68.13 ± 6.14 males ≥60: 68.86 ± 6.47	57.8	6m walk test	< 0.8 m/s	Males ≥60: 150 (14.8) Females ≥ 60: 240 (17.1)	BMI Education level Smoking Drinking Sleep time Dyslipidemia Hypertension Bone mineral density Central adiposity Diabetes Metabolic

							syndrome Coronary heart disease Stroke Tumor Physical activity Total energy intake Protein intake
Zeng et al. (China)	461	females: 69.2 ± 6.5 males: 71 ± 5.7	55.1	6m walk test	< 0.8 m/s	Males: 5.31% Females: 7.50%	Urban residence BMI 2+ comorbidities Smoking Drinking Physical activity Meals per day Unstructured daily routine Hobby engagement Self-rated health
Tchalla et al. (USA)	680	78.1 ± 5.4	62.4	4m walk test, fastest of two trials	< 0.8 m/s	168 (25.0)	Hypertension - plasma VCAM-1 interaction
Kyrdalen et al. (Norway)	108	75-77	62	4m walk test	< 1.0 m/s	48 (44.4)	Education level Impaired vision BMI (Underweight, Overweight) Multimorbidity Polypharmacy Falls Fear of falling Depressive symptoms Trail Making test

Umegaki et al. (Japan)	447	72.3 ± 4.6	45.4	5m walk test	< 1.0 m/s	7 (1.56)	Digit Symbol Substitution Logical Memory II
Adachi et al. (Japan)	308	79.9 ± 3.6	100	10m walk test	< 1.0 m/s	41 (13.3)	Grip strength Mini Mental State Examination Trail Making test Depression Physical activity
Taylor et al. (USA)	7025	65-85+	56.8	3m walk test, fastest of two trials	< 1.0 m/s	984 (14.0)	Chronic pain Education level Dementia Multimorbidity
Kirkness et al. (USA)	2648	White American women: 59.0 ± 8.0 African American women: 62.4 ± 9.1	100	20m walk test	< 1.0 m/s	236 (9.0)	BMI (healthy/ underweight, overweight) Access to medical care Annual income Education level Severe knee osteoarthritis Severe knee pain Back pain Diabetes Hypertension Cancer Heart failure Stroke Ulcer Asthma Lung disease Depression

Frison et al. (France)	982	65.6 - 86.5	59	6m walk test	Lowest quartile of sample (<0.63 m/s)	239 (24.3)	Plasma fatty acids
Busch et al. (Brazil)	1112	60-75+	60.3	3m walk test, slower of two trials	Lowest quartile by sex and height 1. men ≤1.66m: ≤0.68m/s 2. men >1.66m: ≤0.78m/s 3. women ≤1.52m: ≤ 0.63m/s 4. women >1.52m: ≤ 0.68m/s	277 (24.9)	Education level Impairments in activities of daily living Cardiovascular disease Physical activity Grip strength COPD
Wu et al. (Taiwan)	2680	69.0 ± 8.0	52.6	4m walk test	Lowest quartile by sex Men: < 0.75m/s Women: < 0.63m/s	NR	Dietary fiber intake
Eggermont et al. (USA)	585	70-97	63.4	4m walk test, fastest of two trials	Lowest quartile (< 0.784 m/s)	NR	Pain (tender point count, number of pain sites)
Yoshida et al. (Japan)	803	75.7 ± 5.0	59.0	5m walk test	Lowest quartile adjusted for	NR	C-Reactive Protein

					sex		
Kwan et al. (China)	263	77.1 ± 7.5	83.7	5m walk test	Lowest quintile adjusted for sex (Men: <0.89m/s; Women: <0.79 m/s)	93 (35.4)	Mediterranean diet Life-space Social participation
Hirani et al. (Australia)	25D subgroup: 1659 1,25D subgroup: 1536	70-85+	0	6m walk test, mean of two trials	Lowest quintile adjusted for height	436 (13.9)	Vitamin D
Shardell et al. (Italy)	1005	Women: 75.6 ± 7.6 Men: 74.2 ± 7.0	55.8	4m walk test, mean of 2 trials	Lowest quintile by sex and height	Women: 121 (22.2) Men: 99 (22.9)	Vitamin D Parathyroid hormone
Shafie et al. (Singapore)	2192	69.2 ± 0.1	55	10m walk test	≥1 SD below age & sex means of sample	274 (12.5)	Education level Employment status Physical activity Disability
Plouvier et al. (France)	736	55-69	46.0	3m walk test	(Two lowest tertiles) Men: < 1.25 m/s Women: < 1.20 m/s	485 (65.8)	Occupation class and physical demands Physical activity BMI (overweight, obese) Smoking Cardiovascular disorder Musculoskeletal disorder

Ruggero et al. (Brazil)	385	71.4 ± 5.7	64.4	4.6m walk test, mean of three trials	(K-means cluster method) < 0.91m/s	75 (28.1)	Physical activity Stroke Diabetes Urinary incontinence Fear of falling

Table C- 2. Summary of characteristics for studies with longitudinal designs.

Study & Location	Sample Size	Length of follow-up	Age (mean ± SD or range)	% Female	Gait Speed Measurement	Criteria for slow gait/ decline in gait speed	Prevalence of slow gait/decline in gait speed, N (%)	Modifiable Risk Factors Assessed
Montero-Odasso et al. (Canada)	249	5 yrs	76.6 ± 8.6	63	6m walk test	< 0.8 m/s	Baseline: 29 (13.0)	Polypharmacy
Veronese et al. (Italy)	1904	Avg 4.4 yrs	72.5 ±6.0	62.5	4m walk test, best performance of two trials	< 0.8 m/s	NR	Hyperuricemia
Kim et al. (Japan)	538	4 yrs	Nonsarcopenic: 78.5 ± 2.3 Presarcopenic: 77.3 ± 2.0 Sarcopenic: 78.5 ± 2.4 Severe sarcopenic: 80.0 ± 2.1	100	11m walk test, faster of two trials	< 1.0 m/s	137 (25.5)	BMI (underweight) Bone mineral density Calf circumference Timed Up and Go Albumin Vitamin D B 2-globulin Hemoglobin A1c High density lipoprotein Cystatin C

								Physical activity Pain (general, knee) Falls Osteoporosis Heart disease Hyperlipidemia Knee osteoarthritis
Gill et al. (USA)	2246	4 yrs	60.2 ±8.8	53.8	20m walk test	< 1.2 m/s	Follow-up: 400 (15.1)	BMI-waist circumference interaction
Rosano et al. (USA)	Total: 5888 Gait follow-up subgroup : 1019	5 yrs	75.1 ± 5.5	57.6	4.6 m walk test	1.Clinical: < 0.6 m/s 2.Subclinical : 0.6-1.0 m/s	Baseline 1. Clinical (< 0.6 m/s): 644 (10.9) 2. Subclinical (0.6-1.0 m/s): 3164 (53.7) Follow-Up 1.Clinical (< 0.6 m/s): 130 (12.8) 2. Subclinical (0.6-1.0 m/s): 973 (95.5)	Digit symbol substitution White matter hypertensities
Laclaustra et al. (Spain)	1948	Mean 3.5 yrs	68.4 ± 6.2	51.5	2.44m walk test	1. < 2 on SPPB gait (<0.43 m/s or couldn't do) 2. lowest quintile adjusted for sex, height	SPPB gait < 2: 293 (15.7) Lowest quintile: 192 (12.4)	Dietary inflammatory index
Lassale et al. (England)	2437	10 yrs	71.3 ± 7.8	56.5	2.4m walk test, mean of two trials	Lowest quintile by age and sex	332 (14.9)	C-Reactive Protein

García-Esquinas et al. (France)	ENRICA cohort: 1872 AMI cohort: 473 3C cohort: 581	ENRICA cohort: 3.5yrs AMI cohort: 2yrs 3C cohort: 12yrs	ENRICA cohort: 68.7±6.4 AMI cohort: 74.5 ±5.8 3C cohort: 81.8±4.1	ENRICA cohort: 51.6 AMI cohort: 37.8 3C cohort: 63.5	3m walk test	lowest quintile	ENRICA cohort: 279 (14.9) AMI cohort :87 (18.4) 3C cohort:95 (16.4)	Fruit/vegetable consumption
Lana et al. (Spain)	1871	Mean 3.5 yrs	68.8 ± 6.3	51.3	3m walk test	Lowest quintile adjusted for sex and height	NR	Dairy consumption
León-Muñoz et al. (Spain)	1815	Mean 3.5 yrs	68.5 ± 0.3	60.0	3m walk test	Lowest quintile adjusted for sex and height	180 (9.9)	Mediterranean diet
Ayers et al. (USA)	LonGenity cohort: 625 CCMA cohort: 312	LonGenity cohort: 3 yrs CCMA cohort: 2 yrs	LonGenity cohort: 75.21 ±6.4 CCMA cohort: 76.4 ±6.87	LonGenity cohort: 53.3 CCMA cohort: 56.7	8.5m walk test	≥1 SD below age & sex means of sample	Baseline: 1.LonGenity cohort: 68 (10.9) 2.CCMA cohort: 47 (15.1) Follow-up: 1.LonGenity cohort: 81 (14.5) 2.CCMA cohort: 22 (8.3)	Apathy (depressive symptoms)
Verghese et al. (USA)	2306	4 yrs	78.4 ± 0.83	61.4	2.5 m walk test, mean of two trials	≥ 1 SD below age-sex means	Baseline: 691 (17.0)	Muscle weakness (grip strength) Cognitive

						1. < 70yrs: < 0.57 m/s (F), < 0.62 m/s (M) 2. 70-79yrs: < 0.49 m/s (F), < 0.56 m/s (M) 3. 80+ yrs: < 0.38 m/s (F), < 0.45 m/s (M)	Follow-up: 243 (11.0)	impairment Pain Vision impairment Falls Physical activity BMI (obesity) Drinking Poor sleep quality Arthritis Stroke Diabetes Hypertension Heart condition Depression
Simonsick et al. (2018a) (USA)	667	1-5 yrs (mean 2.3 yrs)	60-89	50.8	6m walk test, faster of two trials	≥ 0.05m/s decline in gait speed per year	Meaningful decline at follow-up (%): 32.8%	Pain
Simonsick et al. (2018b) (USA)	579	1-4 yrs (mean 2.2 yrs)	60-89	53.2	6m walk test, faster of two trials	≥ 0.05m/s decline in gait speed per year	Meaningful decline at follow-up (%): 33.2	Fatigability (physical, mental) Energy level Tiredness
Thorpe et al. (USA)	2969	5 yrs	70-79	51.5	6m walk test, faster of two trials	≥ 0.05m/s decline in gait speed per year	749 (31)	BMI (Obesity) Arthritis (knee, hip) Multimorbidity Education level Home ownership Education level
Naples et al. (USA)	2402	4 yrs	74.6 ± 2.9	51.3	20m walk test	1.≥ 0.1m/s decline in gait per year 2.less than	% gait decline ≥ 0.1 m/s per yr: Yr 2-3: 22.4% Yr 3-4: 22.6% Yr 5-6: 23.9%	Drug-disease/ drug-drug interactions

						median speed (< 1.15 m/s)		
Lo-Ciganic et al. (USA)	2405	4 yrs	74.6 ± 2.8	51	20m walk test	≥ 0.1m/s decline in gait per year	Follow-up 1: 491 (22) Follow-up 2: 452 (23)	Statin use
Yokoyama et al. (Japan)	779	4 yrs	71.5 ±5.0	46.7	5m walk test	decline to the lowest baseline quartile level at follow-up	Follow-up: 75 (11.9)	Dietary variety
Chu et al. (China)	1419	1 yr	73.1 ± 6.2	49.5	5m walk test	>1 SD decline in gait speed from baseline value	Follow-up: 96 (7.2)	Vision impairment Falls

Appendix D Overall Characteristics of CLSA Comprehensive Cohort at Baseline

Table D- 1. Characteristics of the baseline CLSA Comprehensive cohort (N=30,097).

Variable	Measure	Missing n (%)	Original data, Unweighted	Original data, Weighted	Imputed data, Weighted
Age, years	Mean ± SE (max, min)	-	62.9 ± 0.06 (45, 86)	59.5 ± 0.061	-
Height, m	Mean ± SE (min, max)	100 (0.3)	1.7 ± 0.0005 (1.18, 2.04)	1.69 ± 0.0006	1.69 ± 0.0006 (1.18, 2.04)
Weight, kg	Mean ± SE (min, max)	130 (0.4)	79.8 ± 0.10 (34.9, 198.85)	80.23 ± 0.12	80.24 ± 0.12 (34.9, 198.85)
Vitamin D, mmol/L	Median,IQR	3100 (10.3)	86.0, 48.0	82.73, 47.22	82.65, 47.33
	Mean ± SE (min, max)		89.7 ± 0.23 (8.0, 385.0)	86.93 ± 0.25	86.83 ± 0.24 (8, 385)
hsCRP, mg/L	Median,IQR	3094 (10.3)	1.2, 2.10	1.11, 2.00	1.12, 2.10
	Mean ± SE (min, max)		2.56 ± 0.031 (0.10, 162.3)	2.44 ± 0.03	2.46 ± 0.03 (0.10, 162.3)
HDL, mmol/L	Mean ± SE (min, max)	3093 (10.3)	1.49 ± 0.003 (0.12, 4.45)	1.49 ± 0.003	1.49 ± 0.003 (0.12, 4.45)
Gait Speed, m/s	Mean ± SE (min, max)	392 (1.3)	0.98 ± 0.001 (0.11, 2.56)	0.99 ± 0.001	0.99 ± 0.001 (0.11, 2.56)
Grip Strength, kg	Mean ± SE (min, max)	2290 (7.6)	33.36 ± 0.069 (0.16, 84.1)	34.74 ± 0.08	34.45 ± 0.08 (0.16, 84.1)
REY I (Immediate Recall)	Mean ± SE (min, max)	1020 (3.4)	5.85 ± 0.011 (0, 14)	6.06 ± 0.01	6.05 ± 0.01 (0, 14)
REY II (Delayed Recall)	Mean ± SE (min, max)	1051 (3.5)	4.04 ± 0.013 (0, 14)	4.28 ± 0.02	4.27 ± 0.014 (0, 14)
AFT	Mean ± SE (min, max)	731 (2.4)	19.67 ± 0.033 (0, 47)	20.30 ± 0.04	20.29 ± 0.038 (0, 47)
MAT	Mean ± SE (min, max)	1486 (4.9)	26.54 ± 0.05 (0, 51)	27.33 ± 0.06	27.28 ± 0.06 (0, 51)
Stroop (Interference)	Mean ± SE (min, max)	424 (1.4)	14.26 ± 0.049 (-83.0, 122.0)	13.12 ± 0.05	13.14 ± 0.05 (-83.0, 122.0)
Depressive Symptoms (CESD-10)	Median,IQR	161 (0.5)	4.0, 5.0	3.68, 5.51	3.69, 5.51
	Mean ± SE (min, max)		5.28 ± 0.027 (0, 30)	5.24 ± 0.031	5.24 ± 0.031 (0, 30)
Physical Activity (PASE)	Median,IQR	1640 (5.4)	130.8, 96.1	139.99, 104.13	139.56, 0.68
	Mean ± SE (min, max)		141.06 ± 0.44 (0, 692.73)	150.70 ± 0.55	150.39 ± 0.54
Sex	n (%)	-			
Female			15320 (50.9)	15301 (50.8)	-
Male			14777 (49.1)	14796 (49.2)	-
Province	n (%)	-			
Alberta			2957 (9.8)	2957 (9.8)	-

Variable	Measure	Missing n (%)	Original data, Unweighted	Original data, Weighted	Imputed data, Weighted
British Columbia			6254 (20.8)	6254 (20.8)	-
Manitoba			3113 (10.3)	3113 (10.3)	-
Newfoundland and Labrador			2214 (7.4)	2214 (7.4)	-
Nova Scotia			3078 (10.2)	3078 (10.2)	-
Ontario			6418 (21.3)	6418 (21.3)	-
Quebec			6063 (20.1)	6063 (20.1)	-
Race	n (%)	-			
White			28771 (95.6)	28610 (95.1)	-
Non-white			1326 (4.4)	1487 (4.9)	-
Level of Education	n (%)	58 (0.2)			
Less than secondary school graduation			1643 (5.5)	1355 (4.5)	1360 (4.5)
Secondary school graduation only			2838 (9.4)	2628 (8.7)	2633 (8.7)
Some post-secondary education			2236 (7.4)	2081 (6.9)	2084 (6.9)
Post-secondary degree or diploma			23322 (77.6)	23989 (79.8)	24020 (79.8)
Trouble getting to bathroom on time	n (%)	34 (0.1)			
Yes			3927 (13.1)	3353 (11.2)	3359 (11.2)
No			26136 (86.9)	26706 (88.8)	26738 (88.8)
Chronic Pain	n (%)	1350 (4.5)			
No			18127 (63.1)	18551 (64.4)	19330 (64.2)
Yes			10620 (36.9)	10239 (35.6)	10767 (35.8)
Sleep Disturbance	n (%)	35 (0.1)			
Never or < once/week			18169 (60.4)	17967 (59.7)	17982 (59.7)
1-2 times/week			4699 (15.6)	4843 (16.1)	4845 (16.1)
3-5 times/week			3604 (12.0)	3727 (12.4)	3730 (12.4)
6-7 times/week			3590 (11.9)	3536 (11.8)	3540 (11.8)
Smoking Status	n (%)	-			
Current smoker			2710 (9.0)	2830 (9.4)	-
Former smoker			13145 (43.7)	12234 (40.6)	-
Never smoker			14242 (47.3)	15033 (49.9)	-
Type of Drinker	n (%)	734 (2.4)			
Regular Drinker			22231 (75.7)	22598 (76.9)	23052 (76.6)
Occasional Drinker			3705 (12.6)	3559 (12.1)	3697 (12.3)
Non-Drinker			3427 (11.7)	3222 (10.7)	3348 (11.1)
Neurodegenerative Disease, Yes	n (%)	110 (0.4)	390 (1.3)	357 (1.2)	379 (1.3)
Memory Problem, Yes	n (%)	102 (0.3)	519 (1.7)	469 (1.6)	491 (1.6)
Macular Degeneration, Yes	n (%)	214 (0.7)	1280 (4.3)	953 (3.2)	969 (3.2)
Cardiovascular Condition, Yes	n (%)	450 (1.5)	4962 (16.7)	3982 (13.2)	4152 (13.8)
Stroke, Yes	n (%)	261 (0.9)	1313 (4.4)	999 (3.3)	1060 (3.5)
Diabetes, Yes	n (%)	110 (0.4)	5310 (17.7)	4713 (15.6)	4740 (15.7)
Hypertension, Yes	n (%)	179 (0.6)	11101 (37.1)	9724 (32.3)	9792 (32.5)

Variable	Measure	Missing n (%)	Original data, Unweighted	Original data, Weighted	Imputed data, Weighted
Cancer, Yes	n (%)	93 (0.3)	4637 (15.5)	3789 (12.6)	3806 (12.6)
Osteoarthritis, Yes	n (%)	611 (2.0)	5847 (19.8)	5047 (16.7)	5186 (17.2)
Sensory Impairment, Yes	n (%)	45 (0.1)	5180 (17.2)	4766 (15.8)	4773 (15.8)
Neuropsychiatric Condition, Yes	n (%)	217 (0.7)	8884 (29.7)	9069 (30.1)	9156 (30.4)
Respiratory Condition, Yes	n (%)	250 (0.8)	5049 (16.9)	4954 (16.5)	5023 (16.7)

Appendix E Characteristics of Analytical Sample versus Excluded Group

Table E- 1. Comparison of characteristics for analytical sample and individuals excluded from Chapter 5 analyses.

Variable	Analytic Sample with Complete Data (n=20,201)	Excluded Group with Missing Data (n=9,896)	*P*
Age, mean ± SE[1]	58.84 ± 0.08	60.95 ± 0.132	< .001
Gait speed, mean ± SE	1.01 ± 0.002	0.97 ± 0.003	< .001
Sex, No. (%)			< .001
Female	9971 (48.6)	5349 (54.2)	
Male	10230 (51.4)	4547 (45.7)	
Race, No. (%)			< .001
White	19479 (95.7)	9292 (92.4)	
Non-white	722 (4.3)	604 (7.6)	
Education, No. (%)			< .001
Less than secondary school graduation	910 (4.0)	733 (6.7)	
Secondary school graduation only	1795 (8.6)	1043 (9.8)	
Some post-secondary education	1439 (6.4)	797 (7.4)	
Post-secondary degree or diploma	16057 (81.0)	7265 (76.1)	

[1] Means, standard errors, and percentages estimated using (trimmed) inflation weights.

Appendix F Sensitivity Analysis – Hierarchical Regression with Imputed Missing Data

Table F- 1. Hierarchical regression models with multiply imputed missing data.

Model 1		
Variable	**B (95% CI)[1]**	***P***
Constant	1.346 (1.332; 1.362)	<.001
Age, years	-.006 (-.006; -.005)	<.001
Sex, female	-.019 (-.024; -.014)	<.001
Province, ON (Ref)		
AB	-.024 (-.035; -.015)	<.001
BC	.036 (.028; .043)	<.001
MB	-.033 (-.041; -.024)	<.001
NL	-.057 (-.066; -.047)	<.001
NS	.080 (.070; .090)	<.001
QC	.008 (.0004; .015)	.038
Race, White (Ref)		
Non-White	-.069 (-.081; -.056)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.022 (-.031; -.013)	<.001
Secondary education only	-.028 (-.036; -.021)	<.001
Less than secondary school graduation	-.072 (-.083; -.062)	<.001
Model 2		
Variable	**B (95% CI)**	***P***
Constant	.757 (.686; .828)	<.001
Age, years	-.005 (-.005; -.005)	<.001
Sex, female	.007 (-.0001; .014)	.053
Province, ON (Ref)		
AB	-.027 (-.037; -.018)	<.001
BC	.028 (.021; .035)	<.001
MB	-.028 (-.036; -.019)	<.001
NL	-.049 (-.058; -.040)	<.001
NS	.085 (.075; .095)	<.001
QC	.011 (.003; .018)	.004
Race, White (Ref)		
Non-White	-.062 (-.074; -.050)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.015 (-.024; -.006)	.001
Secondary education only	-.020 (-.027; -.013)	<.001
Less than secondary school graduation	-.056 (-.067; -.045)	<.001
Height, m	.431 (.392; .469)	<.001
Weight, kg	-.002 (-.002; -.002)	<.001
Neurodegenerative Disease	-.079 (-.104; -.056)	<.001
Memory Problem	-.070 (-.090; -.050)	<.001
Macular Degeneration	-.019 (-.031; -.007)	.002
Model 3		
Variable	**B (95% CI)**	***P***
Constant	.678 (.606; .750)	<.001
Age, years	-.004 (-.004; -.004)	<.001

Sex, female	.003 (-.004; .010)	.406
Province, ON (Ref)		
AB	-.027 (-.037; -.017)	<.001
BC	.026 (.019; .033)	<.001
MB	-.025 (-.034; -.017)	<.001
NL	-.044 (-.053; -.035)	<.001
NS	.089 (.080; .099)	<.001
QC	.018 (.011; .026)	<.001
Race, White (Ref)		
Non-White	-.047 (-.059; -.034)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.011 (-.020; -.002)	.020
Secondary education only	-.012 (-.020; -.005)	.001
Less than secondary school graduation	-.038 (-.048; -.027)	<.001
Height, m	.394 (.356; .433)	<.001
Weight, kg	-.002 (-.002; -.002)	<.001
Neurodegenerative Disease	-.074 (-.098; -.050)	<.001
Memory Problem	-.058 (-.077; -.038)	<.001
Macular Degeneration	-.019 (-.031; -.007)	.002
REY I (Immediate Recall)	.005 (.003; .007)	<.001
REY II (Delayed Recall)	-.002 (-.004; -.0006)	.010
AFT	.002 (.001; .002)	<.001
MAT	.001 (.001; .001)	<.001
Stroop (Interference), sec	-.001 (-.001; -.0005)	<.001
Model 4		
Variable	**B (95% CI)**	***P***
Constant	.697 (.626; .769)	<.001
Age, years	-.004 (-.004; -.003)	<.001
Sex, female	.004 (-.003; .011)	.239
Province, ON (Ref)		
AB	-.028 (-.038; -.018)	<.001
BC	.026 (.018; .033)	<.001
MB	-.026 (-.034; -.018)	<.001
NL	-.045 (-.054; -.036)	<.001
NS	.088 (.079; .098)	<.001
QC	.018 (.011; .025)	<.001
Race, White (Ref)		<.001
Non-White	-.047 (-.059; -.034)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.010 (-.018; -.001)	.030
Secondary education only	-.012 (-.019; -.004)	.002
Less than secondary school graduation	-.033 (-.043; -.022)	<.001
Height, m	.360 (.321; .399)	<.001
Weight, kg	-.002 (-.002; -.002)	<.001
Neurodegenerative Disease	-.064 (-.088; -.040)	<.001
Memory Problem	-.039 (-.059; -.019)	<.001
Macular Degeneration	-.013 (-.025; -.001)	.038
REY I (Immediate Recall)	.004 (.003; .006)	<.001
REY II (Delayed Recall)	-.002 (-.004; -.0004)	.013
AFT	.002 (.001; .002)	<.001
MAT	.001 (.001; .001)	<.001
Stroop (Interference), sec	-.0006 (-.001; -.0003)	<.001
Cardiovascular Condition	-.025 (-.032; -.019)	<.001

Stroke	-.043 (-.055; -.031)	<.001
Diabetes	-.016 (-.022; -.009)	<.001
Hypertension	-.006 (-.011; -.0005)	.032
Cancer	.001 (-.005; .008)	.739
Osteoarthritis	-.022 (-.028; -.016)	<.001
Sensory Impairment	-.016 (-.022; -.009)	<.001
Neuropsychiatric Condition	-.014 (-.019; -.008)	<.001
Respiratory Condition	-.008 (-.014; -.002)	.011
Model 5		
Variable	**B (95% CI)**	***P***
Constant	.710 (.637; .782)	<.001
Age, years	-.003 (-.003; -.003)	<.001
Sex, female	.050 (.041; .058)	<.001
Province, ON (Ref)		<.001
AB	-.030 (-.039; -.020)	<.001
BC	.026 (.019; .033)	<.001
MB	-.021 (-.029; -.013)	<.001
NL	-.048 (-.057; -.039)	<.001
NS	.090 (.080; .100)	<.001
QC	.018 (.011; .025)	<.001
Race, White (Ref)		<.001
Non-White	-.033 (-.045; -.020)	<.001
Education, Post-secondary degree or diploma (Ref)		
Some post-secondary education	-.006 (-.014; .003)	.203
Secondary education only	-.007 (-.014; -.00003)	.049
Less than secondary school graduation	-.023 (-.034; -.013)	<.001
Height, m	.211 (.170; .251)	<.001
Weight, kg	-.001 (-.001; -.001)	<.001
Neurodegenerative Disease	-.045 (-.068; -.021)	<.001
Memory Problem	-.024 (-.043; -.004)	.016
Macular Degeneration	-.008 (-.020; .004)	.180
REY I (Immediate Recall)	.004 (.002; .005)	<.001
REY II (Delayed Recall)	-.002 (-.003; -.0004)	.014
AFT	.001 (.001; .002)	<.001
MAT	.001 (.001; .001)	<.001
Stroop (Interference), sec	-.0004 (-.001; -.00006)	.021
Cardiovascular Condition	-.018 (-.025; -.012)	<.001
Stroke	-.034 (-.046; -.022)	<.001
Diabetes	-.007 (-.013; -.0003)	.039
Hypertension	-.004 (-.009; .001)	.111
Cancer	.004 (-.002; .011)	.202
Osteoarthritis	-.015 (-.021; -.009)	<.001
Sensory Impairment	-.007 (-.013; -.001)	.029
Neuropsychiatric Condition	.0004 (-.005; .005)	.876
Respiratory Condition	-.001 (-.007; .005)	.789
Vitamin D (square root), mmol/L	.003 (.002; .004)	<.001
hsCRP (natural log), mg/L	-.005 (-.008; -.002)	<.001
HDL, mmol/L	.001 (-.005; .008)	.724
Depressive Symptoms (CESD-10)	-.003 (-.003; -.002)	<.001
Trouble getting to bathroom on time	-.032 (-.039; -.024)	<.001
Chronic Pain	-.014 (-.019; -.009)	<.001
Grip Strength, kg	.003 (.002; .003)	<.001
Sleep Disturbance, Never or less than once/week (Ref)		

6-7 times/week	.003 (-.005; .011)	.423
3-5 times/week	.007 (.001; .015)	.026
1-2 times/week	.004 (-.002; .011)	.148
Physical Activity (PASE)	.0001 (.0001; .0002)	<.001
Smoking Status, Never (Ref)		<.001
Current Smoker	-.023 (-.032; -.015)	<.001
Former Smoker	-.006 (-.010; -.001)	.020
Alcohol Consumption, Never (Ref)		
Regular Drinker	.017 (.009; .025)	<.001
Occasional Drinker	.004 (-.006; .014)	.417

[1] Analytic sampling weights applied in hierarchical regression analysis.
[2] Abbreviations: *AFT*, Animal Fluency Test; *CESD-10*, Center for Epidemiologic Studies Depression Scale; *HDL*, High Density Lipoprotein; *hsCRP*, high sensitivity C-Reactive protein; *MAT*, Mental Alternation Test; *PASE*, Physical Activity Scale for the Elderly.

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