2021

TOWARDS EVIDENCE-BASED AND DATA-DRIVEN RECOMMENDATIONS PROMOTING INDEPENDENCE IN LATER LIFE: GAIT SPEED, FALLS, AND ACTIVITIES OF DAILY LIVING IN OLDER ADULTS

Claire Elaine Adam

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By

CLAIRE ELAINE ADAM
DPT, University of Washington, Seattle, Washington, 2005
B.A. Biology and German, Bowdoin College, Brunswick, Maine 1999

Dissertation

presented in partial fulfillment of the requirements
for the degree of

Doctor of Philosophy
in Public Health

The University of Montana
Missoula, MT

November 2021

Approved by:

Scott Whittenburg, Dean of The Graduate School
Graduate School

Erin O. Semmens, Chair
School of Public and Community Health Sciences

Keith Anderson
University of Texas at Arlington School of Social Work

Sophia Newcomer
School of Public and Community Health Sciences

Curtis Noonan
School of Public and Community Health Sciences

Tony Ward
School of Public and Community Health Sciences

Adam, Claire, Ph.D., Autumn 2021 Public Health

Towards evidence-based and data-driven recommendations promoting independence in later life: Gait speed, falls, and activities of daily living in older adults

Chairperson: Erin O. Semmens

Abstract

Background: Falls in older adults are a significant public health challenge. Fall prevention as well as intervention after a fall both are critical to reduce the negative consequences and improve quality of life in older age.

Purpose: 1) Quantify the association between gait speed and fall risk in a cross-sectional analysis for older adults with and without cognitive impairment. 2) Determine if there is an association between change in gait speed and fall risk in a longitudinal analysis including older adults with and without cognitive impairment. 3) Quantify the association between falls and difficulty with activities of daily living (ADLs) and instrumental activities of daily living (IADLs) and determine the trajectory of difficulty with ADLs/IADLs pre- and post-fall for older.

Methods: The study population for this research was the Ginkgo Evaluation of Memory Study, a randomized controlled trial, conducted from 2000-2008, including 3069 older adults from four locations in the United States. The longitudinal study design, number of measures, and rigorous ascertainment of MCI and dementia provided an excellent data set for this research, which included a cross-sectional analysis of gait speed and falls, a longitudinal analysis of change in gait speed and falls, and falls and difficulty with ADLs/IADLs using Cox proportional hazards models, and latent class trajectory modeling to determine trajectories of difficulty with ADLs/IADLs pre- and post- fall.

Results: 1) The results of this study provide evidence of a significant association between faster gait speed and lower fall risk for older adults. 2) A decrease in gait speed of more than 0.15 m/s (mean speed 0.93 m/s) over 12 months is associated with increased risk of falls for older. 3) Falls are associated with an increased risk of difficulty with ADLs/IADLs, which persists and worsens over time for some older adults.

Conclusion: Gait speed and change in gait speed could be used as screening tools for fall risk in older adults with and without mild cognitive impairment. Understanding the characteristics of older adults more likely to have difficulty with ADLs and IADLs post-fall can be utilized to target interventions to decrease fall-related negative outcomes.

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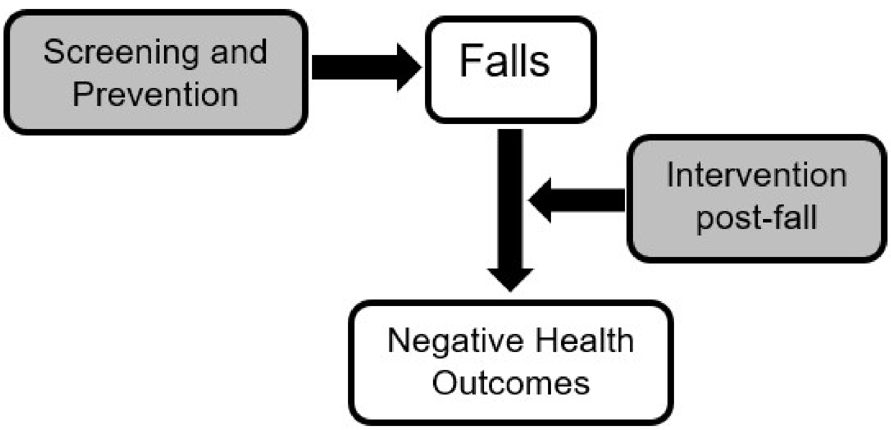
Acknowledgements

I would like to acknowledge and thank my dissertation advisor Dr. Erin Semmens for her support and guidance during this process, specifically her expertise in epidemiology, her scientific integrity, and overall kindness. Thank you to my committee members, Dr. Keith Anderson, Dr. Sophia Newcomer, Dr. Curtis Noonan, and Dr. Tony Ward for their engagement in my work. I would additionally like to thank members of the GEMS research team for being wonderful mentors and collaborators: Dr. Annette Fitzpatrick, Dr. Anjum Hajat, Dr. Sindana Ilango, Dr. Joel Kaufman, Cindy Leary, Christina Park, and Dr. Erin Semmens. A special thanks to Cindy Leary for her assistance with statistical methods and coding. I would like to acknowledge and thank the GEMS participants for their dedication in participating in the original study. Thank you to the Society for Epidemiologic Research for support at their dissertation workshop, and thanks to Dr. Elizabeth Phelan for her mentoring and contributions to my work. Finally, thank you to my family and friends who have provided encouragement throughout this process.

Chapter 1: Introduction

Falls in older adults are common[1] and negatively impact the health and quality of life of older adults.[2] While many falls are preventable, [3,4] the numerous evidence-based interventions for fall prevention[4,5] cannot be implemented unless older adults at risk for falling are identified through screening. While ideally all falls in older adults would be prevented, this is not the reality.[1,6] An effective public health response to falls must focus both on prevention and mitigating the negative outcomes when falls occur (Figure 1).

Figure 1. Comprehensive approach to addressing falls



In order to address both fall prevention and post-fall health outcomes, as illustrated in Figure 1, this dissertation research investigates the association between gait speed and falls and quantifies the association between falls and difficulty with activities of daily living. Understanding the association between gait speed and falls is necessary to determine whether gait speed is potentially a useful screening tool for older adults with and without cognitive impairment. Quantifying difficulty with activities of daily living post-fall furthers knowledge of how falls impact older adults' ability to live independently, potentially leading to interventions to address these difficulties. This introductory chapter will present the epidemiology and public health significance of falls, and for each dissertation Aim presented below, describe the exposures and outcomes of interest, summarize the results of the systematic review, and explain how each Aim addresses the current gaps in the literature.

Aims:

1. Determine the association between gait speed and incident falls among people with and without cognitive impairment in a cross-sectional analysis.

2. Determine the association between change in gait speed and incident falls among people with and without cognitive impairment.

3. Quantify the longitudinal change in difficulty with activities of daily living associated with one or more falls for people with and without cognitive impairment.

1. Falls in older adults: Epidemiology and impacts

A fall is commonly defined as "an unexpected event in which the participants come to rest on the ground, floor, or lower level."[7] Every year, between 20 to 33% of older adults (65+) will fall.[1,2] While there are effective interventions to prevent falls[5], a recent study found that mortality from falls in older adults (75+) has increased from 2000 to 2016, indicating that falls are an ongoing public health concern.[6] In 2016, 122.2 per 100,000 adults aged 75 and older died from falls, an increase from 51.6 per 100,000 in 2000.[6] Another study of fatal falls determined that 71% were preventable or potentially preventable.[3] Falls are the leading cause of hospitalizations (>90%) and emergency department visits for unintentional injuries in adults 65 and over.[8] Approximately 10% of falls result in a serious injury, defined as a fracture or a head injury.[1,9] The injury rate for falls ranges from 33% to 46%.[1,2,10] The estimated annual medical cost of all falls is about $50 billion.[11] These costs stem from hospitalizations, visits to health care providers, and medications, with the highest proportion of costs coming from services such as home health, long-term care facilities, and durable medical equipment.[11]

Multiple studies have found that the rate of falls increases with age.[1,2,11] Many fall risk assessments start for adults at age 65 and over; however, increased fall risk may start earlier than 65, with a recent study finding that rates of trauma visits from falls increased significantly starting at age 55.[12] Women have a greater rate of falls, but men have a greater rate of fatal falls.[1] Health-related risk factors for falls include general poor health, comorbidities such as depression, osteoporosis, diabetes, lung disease, hypertension, and stroke, decreased balance, use of an assistive device, being underweight or overweight, decreased strength, taking certain medications, or multiple medications, gait abnormalities, including slow gait, cognitive impairment, previous falls, vision impairment, and urinary incontinence.[1,2,9-11,13-16] Social factors that contribute to increased risk of falling include lower socioeconomic status, reduced social networks, and living alone.[1,2,9,11] Of older adults who fall, 52% report falling one time in the past 12 months, and 5.7% report falling more than six times in the previous six months.[11] Older adults who live in the community, as opposed to a nursing facility, experience 50% of falls within their home.[1] Falls in the home can result from tripping over furniture or carpets, falling on slippery surfaces such as in the bathroom, and falling in low light situations, such as using the bathroom in the middle of the night. For falls that occur outside of the home, features of the environment such as uneven sidewalks and ground, curbs, and slick surfaces contribute to increased fall risk.[1] Rates of falls are even higher within nursing facilities (approximately 50% of residents annually)[17] and hospitals (3.56 falls/1000 patient days).[18]

There are a variety of health outcomes from a fall, ranging from minor injuries to death. Up to nine months following a hospitalization for a fall, patients reported decreased quality of life, citing difficulty with mobility, self-care, and usual activities, and anxiety and depression.[19] For those with more minor injuries, not requiring hospitalization, they reported limitations in self-care and usual activities, both of which are essential components of independent living.[19] Falls with injuries are also associated with decreases in physical activity, that were measurable three years post-fall.[20] Even those falls that do not require medical care are associated with negative outcomes, notably decreased social participation, decreased ability to perform Activities of Daily Living (ADLs), and increased risk of future falls.[20,21]

Screening for falls can occur in a variety of settings including primary care, geriatric specialty care, emergency departments, and community-based programs.[22-25] Practices for fall screening vary and include asking about prior falls, fear of falling, gait assessment, balance testing, medication review, cognitive screening, and vision assessment.[24,26] The Centers for Disease Control and Prevention's recommended screening for falls is the STEADI algorithm (Stopping Elderly Accidents, Death and Injuries, 2015) which consists of a patient questionnaire, and based on the patient's responses, additional gait, strength, and balance assessments, and for patients who have had multiple falls or falls with injuries, a physical exam to check for dizziness/hypotension, medication review, cognitive assessment, evaluation of feet and footwear, assessment of mobility aids, and a vision check.[27] The STEADI is a comprehensive assessment tool that addresses the primary risk factors for falls in older adults; however completing the STEADI does require healthcare provider training and time. While there are validated approaches to fall screening and most medical providers believe that assessing older adults for fall risk is important, medical providers are not consistently screening patients for falls.[24,26,28] Barriers to implementing screening include lack of awareness of screening tools, time, training/expertise, and reimbursement.[28-30]

2. Aim 1: The Cross-Sectional Association between Gait Speed and Falls

Gait speed has been recommended as and is in use as a screening tool for falls.[31-33] Reasons to use gait to assess fall risk include its association with falls[34] and that it does not require much training, time, or equipment to measure.[31] Gait speed is measured by the time it takes to walk a specific distance divided by that distance. Distances vary in measuring gait speed, however about 4 meters or 15 feet is a commonly used distance to measure gait speed.[35,36] Gait speed can be measured with a dynamic start, where the participant begins walking before timing starts, or a static start, where timing starts as soon as the participant initiates walking.[36] Speeds with a dynamic start are typically faster than those with a static start. Additionally, gait speed is measured as preferred (also called typical, comfortable, self-selected, or usual) or fast (also called rapid or maximal) pace. Anthropometric characteristics such as height, waist circumference, BMI, age, gender, and lower extremity strength are all determinants of gait speed in older adults.[37,38] Gait speed typically decreases with age, and males generally have a faster gait speed than females.[36,39] Poorer health status, cognitive impairment, difficulty with activities of daily living, lower physical activity, lower educational level, pain, depressive symptoms, smoking, decreased social support, and visual impairment are all associated with slower gait speed in older adults.[38,40-43]

2.1 Prior research on Falls and Gait speed

There is overlap between the determinants of both falls and gait speed. Prior research has established an association between slower gait speed and higher risk of falling[9,35,44] although there have been findings of associations between fast gait speed and higher fall risk.[45] In the literature, gait speed is most typically assessed as a cut-point, and less frequently as a continuous variable.[9,35] Gait speed cut-points for older adults range from 0.6 m/s to +1.3 m/s,[45] with 1.0 m/s occurring frequently.[44,46] Variation in the strength of the association between gait speed and fall risk is likely due to differences in study populations, type of measure (continuous vs. cut-points), distance of measurement, dynamic or static start, preferred or fast gait speed, adjustment for covariates, measure of risk, and type of fall (one, multiple, injurious) (Table 1).

Table 1. Associations between Gait Speed Measurements and Fall Risk

Study	N	Age	Measure of Gait Speed	Gait Speed	Distance	Start Type	Fall measure	Fall Risk (95% CI)
			Continuous					
Verghese, et al., 2009[10]	597	70+	Slower speed	Preferred	15 ft	Dynamic	All	RR 1.06 (1.001 to 1.42)
Ward et al., 2015[47]	755	70+	Faster speed	Preferred	15 ft	N/D	Injurious	HR 0.63 (0.33 to 1.20)
			Cut-point					
Quach, et al., 2011[45]	600	78 (mean)	0.6 m/s	Preferred	15 ft	Static	All	IRR 1.60 (1.06 to 2.32)
Dyer, et al., 2020[48]	369	50+	0.67 m/s	Preferred	15 ft	Dynamic	All	IRR 3.48 (2.05 to 5.92)
Luukinen, et al., 1995[49]	1,016	70+	0.77 m/s	N/D	15 ft	N/D	Multiple	RR 1.79 (1.06 to 3.00)
Doi, et al., 2015[44]	2,281	71.5 mean	1.0 m/s	N/D	8 ft	Dynamic	Multiple	OR 1.79 (1.05 to 3.06)
Kyrdalen, et al., 2018[46]	108	78+	1.0 m/s	Preferred	15 ft	Static	Multiple	OR 3.70 (1.18 to 11.65)
Quach, et al., 2011[45]	600	78 (mean)	+1.3 m/s	Preferred	15 ft	Static	All	IRR 2.12 (1.48 to 3.04)

Abbreviations: N/D= Not described

2.2 Gait Speed, Falls, and Mild Cognitive Impairment

2.2.1 Epidemiology of Mild Cognitive Impairment

One way of addressing the variability in the reported association between gait speed and fall risk found in the literature is to look at specific populations. Assessing the relationship between gait speed and fall risk in populations with certain diagnoses is essential to determine if gait speed is a useful measure of fall risk in these populations. Mild cognitive impairment (MCI) is an important diagnosis to assess in relationship to gait speed and fall risk, as it is prevalent among older adults,[50] it is associated with higher risk of falling,[51] and there are a limited number of screening guidelines for this population.[52]

MCI is broadly defined as cognitive impairment that is greater than that associated with typical aging, but not dementia.[50] The specific criteria for MCI vary; however, there is consensus among the most widely used guidelines to include impairment in cognitive performance, both subjective and objective, and independence with activities of daily living.[50,53-55] The incidence of MCI increases with age, from 23/1,000 person years in 75-79 year-olds, to 60/1,000 person years in adults 85 and older.[56] Lower education level is associated with increased risk of MCI.[50] Research into other potential risk factors for MCI such as gender, genetics, and comorbidities have not shown a significant association with MCI.[57] MCI is associated with an increased risk of developing dementia, and is often considered a prodromal stage of dementia, specifically for Alzheimer's Disease. However MCI can be static or transitory, and not all older adults with MCI will develop dementia.[50] Approximately 14% to 38% of older adults who have MCI will revert to normal cognition.[50,58] Higher baseline cognition and increased participation in social activities are associated with a change from MCI back to normal cognition[59]. Lower baseline cognitive function, depressive symptoms, impairment in more than one cognitive domain, and increased age are all associated with increased risk of progression from MCI to dementia.[60]

2.2.2 Associations between Mild Cognitive Impairment and Falls, and Mild Cognitive Impairment and Gait Speed

Multiple studies have found an association between MCI and increased fall risk.[44,51,61-64] Impairment in executive function is considered to be one of the factors responsible for increased fall risk in people with MCI.[51] Deficits in executive function can lead to increased risk-taking behavior due to lack of insight, and difficulty with mobility and divided-attention tasks, putting older adults at risk for falls.[52,61] Older adults with MCI have decreased balance, another risk factor for falls.[65,66] The odds ratios for mild cognitive impairment and fall risk range from 1.32 (95% CI 1.19-1.49)[61] to 1.72 (1.03 to 2.89).[51]

MCI is also associated with decreased gait speed.[64,67,68] Gait speed is associated with global cognition in older adults with cognitive impairment and the strongest association is between decreased executive function and slower gait speed.[69 68]

2.2.3 Systematic Review for Gait Speed, Falls, and MCI

Given the association between gait speed and falls, and MCI and gait speed, gait speed has the potential to be associated with falls in older adults with MCI. However, given the risk factors for falls in older adults with MCI, such as impaired safety awareness[70] and decreased ability to negotiate obstacles,[71] gait speed measured in a clinic or research setting without distractions or hazards, may not adequately assess fall risk in older adults with MCI, or the strength of association between gait speed and fall risk may vary by cognitive status. A systematic review of the literature, utilizing the database "PubMed Medline", and the search terms "Gait Speed AND Falls AND Mild Cognitive Impairment", "Gait Speed AND Falls AND Cognition", "Gait Velocity AND Falls AND Mild Cognitive Impairment", and "Gait Velocity AND Falls AND Cognition", yielded 294 results. After screening, and then excluding results first by duplicates, title, abstract, and then exposure and outcome for full articles, 6 articles were included in the review (Table 2).

Table 2: Systematic Review: The association between gait speed and falls in older adults with mild cognitive impairment.

Study	Location	Study Population	Exposure	Outcome	MCI Criteria	Participants with and without MCI?	Results
Allali, et al., 2017[9]	Australia, Europe, India, and United States	n=2496 Age: 76.6 (mean)	Gait speed- instrumented walkway, 4.6m to 7.9m	Falls, self-report in previous 12 months, 6 months at one location	DSM-IV	Yes	OR: 0.98 (0.97 to 0.99) for gait speed and falls in cognitively healthy participants and OR:0.97 (0.95 to 0.99) for participants with amnestic MCI, units for gait speed not described
Doi, et al., 2015[44]	Japan	n=3400 Age: 71.5 (mean)	Gait speed , usual speed, dynamic start, 2.4 m, 1.0m/s cut-off for slow-gait	Falls, self-report in previous 12 months	Petersen (2004)	Yes	Slow gait and MCI OR: 3.05 (1.74 to 5.37) Slow gait, no MCI OR: 2.49 (1.53 to 4.08) MCI OR: 1.69 (1.13 to 2.53)
Dyer, et al., 2020[48]	9 European Countries	n=369 Age:50+	Gait speed, usual walking speed, dynamic start, 4m, cut-off for slow gait 0.67 m/s	Falls, 18 months after gait speed measure	Mild to moderate Alzheimer's NINCDS-ADRDA	No	Baseline slow gait speed IRR 3.09 (1.82 to 5.22) for falls
Lord, et al., 2020[72]	New Zealand	n=920 Age: 82.6 (mean, Maori), 84.6 (mean, non-Maori)	Gait speed, comfortable pace, 3m	Falls, self-report number of falls in previous 12 months	Motoric Cognitive Risk (MCR) Syndrome- gait speed slower than 1 SD, subjective cognitive impairment, n=17	No- did not specifically classify MCI	MCR OR: 2.45 (1.06 to 5.68) (non-Maori), not significant for Maori
Taylor, et al., 2013[73]	Australia	Community-dwelling n=64 Age:60+	Gait speed, preferred speed, instrumented walkway, dynamic start, 4.6m	Falls, self-recorded on monthly calendar, multiple faller= 2+ falls in 12 months	Mini-mental state exam <24, ACE-R <83|23, clinician diagnosis of cognitive impairment or dementia	No	Multiple fallers significantly slower gait speed than non-multiple fallers, p=0.038
Verghese, et al., 2009[10]	United States	Community-dwelling n=597 Age:+70	Gait speed, "normal pace", instrumented walkway, dynamic start, 4.6m	Falls, self-report, every 2-3 months by telephone	General cognitive status- Blessed Information-Memory Concentration Test	No, did not specifically classify MCI	Gait speed RR: 1.07 (CI: 1.00 to 1.14) for falls, for every 10 cm/ second decrease in speed, model adjusted for score on cognitive test

The studies ranged in size from 64 to 3,400 participants and included participants from 14 countries. Each of the six studies used different criteria for ascertaining mild cognitive impairment, and only two studies [9,44] included participants both with and without cognitive impairment. All of the studies found a significant association between slow gait speed and falls in older adults with cognitive impairment, except in a study from New Zealand which did not see an association for Maori participants.[72] Of the studies that included participants both with and without MCI, one found a stronger association between falls and slow gait speed for participants with MCI compared to those without,[44] and one study found a similar association between gait speed and falls for people without MCI (OR: 0.98 (95% CI: 0.97 to 0.99)) and with MCI (OR:0.97 (0.95 to 0.99)).[9] None of these studies evaluated whether there is an interaction between MCI and gait speed and fall risk.

The overall lack of research on the association between gait speed and falls in older adults with and without MCI and no identified studies assessing an interaction between MCI and gait speed for fall risk, led to the development of Aim 1: Determine the association between gait speed and incident falls among people with and without cognitive impairment in a cross-sectional analysis.

2.2.4 Study Design: The Ginkgo Evaluation of Memory Study

The Ginkgo Evaluation of Memory Study (GEMS) provided the platform for analyses for Aims 1, 2, and 3. GEMS was an NIH funded, randomized controlled trial that took place from 2000 to 2008.[74] The purpose of the study was to determine if *Ginkgo biloba* decreases risk of dementia and cognitive decline in older adults.[74,75] The study found that *Ginkgo biloba* did not decrease the rate of dementia or reduce cognitive decline in the study population.[74,75] 3,069 older adults from four locations in the United States; Sacramento, CA, Pittsburgh, PA, Hagerstown, MD, and Winston-Salem and Greensboro, NC were enrolled in the study.[74] Adults 75 and older were recruited to participate in the study through voter registration and purchased mailing lists.[74] Exclusion criteria for study participation included dementia, use of the following medications and supplements: warfarin, cholinesterase inhibitors, *Ginkgo biloba*, tricyclic antidepressants, antipsychotics, other psychotropic medications, and more than 400-IU vitamin E daily, history of bleeding disorders, hospitalization for depression or use of electroconvulsive therapy in the past 10 years, history of Parkinson's disease or use of Parkinson's medications, abnormal thyroid, liver, B12, hematocrit, or platelet values, disease-related life expectancy of less than 5 years, and known allergy to *Ginkgo biloba.*[74] Participants were randomized to receive *Ginkgo biloba* or placebo.[74] Participants were followed for a median of 6.1 years (7.3 maximum) with study visits every 6 months.[74] Participants left the study due to development of dementia, death, and loss to follow-up.[74]

The rigorous ascertainment of MCI and dementia, and the frequency, duration, and range of measures in GEMS distinguish it from other studies and result in it being an extremely valuable dataset for secondary analysis.[76] The criteria for MCI were based on the International Working Group on MCI guidelines,[53] and included a 10 part neuropsychological test battery that assessed five cognitive domains: attention/psychomotor speed, memory for verbal and visual material, language functions, visuospatial/constructional ability, and executive functions including working memory, and defined as a Clinical Dementia Rating (CDR) score of 0.5, "questionable dementia".[77] Every six months, participants took three cognitive screening tests; the CDR, 3MSE, and the Alzheimer Disease Assessment Scale (ADAS-Cog).[74] If participants scored below a pre-established value on two of three screening tests, based on baseline scores, they underwent the complete neuropsychological battery and based on those results were referred for a full neurological exam and MRI if dementia was suspected.[74] The study adjudication panel then determined if the participant had dementia, and if so, they were excluded from the study, but if not, remained in the study.[74] After study year four, the neuropsychological test battery was given to all participants, and not just those who scored below threshold on the cognitive screening tests.[75] The use of multiple neuropsychological tests in combination with the CDR, which assesses the functional impact of cognitive impairment, provides a more rigorous assessment of MCI than many studies found in the literature, which frequently rely on a cut-point from a single cognitive test to determine MCI.

2.2.5 Outcome: Falls

The outcome of interest for this study, falls, was ascertained every six months in GEMS, beginning at the 12-month study visit (visit four) (Figure 2). Fall history was part of the Medical History questionnaire, and participants were asked, "In the past six months since we last saw you, have you had a fall?", with "yes, no, or don't know" as possible responses. Any participant who responded "yes" to the question was considered to have had a fall in the past six months. The outcome of a fall was dichotomized to no falls/ one or more falls.

2.2.6 Exposure: Gait speed

Gait speed was measured as part of the Functional Assessment which occurred approximately annually for participants, beginning at the baseline study visit (visit two) (Figure 2). Gait speed was measured over a 15-foot walking course with a static start. Participants were initially told to walk three feet at their usual pace, and then if able, completed a 15-foot walk test at their usual pace. Participants who had an assistive device for ambulation could use the device during the 15-foot walk test.

Figure 2. Timeline of measurement of key variables in GEMS

Study Visit	Screening	Baseline	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Time months	0	1	6	12	18	24	30	36	42	48	54	60	66	72	80	86
Falls				x	x	x	x	x	x	x	x	x	x	x	x	x
Gait speed		x		x		x		x	x		x		x		x	
I/ADLs	x			x	x	x	x	x	x		x		x		x	
Cognition	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x

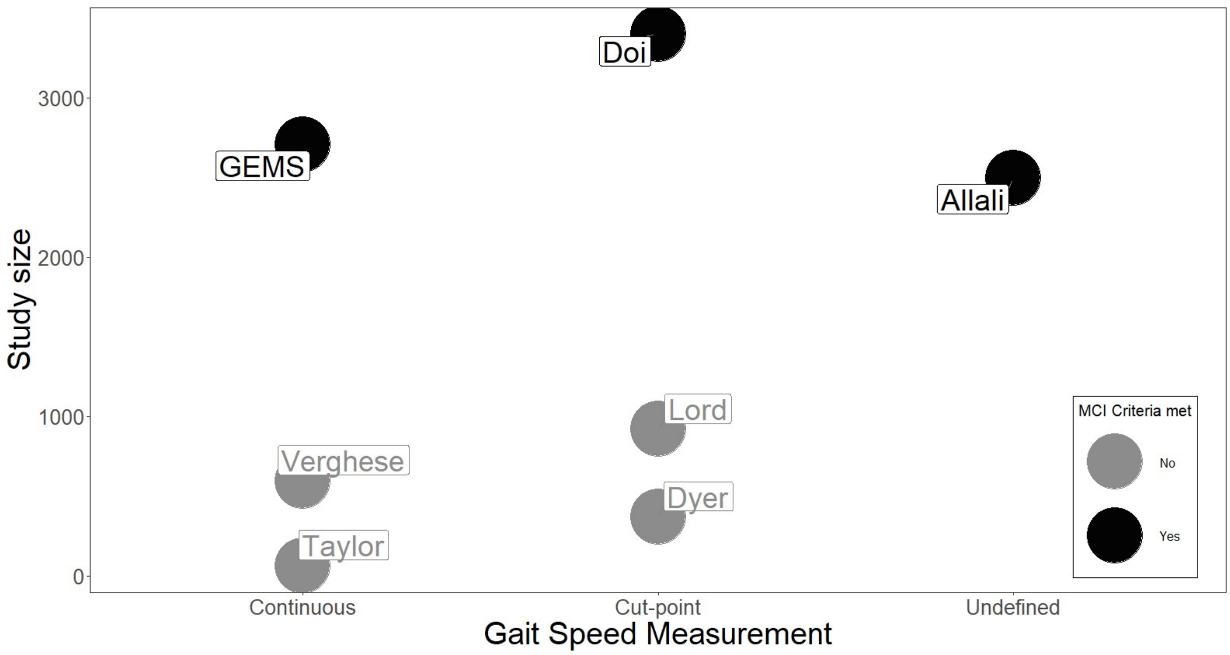
Abbreviations: I/ADL: instrumental activities of daily living, and activities of daily living. "x" marks visits when measurement occurred.

2.2.7 Covariates

GEMS collected information on numerous covariates which are potential confounders and important to adjust for in an analysis of gait speed and falls. These covariates include age, gender, education level, 3MSE score, smoking history, alcohol use, use of an assistive device, and history of heart attack, stroke, or cancer. Data for these covariates were collected at the screening or baseline study visits, except for 3MSE scores, which were completed every six months.

2.2.8 Gaps in literature

Figure 3. Studies analyzing the association between gait speed and falls, by gait speed measurement, study size, and MCI ascertainment.



Utilizing data from GEMS to assess the association between gait speed and falls for older adults with and without mild cognitive impairment addresses several gaps in the literature (Figure 3). Of the previous six studies identified in the systematic review, GEMS has a larger study population than all but one study, which was completed in Japan, and therefore the results might be less generalizable to a population of older adults in the United States.[44] Only two of the previous studies used established MCI criteria,[9,44] while other studies relied on cut-off scores from one test or referred to cognitive impairment in general but did not define it specifically as MCI. The GEMS data allow for the assessment of whether there is an interaction between gait speed and MCI for fall risk, which the other studies did not analyze.

3. Aim 2: The Association between Change in Gait Speed and Falls

3.1 Exposure: Change in Gait Speed

Decrease in longitudinal gait speed is associated with an increased risk of multiple important health outcomes, including disability,[78] dementia,[79,80] cognitive function,[81-83] and death.[84] A longitudinal analysis of change in gait speed has benefits over a cross-sectional analysis including minimizing bias from measurement error,[78] and identifying those with a normal baseline gait speed but with a rate of decline that puts them at higher risk for negative health outcomes, allowing for earlier intervention.[81,83-85] Similarly, decline in gait speed may identify older adults at higher fall risk before they cross a gait speed threshold, allowing for earlier intervention.

3.2 Systematic Review- Change in Gait Speed and Falls

The database "PubMed Medline", was used to complete a systematic review of the literature for change in gait speed and falls with the search terms: "Change Gait Speed AND Falls", and "Decline Gait Speed AND Falls". From this search, 284 articles were identified. After removing duplicates, titles were screened, followed by abstracts, and then full articles. After reviewing 11 full articles, eight were included in the systematic review (Table 3).

Table 3. Systematic Review: Change in Gait speed and Falls

Study	Location	Study Population	Duration	Exposure	Outcome	Cognition	Results
Bowen and Rowe, 2016[86]	United States	Assisted Living n=26 Age: 58-94	4 to 30 weeks	Change in average weekly gait speed, measured continuously by wristband	Witnessed or unwitnessed fall, documented by medical chart review and interview with health care workers	Cognitive Impairment Montreal Cognitive Assessment	Gait speed increase of 0.02 mph from measure 4 weeks pre-fall to 1 week pre-fall,

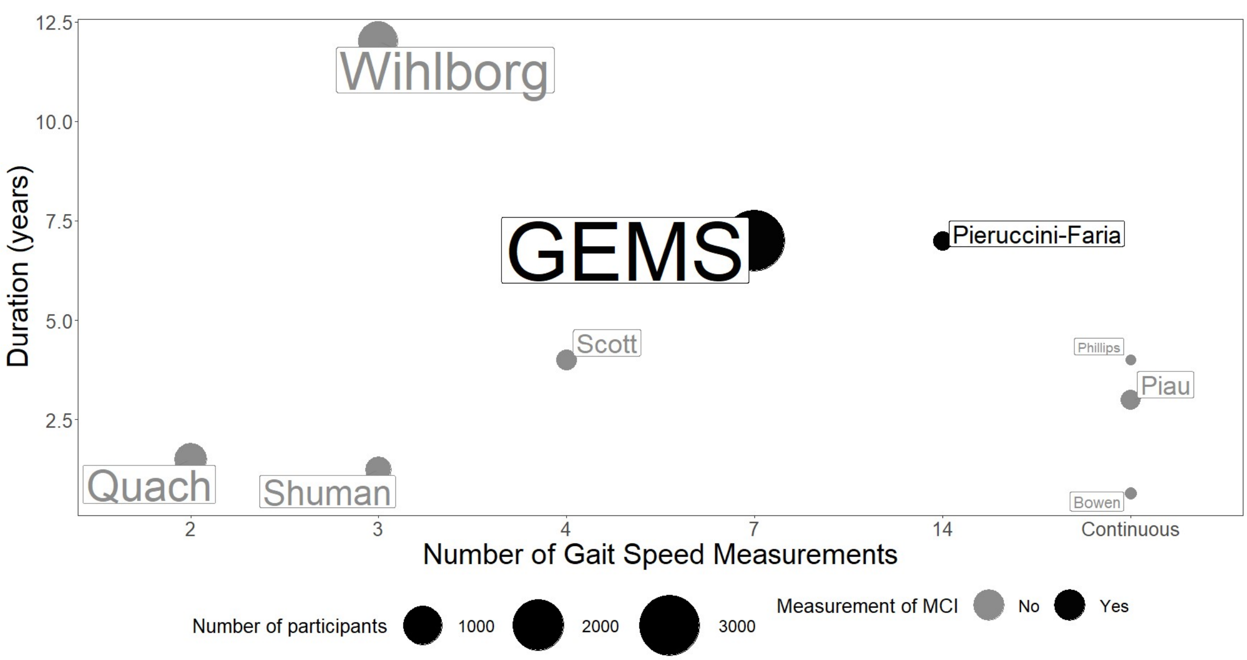
Phillips, et al., 2017[87]	United States	Independent Living Community n=23 Age: 85.2 (mean)	3 to 48 months	Kinect sensor data, within apartment walking, change in gait speed 30 days before a fall	Kinect sensor data, followed up by staff, other observed and self-reported falls	Not assessed	Decline of 2.54 cm/s over 7 days, OR of falling within 3 weeks 4.22 (2.14 to 8.30)
Piau, et al., 2019[88]	United States	Independent n=126 Age: 65+	3 years	Home based sensor system for gait speed, daily walking speed for 3 months before a fall	Weekly electronic questionnaire, participants asked if they had fallen in previous week	Excluded participants with dementia	Decline of 1 cm/s in gait speed in 3 months prior to fall, weekly decline of 0.1 cm, significantly different for fallers than non-fallers
Pieruccini-Faria, et al., 2020[89]	Canada	Community dwelling, all participants with MCI n=110 Age: 65 to 85	7 years, 2 measures/ year	Gait speed using electronic walkway with sensors, usual pace, decline in gait speed is greater than 10 cm/second decrease	Fall, reported in a monthly fall calendar, with face to face follow-up, also looked at multiple falls injurious falls, and injurious falls with ER visits	MCI, using Petersen criteria	Decline in gait speed of > 10 cm/s associated with HR of 4.62 (1.84 to 11.61) for injurious fall with ER visit, no significant association with all falls, multiple falls, all injurious falls
Quach, et al., 2011[45]	United States	Community dwelling n=600 Age: 78 (mean)	18 months	4 meter walk, static start, change in gait speed in 18 months, 4 levels ranging from 0.05 m/s to 0.15 m/s	Falls, monthly postcard calendars	Executive function assessed	Decline in gait speed of greater than 0.15 m/s per year, significantly associated with all falls, and indoor falls, but not outdoor falls , IRR: 1.86 (1.15-3.01)
Scott, et al., 2015[85]	Australia	n=135 Women Age: 70-92 At increased risk of hip fracture	Mean=3.7 years	Assessed 4 times, using electronic walkway, self-selected comfortable pace, dynamic start	Falls, monthly postcard calendars, daily recording, 2 or more falls were recurrent fallers, 1 or fewer were non-recurrent fallers	Not assessed	Increase of gait speed of 1cm/ s from baseline to follow-up OR: 0.96 (0.93, 0.99) for recurrent falls
Shuman, et al., 2020[90]	United States	Community dwelling, n=303 Age: 65+	15 months	Baseline, and 12 weeks later, 4.27 m instrumented walkway, usual gait speed	Monthly for 12 months, report of fall	Not assessed	Change in gait speed, continuous (increment 0.05 m/s), IRR of 0.89 (0.84-0.94) for falls, dichotomous: improvement vs. no change/ decline, IRR of 0.59 (0.41 to 0.84)
Wihlborg, et al., 2015[91]	Sweden	n=1,044 Age: 75+	10 years	Assessed 2x, gait speed in m/s walking 30 m	Fractures, assessed from hospital records	Not assessed	Change in gait speed (each standard deviation), HR of 1.37 (1.14 to 1.64) for hip fracture

The studies ranged in size from 23 to 1,044 participants and were located in four countries. The study duration ranged from four weeks to 10 years. Three of the studies used sensors to record gait speed, and these studies had continuous or daily measurements of gait speed.[86-88] For the other five studies included in the review, the number of gait speed measurements ranged from 2-

14.[45,85,89-91] Change in gait speed ranged from 0.1cm/second per week[88] to 0.15 meters/second per year[45]. For the association between change in gait speed and falls, all studies found an association between decrease in gait speed and increased fall risk, except for one study which found an inverse relationship.[86] The association between change in gait speed and falls was significant for all falls in five studies,[45,86-88,90] for multiple falls in one study,[85] for injurious falls in one study,[89] and for falls with hip fractures in one study.[91] There were four different measures of risk used across the studies. Only one of these studies included ascertainment of MCI, and the study was limited to participants with MCI.[89] None of the studies looked at percent change in gait speed, which is potentially an important measure as it incorporates change in gait speed relative to current gait speed, which has an established association with fall risk.

3.3 Gaps in the literature

Figure 4. Studies analyzing the association between change in gait speed and falls, by frequency of measurement, study duration, study size, and MCI ascertainment.



The overall lack of studies (Figure 4) assessing the association between change in gait speed and fall risk, and particularly the lack of studies incorporating MCI into this analysis, led to the development of Aim 2: Determine the association between change in gait speed and incident falls among people with and without cognitive impairment. In comparison to previous studies evaluating change in gait speed and fall risk, GEMS is larger than any of these studies, and was the second longest in duration. Of the five other studies that did not use sensor-based measurements of gait speed, GEMS, had the second highest number of gait speed measurements, and is the only other study to include MCI. For the current study, annual gait speed was aligned with a six-month reporting period for falls. The extensive measures in GEMS allow for adjustment of potential confounders including recent hospitalization, education, age, gender, medication use, and previous medical history.

4. Aim 3: The Association between Falls and Activities of Daily Living

Despite efforts to prevent falls in older adults, falls frequently occur in this population.[1] While some of the outcomes from falls are very apparent; death, hospitalization, and traumatic injuries, many of the other important but less obvious consequences of falls are not well understood, due to lack of research in this area. For health care providers, public health entities, and community resources to successfully mitigate the impacts of falls, which include helping older adults safely be as independent as possible,[19] continue to be physically active,[20] continue social activities,[21] and prevent future falls,[92] it is necessary to understand the duration and severity of post-fall outcomes. Thus, the approach to addressing the public health challenge of falls must include both fall prevention and post-fall intervention.

4.1 Outcome: Activities of Daily Living

The impact of falls on Activities of Daily Living (ADLs) is an important area of research in understanding outcomes from falls. ADLs were originally developed as a way to quantify functional ability, specifically for people utilizing long-term care.[93] ADLs are described as "a set of basic human functions".[93] The ADLs included in the original index developed by Katz, include "bathing, dressing, toileting, transfer, continence, and feeding", and were found to be associated with two-year mobility, house confinement, and survival.[93] Instrumental Activities of Daily Living (IADLs) are also used to describe functional abilities and include additional activities that are generally considered more complex than ADLs, such as shopping, transportation, and housekeeping.[94] Increased dependence in ADLs and IADLs is associated with increased risk of death and hospitalization.[94] Difficulty and dependence with ADLs is associated with important outcomes such as decreased mental health status,[95] increased out-of-pocket health care expenditures including medications, hospitalizations, nursing services, transportation, and personal hygiene,[96] caregiver burden, and increased risk of institutionalization.[97] Impairment in IADLs is associated with a variety of negative outcomes, including higher risk of institutionalization,[98] increased length of hospital stay,[99] decreased quality of life,[100] increased need for formal and informal care,[101] and increased mortality.[102]

Prevalence of difficulty with ADLs in adults 65 and over ranges from 11%[101] to 34%,[103] depending on the population. Difficulty walking and difficulty bathing are the most common impairments and difficulty eating is the least common.[103,104] For IADL impairment specifically, a study of European countries found a prevalence of 24% of older adults reporting difficulty, with "doing work around the house or garden" being the most common, and "taking medications" and "telephone calls" being the least common.[105] In a study in the United States with a 10 year follow-up period, 70% of participants developed disability with an IADL, and the most common difficulty, after medical care such as giving self-injections, was housework with the least common being answering the phone.[106]

There are a variety of methods for quantifying performance of ADLs and IADLs, including several different indices and scales which are frequently modified, or study authors select their own variables.[93,105,106] Inability to perform I/ADLs independently is often described as "disability,"[101,103]"limitation,"[105,107] or "difficulty".[106] Impairment in I/ADLs is defined as having any difficulty performing an activity[103,105,106,108] or need for assistance with an activity[101] either on a dichotomous scale[101,103,105] or a scored-scale,[106] and may be dichotomized[101,105] or used as a continuous variable.

4.2 Systematic Review: Falls and ADLs

The databased "PubMed Medline", was used to conduct a systematic review of the literature for the association between falls and difficulty with I/ADLs. The search terms used were "ADL trajectory", "Falls and ADL trajectory", "ADLs and Falls", and "Falls AND Disability AND Longitudinal". A total of 575 articles were found, and after screening for duplicates, and then by title, by abstract, and by full article, 11 articles were selected for inclusion in the review (Table 4).

Table 4. Systematic review of the literature for Falls and ADLs/IADLS

Study	**Location**	**Study Population**	**Study Duration**	**Exposure**	**Outcome**	**MCI and Dementia?**	**NDI/ or socioeconomic measure**	**Results**

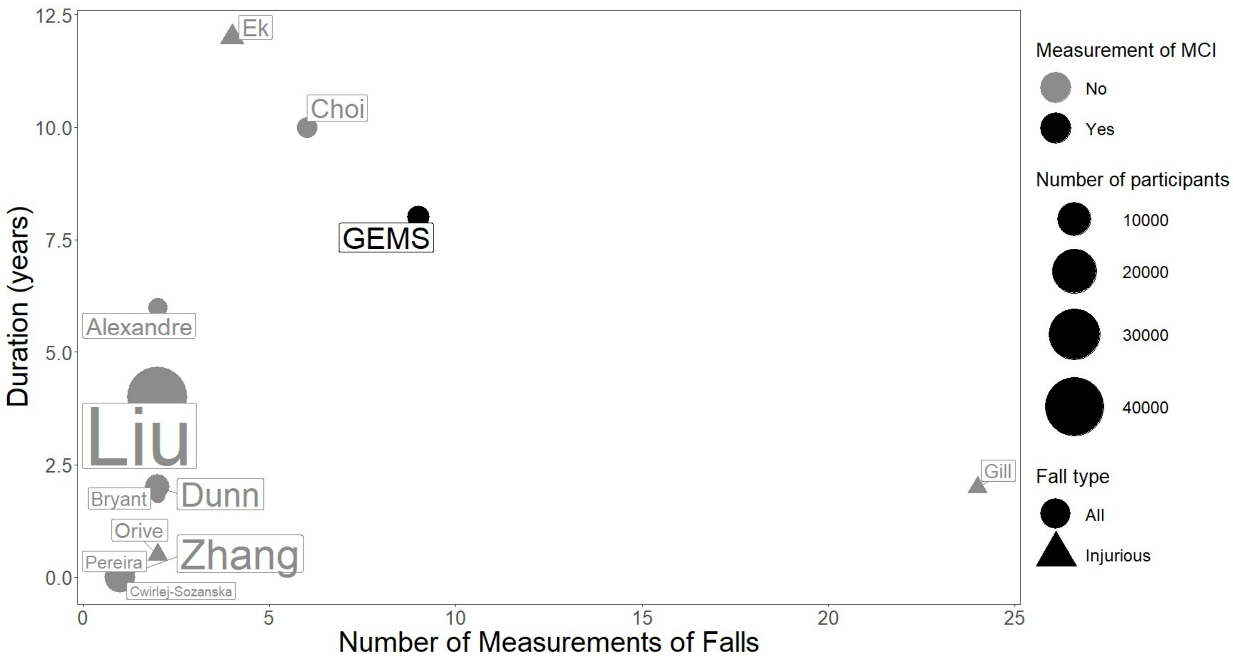
Alexandre, et al., 2012[108]	Brazil	Community-dwelling n=1,634 Age:60+	6 years, 2 assessments	Report of falls in previous 12 months	Disability-difficulty with any of 6 ADL items on modified Katz Index	No	Yes-Social vulnerability index	Falls in previous 12 months OR of 1.38 (0.84 to 2.25) for women, not reported for men
Bryant, et al., 2002[109]	United States	Community-dwelling n=751 Age: 60+	22 months. 2 assessments	Report of falls in previous 12 months	Inability to perform or need for assistance to perform IADL(8) or ADL (7)	No	No	Falls in previous 12 months OR: 1.51 (1.01 to 2.25)
Choi, et al., 2013[110]	United States	Community dwelling n=1,998 Age=65+	10 years, 6 assessments	Report of falls in previous 2 years, injurious falls, and number of falls	ADLS (6), no difficulty or any difficulty, 2 years post fall	No	Yes, household wealth	1 fall OR: 1.31 (0.97 to 1.77) for ADL difficulty, 1 fall with injury OR: 1.78 (1.29 to 2.48), multiple falls, no injury OR: 2.36 (1.80 to 3.09), multiple falls with injury OR: 3.75 (2.55 to 5.53)
Cwirlej-Sonzanska, et al, 2018[111]	Poland	Community-dwelling n=426 Age: 71-80	Cross-sectional	Report of falls in previous 12 months	At least one limitation in either ADL (Katz scale) or IADL (Lawton scale)	No	Income	Falls in previous 12 months OR: 1.85 (1.08 to 3.16) for difficulty with ADL, OR: 2.03 (1.14 to 3.59) for difficulty with IADL
Dunn, et al., 1992[112]	United States	Community-dwelling n=4,270 Age: 70+	2 years, 2 assessments	Report of falls in previous 12 months, single and multiple fallers	Reported difficulty with more ADLs (7) at follow-up than baseline	No	No	Multiple falls in previous 12 months, but not single falls OR: 1.6 (1.2 to 2.0) for functional impairment
Ek, et al., 2020[113]	Sweden	Community-dwelling n=1,426 Age: +60	12 years, 2-4 assessments	Injurious fall, requiring medical care documented with ICD-10 code	ADL (5), IADL (7), combined disability score of 0-14	No	No	Higher risk of annual change in disability for fallers compared to non-fallers, beta (0.34 (0.20 to 0.48) men, 0.32 (0.25 -0.40) women)
Gill, et al., 2013[114]	United States	Community-dwelling n=754 Age: 70+	12 years total, but results for 1 year pre and post fall	Serious fall injuries resulting in hospitalization, monthly interviews, confirmed with medical records	12 ADL and IADL activities, need for personal assistance considered disability	No	No	Pre-fall disability trajectory predicted post-fall disability trajectory

Liu, et al., 2020[115]	China	n=44,447 Age: 50+, 3 waves	4 years, 2 assessments	Falls, frequency and ascertainment not described	ADLs (6) Barthel Index , disability if participant was unable or needed help in at least one activity, IADL (6)	No	No	Falls OR: 1.63 to 1.84 (depending on wave, 95 CIs from 1.43 to 2.06) for ADL disability OR: 1.76 to 1.94 (95% CIs from 1.57 to 2.22) for IADL disability
Orive, et al., 2015[116]	Spain	n=891 Age:65+ Recruited from emergency department	6 months, 2 assessments	Hip fracture because of a fall, presenting to Emergency Department	ADL (10) Barthel Index, IADL (8) (Lawton and Brody Index)	No	No	ADLs Beta: -15.23 IADLs Beta: -19.79 Fracture significantly associated with decrease in ADL and IADL score 6 months later
Pereira, et al., 2020[117]	Portugal	Community dwelling n=588 Age: 65+	Cross Sectional	Report of falls in the previous 12 months including injuries, categorized by fall/ no fall, and by injury level	Composite Physical Function Scale (12 items, including BADL, IADL, and advanced ADL), categorized independent, with help, with difficulty or unable , scores 0 to 24	No	No	Falls without injury or with light injury not associated with physical function (composite of ADL activities) severe fall OR 2.5 (1.05 to 5.95) for moderate physical function, OR: 5.5 (1.5 to 20.2) for low physical function
Zhang, et al., 2021[118]	China	n= 8,108 Age: 65	Cross-sectional	Report of falls, timing not reported	BADLs (6) score of 1 to 3, 1 (complete independence) IADL (8), 3 point scale	Participants with dementia excluded, cognitive impairment classified with 3MSE	No	Falls OR: 1.58 (1.36 to 1.85 for no BADL impairment, but IADL impairment, OR: 1.71 (1.37 to 2.15) for IADL and BADL impairment

The studies included in this review were from seven countries and included study populations ranging in size from 426 participants[111] to 44,447 participants.[115] The duration of the studies lasted from cross-sectional[111,117,118] to 12 years.[113,114] Impairments in I/ADLs were described as "disability" in five studies, and in one study each, "difficulty," "functional decline," "functional dependence," "decline in ADL," "physical dependence," and "limitation". These terms were defined by having difficulty with I/ADLs in three studies, requiring help in two studies, a combination of having difficulty and requiring help in five studies, and was undefined in one study. Six different scales were used, and in four studies, the authors selected the I/ADLs measured. The scales used for I/ADLs were primarily dichotomous (eight studies), combination of dichotomous and continuous scales (two studies), and continuous only (one study). The outcomes used for impairment in I/ADLs were dichotomous (four studies), continuous (five studies), a combination (one study), and a comparative measure (one study). There were three different risk measures used in the studies, odds ratios (eight studies), beta coefficients (two studies), trajectories (one study). Five studies found an association between all falls and impairment in both ADL and IADL function, while three studies found no association between all falls and ADL impairment, and one study found no association between all falls and ADL and IADL impairment. Two studies found an association between multiple falls and ADL impairment, while one study found an association between injurious falls and ADL impairment, and one study found an association between injurious falls and IADL and ADL impairment. One study specifically defined fall with fracture as the exposure and this study found an association with impairment in both ADL and IADL.

4.3 Gaps in the literature and current study

Figure 5. Studies analyzing the association between falls and activities of daily living score, by frequency of measurement, study duration, study size, fall type, and MCI ascertainment.



In comparison to the studies included in the systematic review, the current study, utilizing data from GEMS, has a longer duration than the only other study with more measurements of falls, and is the only study to include ascertainment of MCI (Figure 5). MCI is associated both with increased risk of falls[51] and difficulty with I/ADLs[119,120] and therefore, is an important confounder to adjust for. Utilizing the GEMS dataset also allows for the incorporation of the Neighborhood Deprivation Index (NDI), a socioeconomic measure, which includes information from the census tract level and is a weighted linear combination of percent with a Bachelor degree, percent in managerial occupations, median home value, percent with at least a high school education, percent interest, dividend, or rental income, median household income, and percent with annual household income greater than $50,000.[121] Higher NDI values indicate higher levels of neighborhood deprivation. There is an association between higher neighborhood deprivation[1,123,124] both with falls and impairment in I/ADLs.[125,126] Only three of the studies in the systematic review used a socioeconomic measure in their analyses.[108,110,111] These gaps in the literature led to the development of Aim 3: Quantify the longitudinal change in difficulty with activities of daily living associated with one or more falls for people with and without cognitive impairment.

5. Conclusions

This research will address falls in older adults, which has a significant impact on health at both a population and personal level. The research approaches the challenge of falls from the perspective of prevention and intervention post-fall. Understanding the association between gait speed and falls in older adults is a necessary step to develop screening tools and target them to populations in which they will be most effective. It is especially important to understand this association in older adults with mild cognitive impairment. Older adults with mild cognitive impairment comprise a population that is both understudied and at higher risk of falls,[51] with potentially different underlying risk factors[70,71] for falls than older adults without cognitive impairment. In addition to addressing falls prevention, this research also recognizes that falls in older adults are occurring at alarmingly high rates, which are currently increasing.[6] Given prior research on the outcomes from falls, in order to holistically address falls in older adults, public health has to focus on post-fall intervention in addition to prevention. The current research on outcomes from falls has focused on death, hospitalizations, and injuries, with very few studies evaluating changes in ADL performance, and no studies found assessing this outcome for older adults with MCI. This research will further our understanding of the impact falls have on older adults' ability to perform activities of daily living, essential for independence and safety. This knowledge is necessary to develop interventions that successfully address these impacts by preventing further negative sequelae from falls.

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Chapter 2: The Association between Gait Speed and Falls in Community Dwelling Older Adults with and without Mild Cognitive Impairment

Abstract

Background: Falls are common in older adults and result in injuries, loss of independence, and death. Slow gait is associated with falls in older adults, but few studies have assessed the association between gait speed and falls among those with mild cognitive impairment (MCI).

Methods: The association between gait speed and falls was assessed in 2705 older adults with and without MCI participating in the Ginkgo Evaluation of Memory Study. Gait speed was measured via a 15-foot walk test and fall history through self-report. We used data collected at the 12-month (2001–2003) and 18-month visits (2002–2004).

Results: Participant average age was 78.5 years (sd = 3.2); 45% were female, and 14% had MCI at baseline. The average gait speed was 0.93 m/s (sd = 0.20). Sixteen percent (*n* = 433) and 18% (*n* = 498) reported at least one fall at the 12-month and 18-month visits, respectively. Faster gait speed was associated with decreased risk of falling (RR: 0.95, 95% CI: 0.91, 0.99) for every 10 cm/s increase in gait speed adjusted for age, gender, study arm, site, and MCI status.

Conclusions: The relationship between gait speed and risk of falling did not vary by MCI status (interaction p-value = 0.78).

Introduction

Falls in older adults are common, affecting 20 to 33% of those over the age of 65.[1,2] Death (60 per 100,000 people over 65),[3] injury (46% of falls),[4] medical expenses,[3] increased anxiety and depression, decreased quality of life, and loss of independence[5] all result from falls. Given these negative outcomes and that age-adjusted mortality from falls continues to increase,[6] screening older adults for fall risk is essential in order for effective fall prevention strategies[7-9] to be implemented.

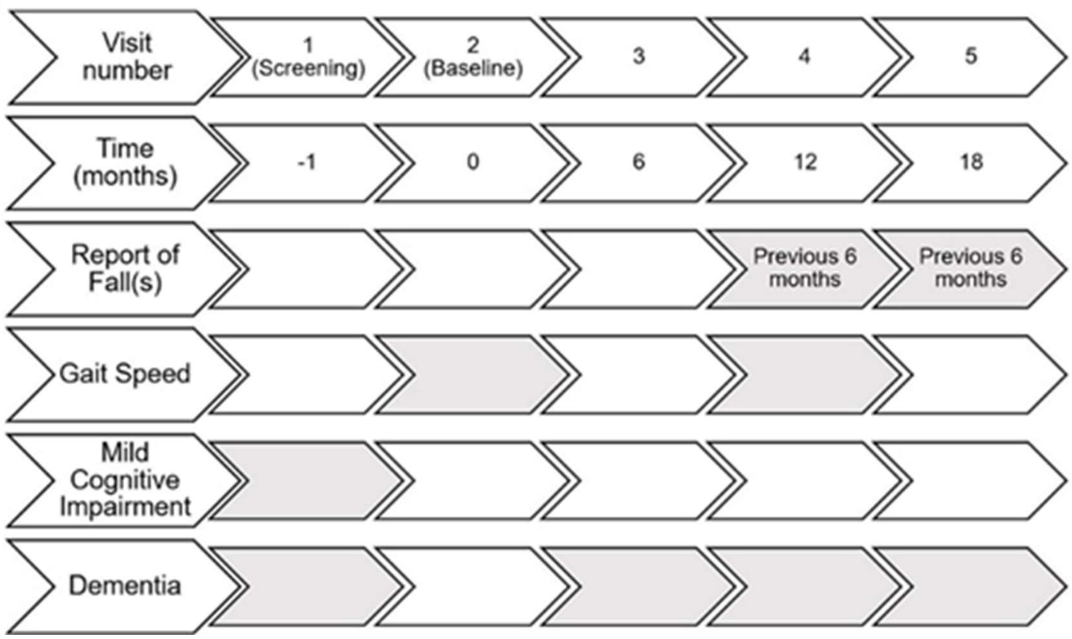
Numerous studies have demonstrated an association between slower gait speed and increased fall risk in the general population of older adults.[4,10,11] However, it is not clear if gait speed is as strongly related to fall risk in those with mild cognitive impairment (MCI),[12] as older adults with MCI have impaired safety awareness and decision making[13] and reduced ability to negotiate obstacles.[14] These impairments are strongly linked to fall risk in a community setting[13,15] but are not tested in well-controlled clinical or research assessments of gait speed, where a participant is asked to walk in a straight line in an environment free of hazards. People with MCI may have decreased executive function, which is a risk factor for falls in older adults, but it is uncertain whether this is adequately tested in gait speed assessments without an added cognitive task.[12,13] To our knowledge, only two studies have examined the relationship between gait speed and falls in a population that included both older adults with and without MCI.[16,17] We hypothesized that gait speed may be more strongly associated with falls in cognitively healthy older adults than those with MCI because factors related to cognition may account for fall risk in older adults with MCI. The objective of this study was to determine if the strength of association between gait speed and falls varied by MCI status in a large population of community-dwelling older adults residing in four, geographically diverse communities in the United States.

Methods

Our study population included 3069 adults aged 75 years and older participating in the Gingko Evaluation of Memory Study (GEMS) in four communities in the United States: Sacramento County, CA, Washington County, MD, Forsyth County, NC, and Pittsburgh, PA.[18,19] GEMS was a double-blind randomized controlled trial conducted from 2000 to 2008 designed to investigate if 240 mg/day of *Ginkgo biloba* decreased the risk of Alzheimer's disease.[18,20] Study methods and their rationale were described in detail in DeKosky et al., 2006 and 2008.[18,20] Exclusion criteria for participating in GEMS included diagnoses such as Parkinson's disease, congestive heart failure, recent cancer, and abnormal blood counts.[20] Additionally, older adults taking medication for cognitive function, anti-coagulants, anti-psychotics, and carbidopa/levodopa were excluded from participating in the study.[20] GEMS was a negative study; there were no differences in cognitive outcomes for participants in the placebo vs. intervention group, thus reducing issues with an effect of *Ginkgo biloba* on MCI. GEMS received Institutional Review Board (IRB) approval from all involved sites and this study was additionally approved by the University of Montana IRB.

Gait speed in GEMS was assessed annually as part of the Functional Assessment. The gait speed measurements used for this analysis were from the 12-month study visit. The gait speed measurement at the 12-month study visit aligns with the beginning of the 6-month period for falls reported during the fall history at the 18-month visit (Figure 1). Gait speed was measured over a 15-foot walking course with a static start. Participants were initially told to walk 3 feet at their usual pace, and then if able, completed a 15-foot walk test at their usual pace. Participants who had an assistive device for ambulation could use the device during the walk test. Gait speeds faster than 1.79 m/s were excluded for both male and female participants. This is the mean usual gait speed plus 3 standard deviations for men aged 70–79 years over a 4-m walking course with a static start.[21] The gait speed for men aged 70–79 was chosen because it is the fastest gait speed for the age range of male and female participants included in this study.[21]

Figure 1. Timeline of GEMS measurements.



Note: Shaded boxes indicate when measurement of the variable of interest occurred.

Fall history was ascertained from the Medical History questionnaire completed every 6 months over the course of the study. Participants were asked, “In the past six months since we last saw you, have you had a fall?”, with “yes, no, or don’t know” as possible responses. Any participant who responded “yes” to the question was considered to have had a fall in the past 6 months. Additional information about the definition of a fall was not provided to participants, however at the screening visit, participants were given instructions to not include falls that occurred during skiing, skating, or other activities that may affect balance, but these instructions were not provided at subsequent visits. For this analysis, fall occurrence as a dichotomous variable from the 12-month study visit was assessed as a potential confounder, and fall occurrence as a dichotomous variable from the 18-month study visit was the outcome of interest (Figure 1).

MCI was ascertained at the screening visit and was determined based on criteria from the International Working Group on MCI.[22,23] Study participants who had a score of 0.5 (questionable dementia) on the Clinical Dementia Rating Scale (CDR) and test scores in the 10th percentile or below on at least two out of ten neuropsychological tests, were determined to have MCI.[22] A full description of the methods for determining MCI are available in Snitz et al. 2009.[22] The prevalence of MCI at the screening visit was 16%.[22] Detailed evaluation of dementia occurred based on the 6-month screening triggered by a participant scoring below threshold on 2 of 3 cognitive tests [modified mini-mental state examination (3MSE), CDR, or Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog)], new dementia diagnosis by a physician not associated with the study, new memory or cognitive difficulty reported by participant or relative, or starting a medication used to treat cognitive function.[19] Sensitivity analyses were conducted to determine if there was a change in relative risk of falls associated with gait speed if participants who developed dementia by the 18-month study visit were excluded from analyses.

In addition to MCI, treatment arm assignment, and study site; age and gender were selected a priori for inclusion in the modified Poisson regression models for their demonstrated association with falls and gait speed.[1,21] We also considered race, education, 3MSE score, history of cancer, heart attack or stroke, smoking, and alcohol as potential confounders. All data for covariates were collected at the screening or baseline study visit, except for 3MSE score, which was assessed at the 12-month study visit. Information on smoking and alcohol use were obtained from a Health Habits Questionnaire administered at the baseline visit. Smoking status was classified as "never", "former", and "current". Alcohol use was divided into 5 categories based on the number of drinks per week and included "none", "less than 1", "1–7", 7.1–14", and "more than 14".

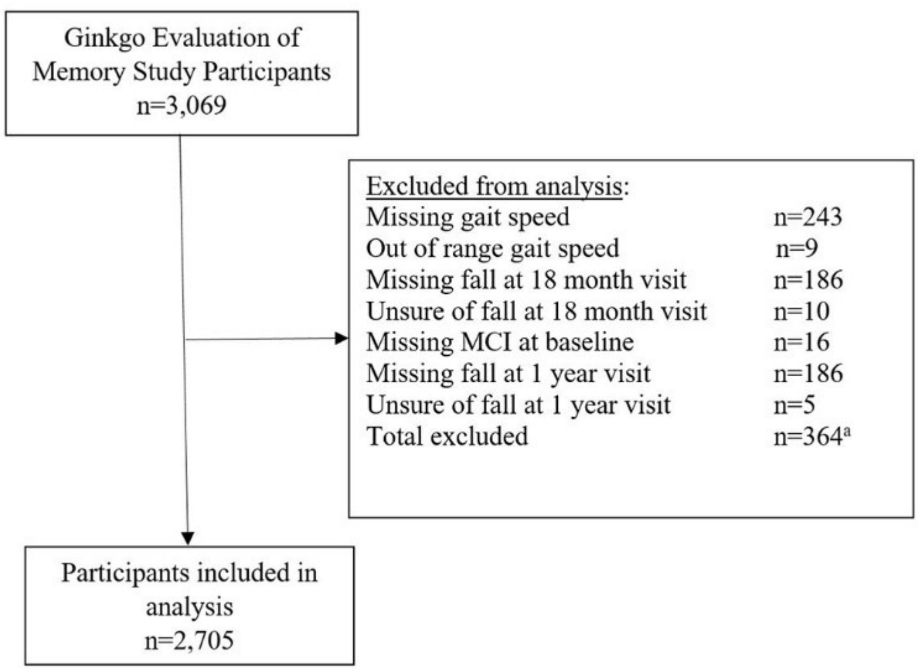
Statistical Analysis

Participants with data for falls at the 18-month visit, gait speed at the 12-month visit, and MCI, determined at the screening visit, were included in the analysis. Participants were excluded if they were missing data for fall history at the 12-month visit or responded "don't know" when asked if they had fallen at the 12-month or 18-month visit. Characteristics of excluded and included participants were assessed for statistically significant differences using t-tests and Chi-square tests. We summarized selected characteristics overall and by gait speed quartiles. We used modified Poisson regression with robust standard errors to evaluate associations between gait speed and risk of falling.[24] We chose modified Poisson regression because it does not have the limitations of convergence seen with binomial regression or the overestimation of errors that occurs with ordinary Poisson regression.[24] Covariates in addition to age, gender, treatment, study site and MCI, were included in the model if they altered the relative risk (RR) for gait speed by 10% or greater. We used a staged approach to model building. We assessed effect modification by MCI by including a multiplicative interaction term containing gait speed and MCI in analyses. All analyses were performed with the statistical software R.

Results

A total of 2705 study participants were included in the analysis (Figure 2). Of the original 3069 study participants, 364 were excluded from the analysis for missing data, uncertainty about falls, or out of range gait speed (greater than 1.79 m/s) [21] for preferred gait speed (Figure 2).

Figure 2. Participants included in analysis.



[a]Some participants were missing data for multiple measurements

Within the complete data set of 2705 participants, 45% of participants were female, the mean participant age at baseline was 78.5 (SD = 3.2) years, and 96% of participants were white (Table 1). For health history, 19% had a history of cancer, 10% history of heart attack, 3% history of stroke, and 14% had MCI at the screening visit. The mean 3MSE score at the 12-month visit was

94.4 (SD = 5.0) and 3% used an assistive device at the 12-month visit. For falls, 16% had a fall at the 12-month visit and 18% had a fall at the 18-month visit. The average gait speed at the 12-month visit was 0.93 m/s (0.20). In terms of health habits, 41% of participants never smoked, and 44% of participants did not drink alcohol. Participants excluded from analysis were significantly older ($p < 0.01$), were more likely to be female ($p < 0.01$), were more likely to be from Forsyth County ($p < 0.01$), and were less educated ($p < 0.01$). There were no statistically significant differences in race or treatment arm assignment.

We observed evidence of a relationship between our exposure of interest (gait speed) and age, gender, MCI, study site, a fall reported at the 12-month study visit, education level, 3MSE score, use of an assistive device, history of a stroke, and alcohol use (Table 1).

Table 1. Participant characteristics by preferred gait speed quartile at 12-month study visit, Ginkgo Evaluation of Memory study (GEMS) (*n* = 2705).

Covariate of Interest	All Participants [a] *n* (%)	Gait Speed, Quartile 1 [b] *n* (%)	Gait Speed, Quartile 2 [c] *n* (%)	Gait Speed Quartile 3 [d] *n* (%)	Gait Speed Quartile 4 [e] n (%)	*p*-Value (Chi-Square or ANOVA)
Age, years (SD)	78.5 (3.2)	79.5 (3.6)	78.4 (3.2)	78.2 (3.0)	77.8 (2.6)	<0.01
Female	1221 (45)	410 (59)	345 (48)	263 (39)	203 (33)	<0.01
Treatment Ginkgo	1365 (51)	357 (51)	363 (51)	352 (52)	293 (48)	0.60
Study Site						<0.01
Forsyth County, NC	623 (23)	181 (26)	180 (25)	148 (22)	114 (19)	
Sacramento County, CA	831 (31)	222 (32)	197 (27)	204 (30)	208 (34)	
Washington County, MD	406 (15)	104 (17)	125 (17)	115 (28)	62 (10)	
Allegheny County, PA	845 (31)	193 (28)	216 (30)	212 (31)	224 (37)	
Fall reported at 12-month visit	433 (16)	149 (21)	110 (15)	95 (14)	79 (13)	<0.01
Education						<0.01
High school or less	943 (35)	274 (39)	260 (36)	244 (36)	165 (27)	
Some college	678 (25)	184 (26)	184 (26)	164 (24)	146 (24)	

College graduate	433 (16)	106 (15)	104 (15)	104 (15)	119 (20)	
Postgraduate	651 (24)	136 (19)	170 (24)	167 (25)	178 (29)	
Health History						
MCI	383 (14)	139 (20)	94 (13)	78 (12)	72 (12)	<0.01
3MSE score (SD)	94.4 (5.1)	93.1 (5.7)	94.5 (4.8)	94.8 (4.8)	95.3 (4.5)	<0.01
Cancer [f]	520 (19)	122 (18)	135 (19)	144 (21)	119 (20)	0.35
Heart attack [g]	255 (10)	69 (10)	69 (10)	62 (9)	55 (9)	0.93
Stroke [h]	73 (3)	29 (4)	21(3)	13(2)	10 (2)	0.02
Smoker [i]						0.22
Never	1091 (41)	287 (42)	308 (43)	257(38)	239 (40)	
Former	1449 (55)	364(53)	372 (53)	378 (56)	335 (57)	
Current	116 (4)	34 (5)	29 (4)	35 (5)	18 (3)	
Alcohol Use (drinks/week) [j]						<0.01
None	1117 (44)	356 (54)	297 (43)	255 (40)	209 (37)	
Less than 1	417 (16)	96 (15)	132 (19)	100 (16)	89 (16)	
1–7	509 (20)	105 (16)	137 (20)	139 (22)	128 (23)	
7.1–14	240 (9)	60 (8)	53 (10)	63 (11)	64 (11)	
More than 14	270 (11)	47 (7)	66 (10)	85 (13)	72 (13)	

Note. Abbreviations: MCI (Mild Cognitive Impairment) ascertained according to 2004 International Working Group criteria, 3MSE (Modified Mini-Mental State Exam) individuals scoring less than 80 at screening were excluded from participating in GEMS [22]. Race and use of an assistive device were excluded from the table, as there were cell counts with fewer than 5 participants; [a] *n = 2705,* [b] *0.19 m/s to 0.80 m/second* [c] *+0.80 to 0.93 m/s* [d] *+0.93 to 1.06 m/s* [e] *+1.06 to 1.69 m/s;* [f] *History of cancer missing for less than five participants,* [g] *History of heart attack missing for 35 participants,* [h] *History of stroke missing for 49 participants,* [i] *History of smoking missing for 49 participants,* [j] *History of alcohol use missing for 152 participants.*

We observed evidence that our primary outcome of interest (report of a fall at the 18-month visit) was associated with age, study site, fall reported at 12-month study visit, MCI, 3MSE score, use of an assistive device, history of stroke, and history of a heart attack (Table 2).

Table 2. Participant characteristics by fall status at 18-month study visit, Ginkgo Evaluation of Memory study (GEMS) (*n* = 2705).

Covariate of Interest	All Participants [a] *n* (%)	No Fall [b] *n* (%)	Fall [c] *n* (%)	*p*-Value (Chi-Square or ANOVA)
Age, years (SD)	78.5 (3.2)	78.4 (3.1)	78.9 (3.4)	<0.01
Gender (female)	1221 (45)	982 (44)	239 (48)	0.17
Treatment -Ginkgo	1365 (51)	1116 (51)	249 (50)	0.86
Study Site				0.02
Forsyth County, NC	623 (23)	497 (23)	126 (25)	
Sacramento County, CA	831 (31)	668 (30)	163 (33)	
Washington County, MD	406 (15)	323 (15)	83 (17)	
Allegheny County, PA	845 (31)	719 (33)	126 (25)	

Fall reported at 12 month visit	433 (16)	274 (12)	159 (32)	<0.01
Education				0.34
Highschool or less	943 (35)	783 (36)	160 (32)	
Some college	678 (25)	545 (25)	133 (27)	
College graduate	433 (16)	358 (16)	75 (15)	
Postgraduate	651 (24)	521 (24)	130 (26)	
Health History				
MCI (yes)	383 (14)	289 (13)	94 (19)	<0.01
3MSE score (SD)	94.4 (5.1)	94.5 (5.0)	93.9 (5.3)	0.02
Use assistive device	86 (3)	52 (2)	34 (7)	<0.01
Cancer [d]	520 (19)	424 (19)	96 (19)	0.98
Stroke [e]	73 (3)	52 (2)	21 (4)	0.02
Heart attack [f]	255 (10)	193 (9)	62 (13)	0.01
Smoker [g]				0.16
Never	1091 (41)	877 (40)	214 (44)	
Former	1449 (55)	1202 (55)	247 (51)	
Current	116 (4)	91 (4)	25 (5)	
Alcohol Use (drinks/week)[h]				0.57
None	1117 (44)	899 (43)	218 (47)	
Less than 1	417 (16)	347 (17)	70 (15)	
1–7	509 (20)	424 (20)	85 (18)	
7.1–14	240 (9)	193 (9)	47 (10)	
More than 14	270 (11)	222 (11)	48 (10)	

Note. Abbreviations: MCI (Mild Cognitive Impairment), 3MSE (Modified Mini-Mental State Exam), Hx (history). Race was excluded from the table, as there were cell counts with fewer than 5 participants. [a] n = 2705 [b] n = 2207 [c] n = 498; [d] History of cancer missing for less than five participants, [e] History of heart attack missing for 35 participants, [f] History of stroke missing for 49 participants, [g] History of smoking missing for 49 participants, [h] History of alcohol use missing for 152 participants.

Following bivariate analysis in addition to the variables specified a priori (age, gender, treatment arm assignment, study site, and MCI), report of a fall at the 12-month study visit was selected as a confounder in the modified Poisson regression models because it changed the relative risk of falls associated with preferred gait speed by 10%.[24] In the unadjusted model including only preferred gait speed at the 12-month visit, a 10 cm/s increase in preferred gait speed was associated with a RR of falling of 0.93 (95% CI: 0.89 to 0.97) (Table 3). In the model adjusted for demographics (age and gender), and treatment arm assignment and study site, a 10 cm/s increase in preferred gait speed was associated with a RR of falling of 0.94 (95% CI: 0.90 to 0.98). In the model adjusted for MCI status, demographics, and treatment arm assignment and study site, a 10 cm/s increase in preferred gait speed was associated with a RR of falling of 0.95 (95% CI: 0.91 to 0.99). In the final model, adjusted for demographics, treatment arm assignment, study site, MCI, and report of a fall at the 12-month study visit, a 10 cm/s increase in preferred gait speed was associated with a RR of falling of 0.96 (95% CI: 0.92 to 1.00). For a model used to assess MCI as an effect modifier, adjusted for demographics, treatment arm assignment, study site, and an interaction term for MCI and gait speed, the p-value for the interaction term was 0.78. For participants without MCI, a 10 cm/s increase in preferred gait speed was associated with a RR of falling of 0.95 (95% CI: 0.90 to 1.00), and for participants with MCI a 10 cm/s increase in preferred gait speed was associated with an RR of falling of 0.94 (95% CI: 0.85 to 1.03). Sensitivity analyses excluding participants diagnosed with dementia by the 18-month visit did not change the relative risk for falls in any of the modified Poisson regression models, except for the RR for people with MCI in the model with the interaction term for MCI and gait speed, however the interaction term remained statistically insignificant (*p*-value = 0.66) (Supplementary Material, Table S1).

Table 3. The association (RR, 95% CI) between preferred gait speed (10 cm/s) and falls in 2705 older adults participating in GEMS.

Model	Relative Risk	95% CI
Unadjusted model	0.93	0.89 to 0.97
Model adjusted for age, gender, treatment arm, and study site	0.94	0.90 to 0.98
Additional adjustment for MCI	0.95	0.91 to 0.99
Additional adjustment for fall at 12-month visit	0.96	0.92 to 1.00
With MCI, additional adjustment for interaction between MCI and gait speed *	0.94	0.85 to 1.03
Without MCI, additional adjustment for interaction between MCI and gait speed *	0.95	0.90 to 1.00

* $p = 0.78$ for interaction between gait speed and MCI.

Discussion

We observed a significant association between slower gait speed and increased risk of falling in older adults including those with MCI. This association persisted in models adjusted for age, gender, treatment assignment, study site, and MCI, but not after adjusting for falls at the 12-month visit. Although those with MCI are at a higher risk of falling,[17,25] we found no evidence that the association between gait speed and fall risk varied by MCI status. These findings support the use of gait speed as a screening tool for fall risk in both cognitively intact as well as cognitively impaired individuals.

The magnitude of the association between gait speed and falls in our study is similar to those of another study evaluating gait speed as a continuous variable and fall risk.[4] Other studies have found an association between slow gait speed and increased fall risk in a population of people with MCI, but these studies have not specifically examined whether the relationship between gait speed and fall risk is stronger in cognitively intact individuals relative to those with MCI.[16,17]

Our study provides evidence that gait speed is a valuable predictor of fall risk even in those with cognitive impairment despite the fact that other factors might influence risk of falls among those with MCI. While these findings are not consistent with our hypothesis, that gait speed may be more strongly associated with falls in cognitively healthy older adults than those with MCI, these findings are consistent with previous work.[26] In a study of older adults with MCI, gait speed and falling were associated, and adding an additional cognitive task to gait speed (dual task) did not improve discrimination between fallers and non-fallers.[26] The identification of potential screening tools for fall risk in older adults with MCI is especially important, given the current lack of recommended screening guidelines for this population.[27]

Our study had a number of strengths. Specifically, it benefitted from inclusion of a relatively large and geographically diverse population of older adults for who we have a robust determination of MCI, including multiple diagnostic tests and expert evaluation. In addition, the study included participants who are considered “old (75–84)” and approaching the status of “oldest-old (85 and older)”. These age-groups are at increasingly high risk of falls,[1] and screening measures for falls are especially important in this population. There was adjustment for several important underlying chronic conditions associated with falls. We utilized a measure of gait speed that requires minimal space and equipment, making it highly relevant to a clinic setting. Moreover, we found that gait speeds in the study population were consistent with gait speeds observed in adults with this age and gender distribution in previous research.[21]

We acknowledge some limitations. While a strength of the study was the inclusion of older adults in the oldest-old age group, the results may not be generalizable to the young-old (65–74 years). In addition, participants were also predominantly white, and the results might not be generalizable to people of other races. Given GEMS exclusion criteria, some chronic conditions were not represented in the data. Missing data were another limitation, with 12% of GEMS participants excluded from the analysis for missing values for falls, gait speed, and MCI. Those excluded from the analysis were more likely to be female, older, and have less education. Fall risk was ascertained by self-report, and was therefore likely underreported in this study; 18% of participants reported a fall; whereas the prevalence of falls found in other studies of adults over

65 is 20% to 33%.[1,2] When examining reported falls by MCI status, 25% of participants with MCI reported a fall, which is within the range reported in the literature for people with MCI .[16,28] However, 17% of participants without MCI reported a fall, which is below the range previously reported for people without cognitive impairment.[16,29] It is possible that underreporting of falls in those without MCI resulted in an underestimate of gait speed associated fall risk in this group. This could have affected our ability to detect a contrast between gait speed impacts on fall risk in those with and without MCI. Finally, while the assessments to determine MCI were robust and the number of participants with MCI was substantial, gait speed and falls were obtained one year and 18 months, respectively, after the initial assessment for MCI. It is possible misclassification of MCI occurred during the follow-up period, as participants may have had a change in MCI status during this time.[30] In a study with a similar population, the Cardiovascular Health Study, over a mean follow-up time of 4.6 years, 18% of people with MCI reverted back to normal cognition, 25% of people with normal cognition developed MCI, and 51% with MCI developed dementia.[31] We were able to address potential misclassification of participants who had MCI or normal cognition at baseline and developed dementia in sensitivity analyses by excluding participants who developed dementia by the 18-month study visit, and results did not change (Supplementary Material, Table S1).

Conclusions

Our findings add to the evidence that gait speed and fall risk are associated for older adults with and without MCI. Importantly, from our study there was no evidence that the relationship between gait speed and fall risk varied by MCI status, providing support for the use of gait speed as a screening tool for falls for people with and without MCI.

Supplement 1.

Table S1. Sensitivity analysis, the association (RR, 95% CI) between preferred gait speed (10 cm/second) and falls in 2,679 older adults participating in GEMS, excluding participants diagnosed with dementia by the 18-month study visit.

Model	**Relative Risk**	**95% CI**
Unadjusted model	0.93	0.89 to 0.97
Model adjusted for age, gender, treatment, and clinic	0.94	0.90 to 0.99
Additional adjustment for MCI	0.95	0.90 to 0.99
Additional adjustment for fall at 12-month visit	0.96	0.92 to 1.00
With MCI, additional adjustment for interaction between MCI and gait speed*	0.93	0.85 to 1.02
Without MCI , additional adjustment for interaction between MCI and gait speed*	0.95	0.90 to 1.00

*p=0.66 for interaction between gait speed and MCI

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Chapter 3: Longitudinal analysis of change in gait speed and falls for older adults with and without mild cognitive impairment

Abstract

Background: While many studies have established an association between slower gait speed and increased fall risk, few studies have looked at the association between change in gait speed and falls.

Objective: The purpose of this study is to determine whether there is an association between change in gait speed and future fall risk in older adults with and without mild cognitive impairment.

Methods: This study utilized data from 2779 participants in the Ginkgo Evaluation of Memory Study. Falls were reported every six months, and gait speed was ascertained annually. The relationship between 12-month change in gait speed and risk of falls was quantified.

Results: Slower change (0.15m/s) in gait speed was associated with increased risk of falls in models adjusted for age, gender, hospitalization, polypharmacy, study characteristics, previous falls, previous gait speed, and cognitive impairment, compared to no change or minimal change HR:1.13 (95% CI: 1.01 to 1.26) for slower gait speed. Faster change (0.15m/s) in gait speed (10%) was not significantly associated with fall risk, HR 0.94 (0.84 to 1.07) for faster gait speed. The association between change in gait speed and fall risk did not vary by cognitive status (p=0.39)

Conclusions: Change in gait speed is associated with fall risk in older adults and may be a valuable tool to identify older adults with a higher fall risk.

Introduction

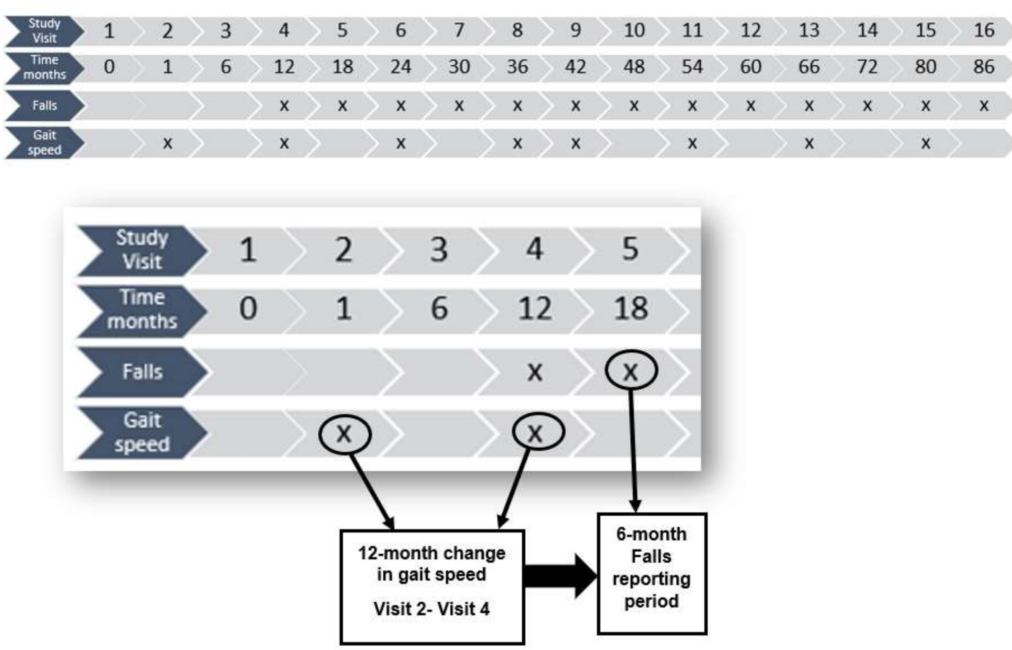
Falls in older adults are a common occurrence,[1] and have a significant impact on health at both the population and individual level.[1,2] Gait speed has an established association with fall risk,[3-5] however most research assessing the relationship between gait speed and falls has focused on using a gait speed cut-off,[6] frequently 1 m/s,[7,8] or gait speed as a continuous variable.[5] A decline in gait speed is associated with an increased risk of multiple negative health outcomes,[9,10] including disability,[11] and may also be associated with increased fall risk,[12] however, there are only a few studies looking at the association between change in gait speed and falls in older adults.[13-20] Many of these studies are limited by small study populations,[18,20] or short study duration and infrequent measures of gait speed.[13,15] Only one of the identified studies specifically investigated change in gait speed and fall risk for older adults with mild cognitive impairment (MCI),[17] a population at increased risk of falling.[21] A significant association was observed between decrease in gait speed and increased risk of injurious falls, but the study population only included older adults with MCI.[17]

The purpose of this study was to determine if there is an association between change in gait speed and fall risk in older adults, and to determine if this association differs by cognitive status. Using change in gait speed could lead to earlier identification of older adults with higher fall risk while they are on a trajectory of decline towards gait speed thresholds for fall risk but have not yet reached those thresholds. Our hypothesis is that change in gait speed is associated with fall risk in older adults, and that the strength of association varies by cognitive status. There is evidence that some of the risk factors for falls in older adults with MCI differ from those without cognitive impairment, and that these risk factors, such as decreased safety awareness[22] may not be adequately assessed with gait speed in a clinic or research setting.

Methods

This study utilized data from the Ginkgo Evaluation of Memory study (GEMS), completed in 2008. At baseline, GEMS included 3,069 adults 75, and older, from four different locations in the United States. Study participants were all community-dwelling at baseline. Study visits were every six months for up to eight years. There have been multiple publications from GEMS where further details on study design and methods can be found.[23-25] The original study received Institutional Review Board approval from all study sites. The study reported here was approved by the University of Montana IRB.

Figure 1. Timing of longitudinal outcome and exposure measurements in GEMS.



Outcome Measure

The outcome of interest for this study was falls. Beginning at the one-year study visit, at every subsequent 6-month study visit, participants were asked if they had had any falls in the previous six months (Figure 1). Participants could respond “yes,” “no, or “don’t know.” The period for falls was from zero to six months after gait speed was measured. The fall outcome was dichotomized to no falls, or one or more falls reported in the six-month period. Additional information was provided about the number of falls, and whether participants sought medical care for falls. Responses from participants who answered “don’t know” were coded as missing. Falls were combined as the number of cumulative previous falls and categorized as zero falls, one fall, and two or more falls based on distribution in the data set and interpretability.

Exposure Measure

The exposure of interest in this study was gait speed. Gait speed was measured approximately annually as part of the Functional Assessment performed in GEMS (Figure 1). Due to changes in the GEMS protocol, after year four of the study some participants had gait speed measurements that were six months or eighteen months apart for one visit. Gait speed was measured from a static start over 15 feet. Time to walk 15 feet was converted to gait speed in meters per second (m/s) and then 10 centimeters per seconds (10 cm/s) for models. Any gait speed faster than 1.93 was excluded from analyses as these values exceeded the mean preferred gait speed plus three standard deviations for males 75-84 and this was used as the exclusion criteria for both men and women.[26] Change in gait speed was the metric of primary interest. Gait speed change was aligned with the fall reporting period and was measured as the difference between gait speed 12 months prior to the fall reporting period, and gait speed measured at the start of the fall reporting period (Figure 1). Change in gait speed was categorized based on clinically measurable differences in gait speed,[6,27] change in gait speed used in prior studies,[13,17] and the distribution of change in gait speed among study participants. Categories for 12-month change in gait speed included greater than 0.15 m/s faster, no change (0.15 m/s faster to 0.15 m/s slower), slower by more than 0.15 m/s. Change in gait speed was also assessed as a percentage to include a measure of change relative to gait speed. Percent change in gait speed was the 12- month change in gait speed variable, divided by gait speed 12 months prior to the fall reporting period multiplied by 100. Categories for percent change in gait speed were greater than 10% increase in gait speed, no change in gait speed (10% faster to 10% slower), and more than 10% slower. Associations between percent change in gait speed and falls were not found in the literature, therefore, categories were based on distribution of percent change in gait speed among participants and sensitivity analyses. Previous gait speed, 12 months prior to current gait speed, was also included in the model both as a continuous variable, and in categories of 0 to 0.8m/s, +0.8 m/s to 1.0 m/s, +1.0 m/s.

Covariates

Covariates considered for inclusion in analyses were cognition, medications, hospitalizations, previous health history, education, and assistive device use. A three-level time-varying covariate for cognition was created. The three levels of cognition include normal cognition, MCI, and dementia. MCI was determined based on the International Working Group on Mild Cognitive Impairment guidelines[24,28] and was ascertained at baseline, and then annually beginning at study year 4. MCI status at baseline was carried forward until the annual assessments began. Participants were screened for dementia at each six-month study visit and dementia was ascertained through a multi-step process described in detail by DeKosky, et al. 2006.[23] Participants were asked at each study visit about their medication use. Prescription medication use was included as a dichotomous covariate for polypharmacy (five or more prescription medications),[29] which is associated with increased fall risk.[30] Participants were asked if they had an at least a one-night stay in the hospital in the previous six months. Hospitalization for any reason was included in the analysis as a dichotomous variable. At baseline participants were asked if they had a history of cancer, heart attack, or stroke. Education was included as a continuous variable. Assistive device use was considered, but was not included as 96% of observations for gait speed participants did not use an assistive device

Statistical Analysis

Covariates selected *a priori* included gender, treatment (yes/no Ginkgo), study site, and cognition. History of heart attack, stroke, or cancer, hospitalization in the previous six months, polypharmacy, previous gait speed, and education, were all considered for inclusion in the model. Covariates that changed the hazard ratio for gait speed and falls in the bivariate analysis were included in the full models. All analyses were completed with the statistical software R.

<u>Modeling Approach</u>

Cox proportional hazards models for recurrent events were used for the primary analyses.[31] Effect modification by cognition was assessed using models with an interaction term for change in gait speed and percent change in gait speed and cognition. Extended Cox proportional hazards models (Prentice-Williams-Peterson model (PWP)) were used for sensitivity analyses with cumulative falls as strata to account for the possibility that the hazard of falling after experiencing one fall is different than the hazard of falling after multiple falls.[32-34] The time axis for this modeling approach was age using the counting process data format.[31-33] Schoenfeld residuals were assessed to check the proportional hazards assumption.[31] Gender, study site, treatment, and polypharmacy were adjusted as stratified variables in the model based on evidence that they did not meet proportional hazards assumptions.[31]

Imputation

When there was missing information for the visit date, age was imputed based on the baseline age and the current visit number, assuming all visits were six months apart. Imputed age was then used when there was missingness for the time axis variables. Missing change in gait speed was imputed in a two-part process. First, if available, the reason for missingness was used to impute gait speed. For the following reasons, gait speed was recorded as 0.01 m/s: "tried but unable, you felt it was unsafe, participants felt it was unsafe, participant cannot walk even with support, participant unable to understand instruction." If the reason was further described, for participant characteristics, such as an injury, gait speed was recorded as 0.01 m/s, but for structural reasons, such as not enough space, or study specific reasons, such as measurement was forgotten, values were imputed. Updated change in gait speed values were calculated based on this first round of imputing. For continued missing change in gait speed, previous gait speed, hospitalization, and polypharmacy, multiple imputation with expectation maximization with bootstrapping with five imputations using Amelia in R, which accounts for time-varying covariates, was used.[35] Pooled confidence intervals were calculated using Rubin's Rules.[36] Hazard ratios and 95% confidence intervals from the original analyses were then compared with the results from the analyses with imputed data.

Competing Risks

GEMS was not originally designed to assess the association between change in gait speed and falls, and over time, some participants left the study early due to censoring if they developed dementia, death, or loss to follow-up. The purpose of this analysis was to determine if participants who left the study before visit eight (study year three), had a risk of falling that differed from those participants who remained in the study past visit eight at changed the association between change in gait speed and falls. Inverse probability weighting was used for this analysis. Weights were created based on the association between covariates used in the full model and risk of leaving the study early. Analyses were done including all participants who left the study early. These weights were then added to the fully adjusted model for change in gait speed and falls to determine if the HR for change in gait speed and falls changed when people who were more likely to leave the study early were upweighted.

Results

Participants

Table 1. Baseline characteristics of GEMS participants included in analyses of change in gait speed and fall risk (N = 2,775)

Characteristic	Mean or n (SD or %)
Age	78.5 (3.2)
Gender- Female	1255 (45%)
Race (White)	2649 (96%)
Treatment- Ginkgo	1411 (51%)
Clinic Site	
Forsyth County, NC	641 (23%)
Sacramento County, CA	842 (30%)
Washington County, MD	413 (15%)
Allegheny County, PA	879 (32%)
MCI at baseline	418 (15%)
Education- years	14.5 (3.1)
Polypharmacy-yes	819 (30%)
Heart attack*	255 (9%)

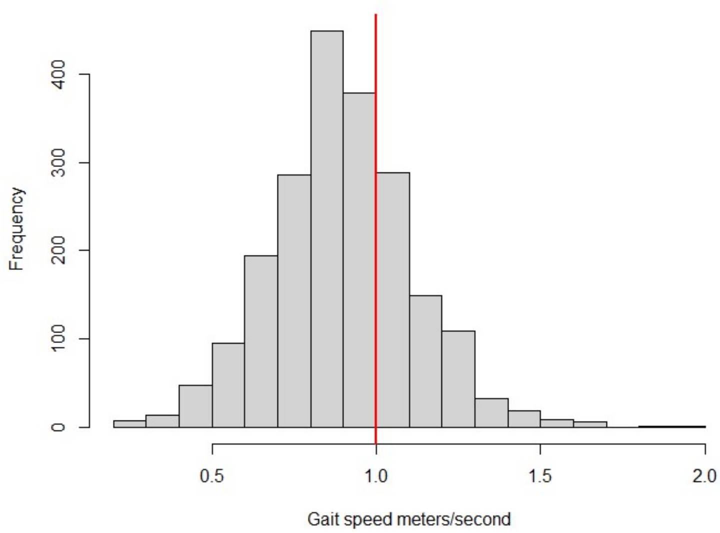
Stroke*	73 (3%)
Cancer*	517 (19%)

*Missing: Heart attack (36), stroke (49), cancer (1)

Of the original 3,069 GEMs participants, 2,775 participants were included in these analyses with 10,654 observations. Participants were excluded from analyses for missing data for falls (n=131), change in gait speed (n=128), polypharmacy (n=1), hospitalizations (n=3), and for the time axis (n=31).

Using the 1.93 m/s gait speed cut-off, 38 observations ranging from 1.99 to 45.7, median 2.95 m/s were excluded from analysis, but this did not change the number of participants in the analysis. The mean gait speed for remaining participants was 0.93 m/s. Of the 1337 participants who experienced a fall during the study period, 30% (617) had a gait speed faster than 1.0 m/s prior to falling (Figure 2).

Figure 2. Distribution of gait speed prior to a fall among older adults in GEMS, N=1337, observations=2090



**Gait speed slower than 1 m/s is a commonly used threshold for increased fall risk*[7,8]

Decreased gait speed of more than 0.15 m/s was associated with a HR for falls in the next 6 months of 1.13 (95% CI: 1.01 to 1.26) in a model adjusted for gender, treatment (Ginkgo), study site, previous gait speed category, cognitive status, polypharmacy, hospitalization, and previous number of falls with age as the time axis (Table 2). Increased gait speed of more than 0.15 m/s is associated with a HR 0.97 (95% CI: 0.87 to 1.08) for falls in the next 6 months in a fully adjusted model. For percent change in gait speed, a 10% or greater decrease in gait speed was associated with a HR of 1.11 (95% CI: 1.00 to 1.23) for falls in the next 6 months and a HR of 0.97 (95% CI: 0.87 to 1.08) for an increase in gait speed of 10% or more (Table S1).

Table 2. The association between change in gait speed and fall risk in older adults from GEMS (N=2775, observations=10,654)

Model	Observations N (%)	HR	95% CI
1. Adjusted for change in gait speed, gender**, study site**, treatment (Ginkgo)**, and previous gait speed category			
Reference is no change (0.15 m/s faster to 0.15 m/s slower)	6702 (63%)		
0.15 m/s faster	1723 (16%)	0.90	0.80 to 1.02
0.15 m/s slower	2229 (21%)	1.17	1.05 to 1.30
2. 1+cognitive status			
0.15 m/s faster	1723 (16%)	0.91	0.80 to 1.02
0.15 m/s slower	2229 (21%)	1.16	1.04 to 1.29
3. 2+ hospitalization and polypharmacy**			
0.15 m/s faster	1723 (16%)	0.90	0.80 to 1.02
0.15 m/s slower	2229 (21%)	1.13	1.01 to 1.26
4. 3+ previous falls (0,1,2+)			
0.15 m/s faster	1723 (16%)	0.94	0.84 to 1.07
0.15 m/s slower	2229 (21%)	1.13	1.01 to 1.26
5. 4 + interaction with cognitive status			
0.15 m/s Faster* normal cognition	1433 (14%)	0.91	0.80 to 1.04
0.15 m/s Slower* normal cognition	1821 (17%)	1.13	1.00 to 1.28
0.15 m/s Faster*MCI	266 (3%)	1.05	0.80 to 1.38
0.15 m/s Slower*MCI	364 (3%)	1.07	0.84 to 1.37

Abbreviations: MCI (Mild Cognitive Impairment) **stratified

Proportional hazards assumptions were met for all models. The interaction between change in gait speed category and cognitive status was not statistically significant (p=0.39). Previous falls were included in the final models as a categorical variable rather than as strata as there was no evidence of an interaction between previous number of falls and change in gait speed (p=0.89), and previous falls as a categorical variable met proportional hazards assumptions (Table S2).

Imputation

Imputation increased the number of observations from 10,654 to 14,083 (Table S3). Using the first stage of imputation for gait speed, incorporating reason for missingness, 254 values were imputed. In the second stage, using multiple imputation, data were imputed for hospitalizations (<1%), polypharmacy (<1%), previous fall category (<1%), previous gait speed (17%), and change in gait speed (21%). Change in gait speed point estimates for hazard ratios increased for faster gait speed by .02 and decreased for slower gait speed by .05. The width of the 95% CIs were similar for imputed and non-imputed models, however the CI for slower gait speed shifted to included 1. The 95% CI remained overlapping between imputed and non-imputed models and did not change the interpretation of the association between change in gait speed and fall risk.

Competing Risks

Inverse probability weights were used for the competing risks analysis (lost to follow-up, n=530 (19%), truncated 6% to 94%). Using the weights for change in gait speed, altered the point estimates for HR for fall risk by .02 or less, and widened the 95% CIs (Table S4). The point estimate for the HR was the same in the weighted model (1.10) for decreased gait speed and higher in the weighted model for increased gait speed (0.99 vs. 0.97). All the confidence intervals were overlapping and weighting the models did not change the interpretation of the association between change in gait speed and fall risk.

Discussion

The results of these analyses provide evidence of an association between decreased gait speed and fall risk for older adults with and without mild cognitive impairment for any type of fall. The association between change in gait speed and fall risk did not vary by cognitive status or previous number of falls. While both change in gait speed and percent change in gait speed were associated with fall risk, we found that the effect sizes for these measures were similar, and therefore change in gait speed could be used rather than calculating percent change. Change in gait speed could potentially be used in conjunction with gait speed thresholds to identify more older adults at higher risk of falls. In our study, we found that prior gait speed for 30% of observations for falls were above the commonly used 1m/s threshold.

Our study was unique in comparison to the other studies on change in gait speed and fall risk we identified, as it included older adults both with and without mild cognitive impairment and assessed whether there is an interaction between change in gait speed and cognition. Additionally, we utilized PWP models to account for potential interactions between previous falls and change in gait speed. In comparison to two previous studies that used similar timing and sizes of change in gait speed, our results aligned with one other study that found an association between slower gait speed of greater than 0.15 m/s and increased risk of all fall; however this study did not include participants with MCI.[13] Our results differed from another study only including participants with MCI that found an association between more than 0.1 m/s decrease in gait speed and falls with injuries requiring ER visit, but not all falls.[17] Because there is evidence that the hazard of falling increases with each previous fall; we looked for but did not find an

interaction between change in gait speed and previous number of falls.[33] The prior research; however, did not look specifically at the relationship between gait speed and falls.[33]
Our study had numerous strengths, including a large number of participants with frequent measures of gait speed and falls over multiple years. Numerous potential confounders such as polypharmacy and hospitalizations, were available in the dataset to include in the model. While there was some missingness of gait speed and censoring and lost to follow-up, sensitivity analyses including multiple imputation and competing risks did not alter conclusions. Frequent assessment of dementia allowed for identification of participants who had transitioned from normal cognition or MCI to dementia during the study period.

While the study had excellent ascertainment of MCI, the timing of the measurement of MCI was a potential limitation of the study. Assessment of MCI varied during the study and after baseline MCI ascertainment did not occur for the first four years of the study but was then measured annually. In this first four-year period, some participants may have transitioned between normal cognition and MCI without this being captured in the analysis. Additionally, some falls data were not incorporated into the analyses as they did not align with the measurement of gait speed.

Conclusions

Our study provides evidence of an association between change in gait speed and falls for older adults with and without mild cognitive impairment. Using change in gait speed as a screening tool has the potential to identify older adults with increasing fall risk before they reach a commonly used gait speed threshold for fall risk. As seen in our study, 30% of falls occurred at gait speeds above 1.0 m/s, a commonly used threshold. Our results also add to the evidence that change in gait speed can be used to assess fall risk in individuals with MCI, potentially adding another screening tool to use with this population at high risk for falls. Increased and earlier identification of older adults with increased fall risk is essential for tackling the growing public health challenge of falls[37,38] in older adults.

Supplement

S1: The association between percent change in gait speed and fall risk in older adults from GEMS (N=2775, observations=10,654)

Model	Observations N (%)	HR	95% CI
1. Adjusted for gender**, study site**, treatment (Ginkgo), previous gait speed category, cognitive status, hospitalization, polypharmacy**, and previous number of falls			
Reference is 10% faster to 10% slower	4579 (43%)		
10% faster	2806 (26%)	0.97	0.87 to 1.08
10% slower	3269 (31%)	1.11	1.00 to 1.23

**Stratified

S2: The association between change in gait speed and fall risk in older adults from GEMS, stratified by total previous number of falls (0, 1, 2+) N=2775, observations=10,654

Model	Observations N (%)	HR	95% CI
1 Adjusted for gender**, study site**, treatment (Ginkgo), previous gait speed category, cognitive status, hospitalization, polypharmacy**, and previous number of falls, and interaction term for change in gait speed and previous fall category			
0.15 m/s faster *no previous falls	1030 (10%)	0.87	0.71 to 1.07
0.15 m/s faster *1 previous fall	312 (3%)	0.98	0.73 to 1.31
0.15 m/s faster * 2+ previous falls	381 (4%)	0.94	0.78 to 1.14
0.15 m/s slower * no previous falls	1244 (12%)	1.10	0.91 to 1.31
0.15 m/s slower * 1 previous fall	426 (4%)	1.19	0.91 to 1.55
0.15 m/s slower * 2+ previous falls	559 (5%)	1.05	0.89 to 1.24

**Stratified

S3. The association between change in gait speed and fall risk in older adults from GEMS, using multiple imputation for missing data.

Model	Observations N	HR	95% CI
1. Adjusted for gender**, study site**, treatment (Ginkgo), previous gait speed category, cognitive status, hospitalization, polypharmacy**, and previous number of falls	10,654		
Reference is no change (0.15 m/s faster to 0.15 m/s slower)			
0.15 m/s faster		0.94	0.84 to 1.07
0.15 m/s slower		1.13	1.01 to 1.26

2. 1- with pooled results from 5 imputations	14,083		
0.15 m/s faster		0.96	0.85 to 1.09
0.15 m/s slower		1.08	0.96 to 1.21

*Stratified

S4. The association between change in gait speed and fall risk in older adults from GEMS, weighted for the competing risk of leaving the study early (before visit 8). N=2572 observations=9,368

Model	HR	95% CI
Unweighted		
Adjusted for gender**, study site**, treatment (Ginkgo), previous gait speed category, cognitive status, hospitalization, polypharmacy**, and previous number of falls		
Reference is no change (0.15 m/s faster to 0.15 m/s slower)		
0.15 m/s faster	0.97	0.85 to 1.10
0.15 m/s slower	1.10	0.98 to 1.24
Weighted[+]		
Adjusted for gender*, study site*, treatment (Ginkgo), previous gait speed category, cognitive status, hospitalization, polypharmacy*, and previous number of falls		
Reference is no change (0.15 m/s faster to 0.15 m/s slower)		
0.15 m/s faster	0.99	0.85 to 1.15
0.15 m/s slower	1.10	0.96 to 1.26

[+]Weights truncated to between >5% and <95% to remove negative values. **Stratified

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Chapter 4: Falls and trajectories of activities of daily living in older adults with and without cognitive impairment.

Abstract

Background: Understanding the impact of falls on activities of daily living is necessary for developing post-fall interventions.

Objective: The purpose of this study is to determine the association between falls and difficulty with activities of daily living (ADLs) and instrumental activities of daily living (IADLs), and to model trajectories of difficulty with I/ADLs pre- and post-fall.

Methods: This study included 3069 participants from the Ginkgo Evaluation of Memory Study. Self-reported falls and I/ADL scores were ascertained every 6 months for up to 7 years. Cox proportional hazards models and latent class trajectory modeling were used for statistical analyses.

Results: A fall or falls reported in the previous 6 months was significantly associated with difficulty with ADLs HR: 1.19 (95% CI 1.09 to 1.29) and IADLs HR 1.25 (95% CI 1.13 to 1.38) in a fully adjusted model. The risk of difficulty with ADLs and IADLs increased with more falls. Based on trajectory modeling, about 20% of participants had increasing difficulty with ADLs and IADLs after their first fall during the study.

Conclusions: Falls are associated with an increased risk of difficulty with ADLs and IADLs. This difficulty persists and worsens over time for some individuals who fall.

Introduction

Falls in older adults are common[1] and are associated with multiple negative health outcomes ranging from death and injury[2] to decreased social participation[3] and mental health.[2] While many falls are preventable,[4] a large number of older adults fall each year.[1,5] Intervention post-fall is important in preventing further declines in health.[6,7]

To maximize quality of life and develop targeted post-fall interventions, it is critical to understand the magnitude and duration of post-fall outcomes. Difficulty in performing Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs) is associated with a variety of negative health outcomes including increased risk of institutionalization,[8] decreased mental health,[9] increased need for formal and informal care,[10] hospitalization, and mortality.[11] A limited number of studies have looked at the association between falls and dependency with I/ADLs. While most found an association between falls and impairment in I/ADLs, the type of fall (all, injurious, multiple) varied across studies and, many of the studies were cross-sectional or had a short follow-up time,[12-22] making it challenging to characterize the range of post fall trajectories and also to identify those more susceptible to poorer post-fall trajectories. In addition, no study has specifically looked at the association between falls and I/ADL impairment in older adults with mild cognitive impairment (MCI). Older adults with MCI are a vulnerable, understudied population, and MCI is associated both with increased risk of falls[23] and with increased risk of I/ADL impairment.[24,25]

The purpose of this research was to quantify the association between falls and difficulty with I/ADLs, characterize the trajectory of difficulty with I/ADLs pre- and post- fall, and identify those at most risk of steep declines in I/ADLs function.

Methods

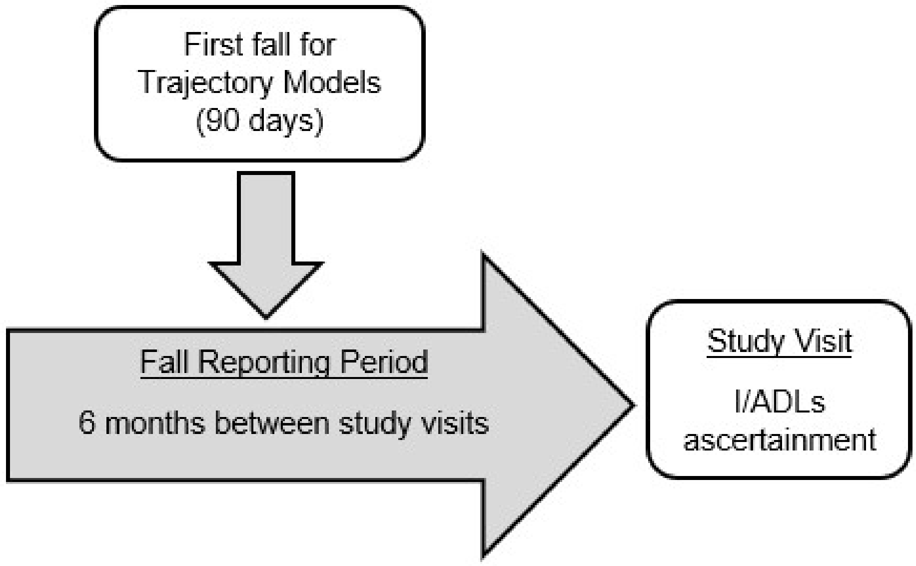
Study Population

This study utilized data from the Ginkgo Evaluation of Memory Study (GEMS). Multiple papers have been published from GEMS with further description of the methodology,[26,27] but briefly, GEMS was a randomized controlled trial (RCT), designed to investigate whether taking *Ginkgo biloba* supplements decreased the risk of dementia and cognitive decline in older adults.[28,29] *Ginkgo biloba* had no effect on dementia or cognitive decline.[28,29] GEMS took place from 2000 to 2008 and included 3,069 older adults, who were community-dwelling at study-entry. There were four study sites: Sacramento, CA, Pittsburgh, PA, Hagerstown, MD, and Winston-Salem and Greensboro, NC. Participants were followed for a median of 6.1 years.[28] While enrolled, participants had study visits every 6 months. IRBs at the four study sites approved the GEMS RCT, and the University of Montana IRB approved the study described here.

Fall ascertainment

Participants were asked at each 6-month study visit, beginning at the one-year study visit "In the past six months since we last saw you, have you had a fall?" and participants could respond, "yes," "no," or "don't know". If they responded "yes," they were then asked how many times they had fallen in the past six months, and "did any fall require medical treatment such as a visit to a physician's office, emergency room or an overnight hospitalization?", to which they could

Figure 1. Timing of the measurement of falls and I/ADLs in GEMS.



respond “yes,” “no,” or “don’t know”. Falls were dichotomized as “yes/no” for a fall in the previous 6 months. Any response of “don’t know” was coded as missing. First fall periods were included in analyses as the first 6 month fall reporting period in the study with a fall (Figure 1). The effect of cumulative falls was also evaluated. Cumulative falls are the total number of falls that occurred in the 6-month reporting period added to all previous falls that had occurred during the study, and were categorized into 0, 1, 2, 3-5, 6-9, and 10+ falls. Categories were based on the distribution of falls and clinical relevance. Medically treated falls were included as a dichotomous variable in the Cox models and were characterized as any fall or falls in the 6-month reporting period that participants sought medical care for. ADL and IADL trajectories were modeled pre- and post- first reported fall (one year study visit or later). The timing of the first fall was set to 90 days before the study visit when the fall was reported, which was the midpoint of the 6-month fall reporting period (Figure 1).

Activities and Instrumental Activities of Daily Living

The outcome of interest was change in score on the GEMS Activities of Daily Life (ADL) questionnaire. The ADL questionnaire was answered by participants at the screening visit and then every 6 months starting at the 1-year visit until the 4-year visit, and then annually for the rest of the study for a total of up to 10 measures. The results from the questionnaire were divided into two composite scores, one for ADLs and one for IADLs. Participant's I/ADLs score increased by one point respectively, for each activity participants reported having difficulty with (Table 1).

Table 1. ADLS and IADL Items on the GEMS Activities of Daily Life Questionnaire*

Difficulty with ADLs *For each item:* Yes=1 point No= 0 points Could do it but don't for reason other than health=0 points Don't know= NA	**Difficulty with IADLS** *For each item:* Yes=1 point No= 0 points Could do it but don't for reason other than health=0 points Don't know= NA
Do you have any difficulty?	*Because of health or physical problems, do you have any difficulty or are you unable to?*
1. Walking around your home	1. Do light housework
2. Getting out of a bed or a chair	2. Shop for groceries
Because of health or physical problems, do you have any difficulty or are you unable to?	3. Shop for personal items
3. Eat, including feeding yourself	4. Prepare your own meals
4. Dress yourself	5. Manage your money such as paying bills
5. Bathe or shower	6. Take medications
6. Use the toilet, including getting to the toilet	7. Use the telephone

**Modified from GEMS study forms*

Covariates

<u>Cognition</u>

Impaired cognition is associated both with increased risk of falling,[23,30,31] and decreased ability to perform ADLs.[22,24] Cognition was included as time-varying covariate including intact cognition, mild cognitive impairment (MCI), and dementia. Participants were screened for dementia at each study visit, and participants who were diagnosed with dementia were then censored from the study. Mild cognitive impairment was ascertained as baseline, and then beginning in 2004, at year four of the study, annually. Participant's cognitive status at baseline was carried forward from baseline until annual assessments began unless they were diagnosed with dementia in the interim. Participants were given a neuropsychological test battery comprised of 10 tests covering five cognitive domains and the Clinical Dementia Rating (CDR) scale.[26] Participants who were impaired on two or more tests, based on cut-points from participants in the Cardiovascular Health Study, and scored 0.5 on the CDR, were determined to have MCI.[26]

Neighborhood deprivation index

Neighborhood deprivation index (NDI) characterizes neighborhoods at the census tract level, and utilized information from the 2000 US Census.[32] NDI is a weighted linear combination of percentage of people within a census tract with a Bachelor degree, in managerial occupations, with at least a high school education, with an annual household income greater than $50,000, and the percent interest, dividend, or rental income, median home value, and median household income.[32] A higher NDI score indicates greater neighborhood deprivation. NDI is associated with both increased risk of falls[1,33,34] and decreased ability to perform ADLs[35,36] NDI was included as a time-varying covariate to account for participants who moved during the study period.

Additional Covariates

Other covariates considered for inclusion in the models include medication use, hospitalization in the previous 6 months, and education. Education was assessed at the baseline visit, whereas medication use and hospitalization, were assessed at each 6-month study visit. Education was assessed as a continuous variable. Medication use was included as the number of prescription medications a participant was taking at each study visit and was categorized as no polypharmacy (0-4 medications) and polypharmacy (5+) medications. Participants reported hospitalizations for the previous 6 months, with a hospitalization defined as at least a one-night stay in the hospital for any reason. The variable was dichotomized as yes/no for any hospitalization in the previous 6 months.

Statistical Approach

To estimate the association between falls and difficulty with I/ADLs, Cox proportional hazards models were used. Because most of the scores for ADLs (79%) and IADLs (83%) were zero, the decision was made to dichotomize the outcome to difficulty with ADLs or IADLs and use Cox proportional hazards models for recurrent events. Covariates including age (continuous, time-varying), gender (categorical, time independent), NDI (categorical-quartiles, time-varying), and cognition (categorical- intact, MCI, and dementia , time-varying) were chosen *a priori* for their known association both with falls and ADLS.[1,21,24,30,34,35] Study site (categorical, time-independent) and whether participants received *G. biloba* or placebo (categorical, time independent) were also included as covariates in the model to adjust for any potential impacts of the study design. Age was the time axis in the analysis using the counting process, with the starting age, age at the previous study visits, and the stopping age, age at the time of the study visit.[37] Polypharmacy (categorical, time-varying), hospitalization (categorical, time-varying) in the previous 6 months, and education (continuous, time-independent) were all assessed as potential confounders through bivariate analysis. Medically treated falls, multiple falls, and previous number of falls as strata were also included in the models. Analyses with cognition as an interaction term were included to assess cognition as an effect modifier, using the Wald test to assess for a significant difference in the association between previous falls and the three different levels of cognition. I/ADL scores were dichotomized (no difficulty/ difficulty with one or more items on the questionnaire) for analysis with Cox proportional hazards models and used as a continuous variable for trajectory modeling. Schoenfeld residuals were used to assess the proportional hazards assumption. The study site, treatment, total number of falls, and polypharmacy were stratified when adjusted for in the Cox models, and cognitive status was stratified when adjusted for in the models with IADL difficulty as an outcome, as there was evidence that these covariates did not meet proportional hazards assumptions.[37] All analyses were completed using R statistical software

Latent class trajectory modeling was used to understand the trajectory of I/ADLs for all participants by age.[38,39] Latent class trajectory modeling has been used to characterize trajectories of disability post serious fall injury.[18] Latent class trajectory modeling provides visualization of the types and durations of impairment post fall, and the participant characteristics associated with these trajectories, increasing understanding of which populations are at highest risk post-fall. Pre-and post-first fall I/ADL trajectories were modeled only for those participants who reported a fall during the study. Pre-fall time was considered to start at the 12-month visit, as that was the first time falls were reported during the study. Participant characteristics associated with each latent class were reported for each model. The number of latent classes was determined based on BIC, having at least 1% of the study population in each class, and having a mean posterior probabilities for each class of greater than 70%.[38] All analyses were completed using the lcmm package in R statistical software.[39]

Results

The Cox proportional hazards models included 2900 participants. Participants were excluded for missingness for falls/ number of falls (n=129), NDI (n=17), age at previous visit for time axis (n=22), and medically treated falls (1). At baseline, 20% of participants had difficulty with ADLs and 15% had difficulty with IADLs. This increased to 25% for ADLs, and 23% for IADLs for participants at their last observed study visit. Transferring in and out of a bed or chair, followed by walking around the home were the most common ADLs participants had difficulty with both at baseline and the last observed visit. The IADL the most participants had difficulty with both at baseline and last observed visit, was using the phone, followed by grocery shopping. Table 2. provides the characteristics of participants included in the Cox models, by fall status.

Table 2. Participant characteristics of older adults from GEMS by fall status (n=2900)

Characteristic	All n=2900 (n and %, or mean and SD)	No Falls during study period n=796 (27%)	At least one Fall during study period n=2104 (73%)	P-value
Max visit number	12.0 (3.2)	10.9 (3.8)	12.4 (2.8)	<0.01
Age at baseline	78.6 (3.2)	78.4 (3.1)	78.7 (3.3)	0.05
Gender (Female)	1335 (46%)	340 (43%)	995 (47%)	0.03
Treatment (Ginkgo)	1464 (51%)	398 (50%)	1066 (51%)	0.78
Clinic				<0.01
Forsyth County, NC	683 (24%)	195 (25%)	488 (23%)	
Sacramento County, CA	858 (30%)	203 (26%)	655 (31%)	
Washington County, MD	437 (15%)	107 (13%)	330 (16%)	
Allegheny County, PA	922 (32%)	291 (37%)	631 (30%)	

Education (years)	14.4 (3.1)	14.4 (3.1)	14.4 (3.1)	0.97
MCI at baseline (yes)	465 (16%)	142 (18%)	323 (15%)	0.11
NDI (quartile) at baseline				0.06
1 (-7.73 to -2.25)	717 (25%)	224 (28%)	493 (23%)	
2 (-2.25 to 0.04)	724 (25%)	184 (23%)	540 (26%)	
3 (0.04 to 2.22)	732 (25%)	190 (24%)	542 (26%)	
4 (2.22 to 12.96)	727 (25%)	198 (25%)	529 (25%)	
Any Polypharmacy during study (yes)	1854 (64%)	459 (58%)	1395 (66%)	<0.01
Any Hospitalization during study (yes)	1692 (58%)	393 (49%)	1299 (62%)	<0.01

There were significant differences between participants who did not fall during the study period, and participants who had at least one fall during the study period in their maximum visit number in their age at baseline, gender, study site, polypharmacy, hospitalization, and maximum study visit (Table 2).

Table 3: The association between a first fall period with a fall during the study and difficulty with ADLS or IADLS in older adults from GEMS N=2870 individuals and 11800 observations

Model	HR	95% CI
1.ADL~ First fall period Adjusted for gender, study site*, and treatment (Ginkgo)*	1.43	1.29 to 1.59
2. 1+ Cognitive status, polypharmacy*, NDI, and hospitalization	1.38	1.25 to 1.53
1a. IADL difficulty~ First fall period Adjusted for gender, study site*, and treatment (Ginkgo)*	1.28	1.13 to 1.45
2a. 1a+ Cognitive status, polypharmacy*, NDI, and hospitalization	1.24	1.08 to 1.41

*Abbreviations: NDI (Neighborhood deprivation index) *stratified*

Following the first fall reporting period with a fall, the risk of having difficulty with ADLs significantly increased with a HR 1.38 (95% CI 1.25 to 1.53) and for IADLs HR: 1.24 (95% CI: 1.08 to 1.41) in a model fully adjusted for gender, study site, study treatment, cognitive status, NDI quartile, polypharmacy, and prior hospitalization, with age as the time axis (Table 3.) Based on Schoenfeld residuals, proportional hazards assumptions were met for the fully adjusted models for ADLs and IADLs.[37]

Table 4. The association between cumulative number of falls during the study period and difficulty with ADLs or IADLs in older adults from GEMS N=2900 and 18931 observations

Model	Observations (n)	HR	95% CI
ADL			
1. Cumulative falls			
Adjusted for gender, study site*, and treatment*			
Reference: No falls	10275		
1 fall	3801	1.18	1.07 to 1.31
2 falls	1911	1.33	1.17 to 1.50
3-5 falls	1859	1.75	1.56 to 1.97
6-9 falls	632	2.14	1.85 to 2.48
10+ falls	453	2.60	2.18 to 3.09
2. 1+ Cognitive status, polypharmacy*, NDI, and hospitalization			
1 fall	3801	1.14	1.03 to 1.26
2 falls	1911	1.26	1.11 to 1.42
3-5 falls	1859	1.61	1.43 to 1.81
6-9 falls	632	1.95	1.69 to 2.26
10+ falls	453	2.24	1.89 to 2.66
3**. 2+ interaction with cognitive status**			
3. Intact cognition			
1 fall	3082	1.12	1.01 to 1.26
2 falls	1542	1.32	1.15 to 1.51
3-5 falls	1375	1.59	1.39 to 1.81
6-9 falls	420	1.99	1.67 to 2.37
10+ falls	280	2.28	1.85 to 2.80
3. MCI			
1 fall	623	1.28	1.03 to 1.60
2 falls	318	1.02	0.78 to 1.33
3-5 falls	410	1.67	1.35 to 2.07
6-9 falls	161	1.92	1.47 to 2.50
10+ falls	137	2.00	1.44 to 2.78
3. Dementia			
1 fall	96	0.80	0.43 to 1.49
2 falls	51	1.19	0.65 to 2.17
3-5	74	1.56	0.93 to 2.63
6-9 falls	41	1.66	0.90 to 3.04
10+ falls	36	2.82	1.69 to 4.73
IADL			

1a. Cumulative falls Adjusted for gender, study site*, treatment (Ginkgo)* Reference: No falls 1 fall 2 falls 3-5 6-9 falls 10+ falls	 10275 3801 1911 1859 632 453	 1.05 1.24 1.55 1.67 2.15	 0.92 to 1.19 1.07 to 1.44 1.36 to 1.77 1.40 to 2.00 1.74 to 2.65
2a. 1a+ Cognitive status*, polypharmacy*, NDI, and hospitalization 1 fall 2 falls 3-5 falls 6-9 falls 10+ falls	 3801 1911 1859 632 453	 1.01 1.21 1.40 1.43 1.93	 0.89 to 1.15 1.04 to 1.41 1.22 to 1.61 1.19 to 1.72 1.55 to 2.39
3a. 2a+ interaction with cognitive status			
3. Intact cognition 1 fall 2 falls 3-5 falls 6-9 falls 10+ falls	 3082 1542 1375 420 280	 0.95 1.26 1.34 1.38 2.03	 0.82 to 1.10 1.07 to 1.50 1.13 to 1.59 1.10 to 1.73 1.56 to 2.65
3a. MCI 1 fall 2 falls 3-5 falls 6-9 falls 10+ falls	 623 318 410 161 137	 1.28 1.03 1.63 1.71 1.59	 1.01 to 1.61 0.75 to 1.40 1.28 to 2.07 1.24 to 2.35 1.13 to 2.23
3a. Dementia 1 fall 2 falls 3-5 falls 6-9 falls 10+ falls	 96 51 74 41 36	 1.19 1.18 1.24 0.98 4.25	 0.64 to 2.22 0.60 to 2.35 0.69 to 2.24 0.50 to 1.93 1.94 to 9.28

*Abbreviations: NDI (Neighborhood deprivation index), *stratified*

Cox proportional hazards models assessed the association between the cumulative total number of falls during the study (categorical) and the risk of difficulty with ADLs or IADLs (Table 4). Out of 18,931 observations, 54% (10275) were for no falls, 20% (3801) were for one fall, 10% (1911) were for 2 falls, 10% (1859) were for 3-5 falls, 3% (632) were for 6-9 falls, and 2% (453)

were for 10 or more falls. The risk of difficulty with ADLs increased with each increase in number of falls category, with 1 fall associated with HR 1.14 (95% CI: 1.03 to 1.26) and 10 or more falls associated with the highest risk, HR 2.24 (95% CI: 1.89 to 2.66) in a model fully adjusted for gender, study site, study treatment, cognitive status, NDI quartile, polypharmacy, and prior hospitalization, with age as the time axis (Table 4). Falls generally were a predictor of ADL difficulty regardless of cognition status, and the interaction between cognition status and number of falls was not significant for ADLs (Wald test, p=0.31). Proportional hazards assumptions were met for models 2 and 3 and 1a through 3a, but not for model 1.

For IADLs, one fall was not associated with increased risk of difficulty, HR:1.01 (95% CI 0.89 to 1.15) but two or more falls were associated with increased risk of difficulty with that risk increasing with the number of falls, with an HR of 1.93 (95% CI: 1.55 to 2.39) for 10 or more falls in a model fully adjusted for gender, clinical site, study treatment, cognition, polypharmacy, NDI and hospitalization. The impact of falls on IADLs varied significantly by cognitive status (Wald test, p=0.01).

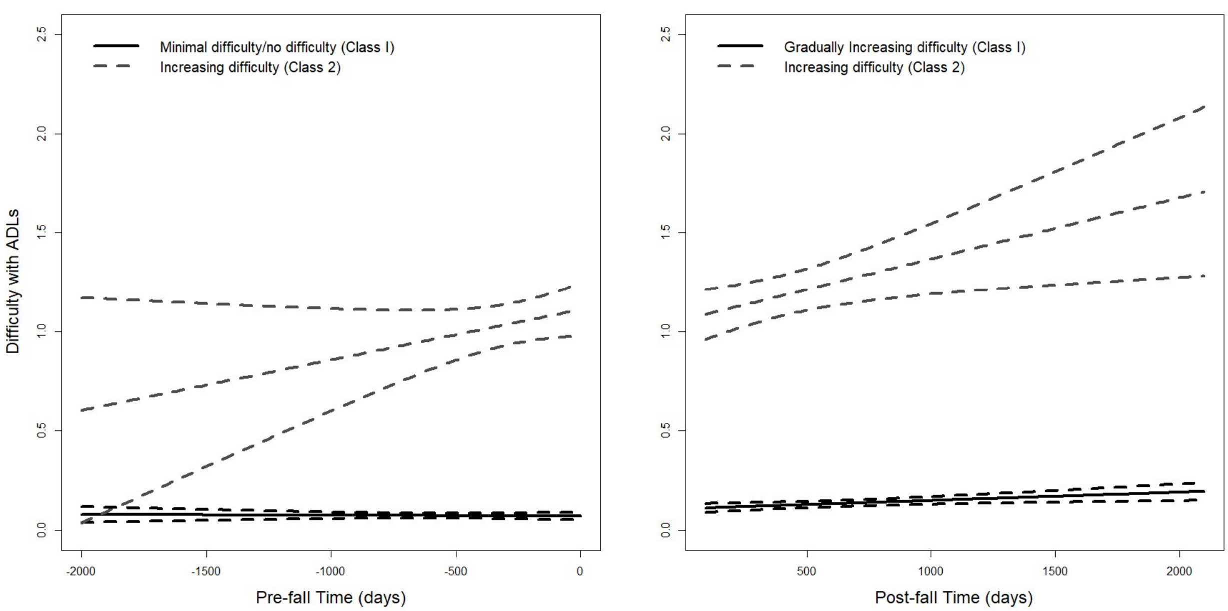
Table 5. The association between all falls and medically treated fall/falls in a 6 month fall reporting period and difficulty with ADLs or IADLs in older adults in GEMS, N=2900 and 18931 observations

Model	HR	95% CI
ADL		
1. 1 or more fall(s) in 6 months	1.19	1.09 to 1.29
2. 1 or more medically treated fall(s) in 6 months	1.15	1.01 to 1.30
IADL		
1a. 1 or more fall(s) in 6 months	1.25	1.13 to 1.38
2a. 1 or more medically treated fall(s) in 6 months	1.40	1.21 to 1.61

All models adjusted for gender, study site*, treatment (Ginkgo)*, cognitive status, polypharmacy*, NDI (Neighborhood deprivation index), and total number of falls*. *stratified

One or more falls in the 6-month fall reporting period, was significantly associated with a higher risk of ADL difficulty in a fully adjusted model for gender, study site, study treatment, cognition, polypharmacy, NDI, and stratified by total number of falls, HR 1.19 (95% CI: 1.09 to 1.29) (Table 5). The association between difficulty with ADLs and one or more medically treated falls in the 6-month reporting period was similar to that for one or more falls (HR: 1.15; 95% CI: 1.01 to 1.30) in a fully adjusted model for gender, study site, study treatment, cognition, hospitalization, polypharmacy, NDI, and stratified by total number of falls. Difficulty with IADLs were significantly associated with one or more falls HR 1.25 (95% CI: 1.13 to 1.38) and one or more medically treated falls HR 1.40 (95% CI: 1.21 to 1.61) in the six month reporting period in a fully adjusted model for gender, study site, study treatment, cognition, polypharmacy, NDI, and stratified by total number of falls (Table 5). All models met the proportional hazards assumption.

Figure 2. Plot of the latent class mean predicted trajectories for first fall and ADL score, n=1513.



Trajectory models included all participants with a fall during the study period and evaluated the relationship between a first observed fall and difficulty with I/ADLs score (Figures 2 and 3). Out of the 2141 participants who fell during the study period, the 1513 participants who had ADL and IADL scores and observations both pre-and post-fall were included in the trajectory models. Trajectory models for difficulties with ADLs pre-and post-fall included two latent classes (Figure 2). Pre-fall, 82% of participants (1235) were in class 1, described as minimal /no difficulty with ADLs, and 18% (278) were in class 2, described as increasing difficulty with ADLS. Post-fall, 82% (1244) of participants were in class one, gradually increasing difficulty with ADLs, and 18% (269) were in class two, increasing difficulty with ADLs. The mean posterior probabilities for each class were 95% for class 1 and 91% for class 2 pre-fall, and 95% for class 1 and 93% for class 2, post-fall; all meeting the criteria for class membership of >70%.[38] Pre-fall, participants in class 2 on average had difficulty with at least one out of six ADLs which could be difficulty with walking around their home, bathing or showing, using the toilet, feeding themselves, transferring in and out of a bed or chair, or dressing themselves. For participants in class 2 post-fall, they were on a trajectory to have difficulty with at least two ADLs on average.

Table 6. Participant characteristics by latent class for trajectories of difficulty with ADL pre- and post-fall (n=1513)

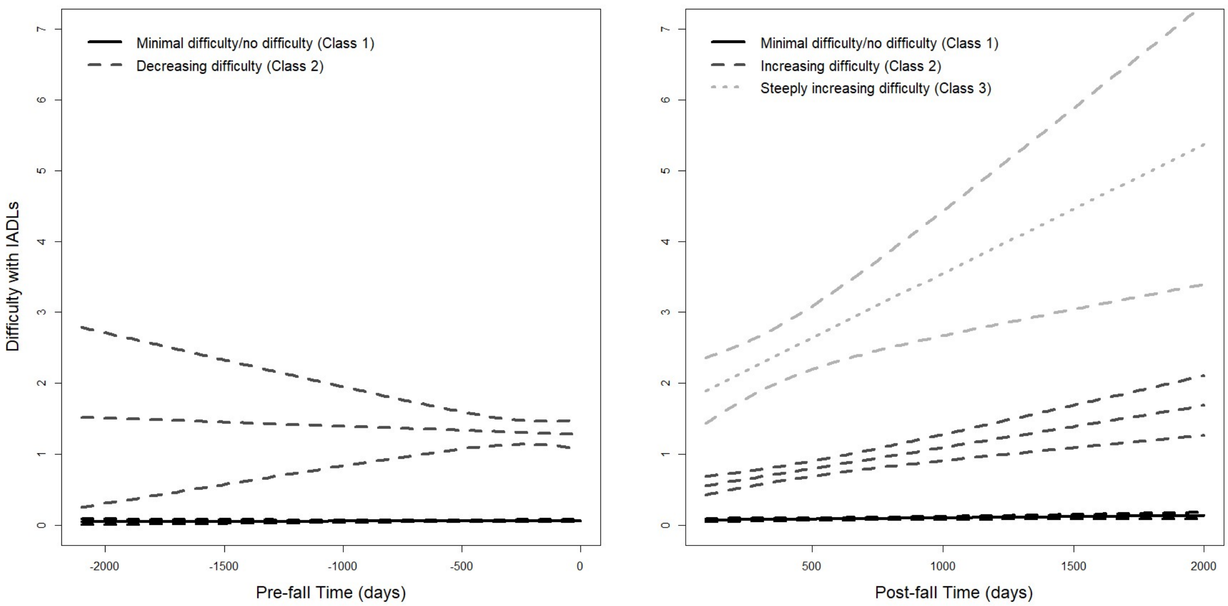
	Pre-Fall (n=1513)			**Post-Fall (n=1513)**		
Characteristic	**Class 1 (n=1235)**	**Class 2 (n=278)**	**p-value**	**Class 1 (n=1244)**	**Class 2 (n=269)**	**p-value**
Measured at Baseline						
Age	78.4 (3.2)	79.1 (3.5)	<0.01	78.4 (3.0)	79.4 (3.9)	<0.01
Gender (female)	541 (44%)	137 (49%)	0.11	520 (42%)	158 (59%)	<0.01
Treatment (Ginkgo)	621 (50%)	142 (51%)	0.86	625 (50%)	138 (51%)	0.80
Study Site			<0.01			<0.01

Forsyth County, NC	298 (24%)	54 (19%)		290 (23%)	62 (23%)	
Sacramento County, CA	356 (29%)	110 (40%)		376 (30%)	90 (34%)	
Washington County, MD	175 (14%)	63 (23%)		181 (15%)	57 (21%)	
Allegheny County, PA	406 (33%)	51 (18%)		397 (32%)	60 (22%)	
Education	14.6 (3.1)	14.3 (3.1)	0.17	14.6 (3.1)	14.2 (3.2)	0.07
Measured at max pre-fall and post-fall study visit						
Max study visit	6.7 (2.5)	6.4 (2.3)	0.02	13.1 (2.3)	12.7 (2.7)	<0.01
MCI	175 (14%)	62 (22%)	<0.01	293 (24%)	75 (28%)	0.03
NDI *			<0.01			<0.01
1	319 (26%)	46 (17%)		321 (26%)	45 (17%)	
2	326 (27%)	63 (23%)		322 (26%)	73 (27%)	
3	292 (24%)	84 (30%)		296 (24%)	68 (25%)	
4	292 (24%)	84 (30%)		299 (24%)	82 (31%)	
Any Polypharmacy	787 (64%)	202 (73%)	<0.01	781 (63%)	208 (77%)	<0.01
Any Hospitalization	734 (59%)	186 (67%)	0.03	734 (60%)	186 (69%)	<0.01
Pre-fall Class			NA			<0.01
1	1235(100%)	0 (0%)		1100 (89%)	135 (11%)	<0.01
2	0 (0%)	278(100%)	NA	144 (52%)	134 (48%)	
Total number of falls	NA	NA	NA	3.1 (5.2)	5.1 (6.9)	<0.01
Total number of fall reporting periods with falls	NA	NA	NA	2.2 (1.5)	2.9 (1.8)	<0.01
Any medically treated fall	NA	NA	NA	545 (44%)	144 (54%)	<0.01

*Missing values: NDI (7) Abbreviations: MCI (Mild cognitive Impairment), NDI (Neighborhood Deprivation Index)

For the pre-fall classes, there was a significant difference between age at baseline, study site, MCI, NDI, the maximum study visit number, any polypharmacy, and any hospitalization (Table 6). For post-fall classes, there was a significant difference in age at baseline, gender, study site, MCI, NDI, the maximum study visit number, any polypharmacy, any hospitalizations, pre-fall class, total number of falls, total number of reporting periods with a fall, and any medically treated fall.

Figure 3. Plot of the latent class mean predicted trajectories for falls and IADL score (n=1513)



For IADLs, two pre-fall trajectories were identified, class 1 (minimal difficulty/no difficulty) with 1298 (86%) participants and class 2 (decreasing difficulty) with 215 (14%) of participants and three post-fall trajectories, class 1 (minimal difficulty/no difficulty) with 1222 (81%) participants, class 2 (increasing difficulty) with 192 (13%) participants, and class 3 (steeply increasing difficulty) with 99 (7%) participants (Figure 3). Mean posterior probabilities were 97% and 96% for pre-fall class 1 and 2, respectively, and 945, 84%, and 87% for post-fall classes 1,2, and 3, respectively. Participants in pre-fall class 2 have difficulty with one to two IADLs such as difficulty with light housework and preparing meals. For participants in Class 3 post-fall, within about a year post-fall, they are on a trajectory to have difficulty with three

IADLs on average, which increases to difficulty with five out of seven IADLs on average by about 4 years post-fall.

Table 7. Participant characteristics by latent class for trajectories of difficulty with IADL pre- and post-fall (n=1513)

	Pre-Fall (n=1513)			Post-Fall (n=1513)			
Characteristic	**Class 1 (n=1298)**	**Class 2 (n=215)**	**p-value**	**Class 1 (n=1222)**	**Class 2 (n=192)**	**Class 3 (n=99)**	**p-value**
Measured at Baseline							
Age	78.4 (3.2)	79.4 (3.5)	<0.01	78.3 (3.0)	79.7 (3.6)	79.8 (4.05)	<0.01
Gender (female)	583 (45%)	95 (44%)	0.90	533 (44%)	82 (43%)	63 (64%)	<0.01
Treatment (Ginkgo)	648 (50%)	115(54%)	0.37	617 (51%)	94 (51%)	47 (48%)	0.84
Study Site			<0.01				<0.01
Forsyth County, NC	296 (23%)	56 (26%)		288 (24%)	35 (18%)	29 (29%)	
Sacramento County, CA	383 (30%)	83 (39%)		365 (30%)	71 (37%)	30 (30%)	
Washington County, MD	197 (15%)	41 (19%)		178 (15%)	43 (22%)	17 (17%)	
Allegheny County, PA	422 (33%)	35 (16%)		391 (32%)	43 (22%)	23 (23%)	
Education	14.6 (3.0)	14.3(3.7)	0.32	14.7 (3.1)	14.0 (3.2)	14.0(2.9)	<0.01
Measured at max pre-fall and post-fall study visit							
Max study visit	6.7 (2.4)	6.6 (2.6)	0.78	13.2 (2.3)	13.1 (2.3)	11.6 (3.0)	<0.01
MCI	182 (14%)	55 (26%)	<0.01	268 (22%)	60 (31%)	40 (40%)	<0.01
NDI *			<0.01				0.05
1	333 (26%)	32 (15%)		308 (25%)	40 (21%)	18 (18%)	
2	326 (25%)	63 (29%)		316 (26%)	54 (28%)	25 (25%)	
3	325 (25%)	51 (24%)		303 (25%)	42 (22%)	19 (19%)	
4	308 (24%)	68 (32%)		290 (24%)	54 (28%)	37 (37%)	
Any Polypharmacy	830 (64%)	159 (74%)	<0.01	774 (63%)	137 (71%)	78 (79%)	<0.01
Any Hospitalization	778 (60%)	142 (66%)	0.10	729 (60%)	123 (64%)	68 (69%)	0.13
Pre-fall Class			NA				<0.01

1	1298 (100%)	0 (0%)		1126(87%)	128 (10%)	44 (3%)	<0.01
2	0 (0%)	215 (100%)	NA	96 (45%)	64 (30%)	55 (26%)	
Total number of falls	NA	NA	NA	3.1 (4.9)	5.3 (9.1)	3.7 (4.2)	<0.01
Total number of fall reporting periods with falls	NA	NA	NA	2.2 (1.6)	3.0 (1.8)	2.1 (1.2)	<0.01
Any medically treated fall	NA	NA	NA	531 (44%)	102 (53%)	56 (57%)	<0.01

*Missing values: NDI (7) Abbreviations: MCI (Mild cognitive Impairment), NDI (Neighborhood Deprivation Index)

Characteristics that were significantly different between pre-fall classes for IADLs include, age at baseline, study site, MCI, NDI, the maximum study visit number, and any polypharmacy (Table 7). For post-fall trajectories, there were significant differences between age at baseline, gender, study site, education, MCI, the maximum study visit number, any polypharmacy, pre-fall class, total number of falls, total number of fall reporting periods with falls, and any medically treated fall (Table 7).

Discussion

Older adults who fall even one time, have a significant risk of difficulty with ADLs. This risk increases each time they fall, for both IADLs and ADLs. Based on trajectory modeling, about 20% of older adults (18% in class 2 for ADLS, and 20% in class 2 and 3 for IADLS) who fall have increasing difficulty with I/ADLs post-fall that not only persists over time but worsens. Having difficulty with just one ADL or IADL, such as being able to get in or out of a chair or bed or use the phone, the two most common impairments in those who fell, can greatly impact an older adult's ability to safely live independently. Difficulty with more ADLs is associated with increased risk of 1-year mortality and hospitalization.[11] These results highlight the importance of both fall prevention and intervention post-fall to mitigate declines in independent function.

The hazard ratios are similar to the odds ratios for ADL and IADL difficulty in two previous studies[13,15,19], and lower than one study[15] out of studies that found an association between any falls and difficulty with ADLs. Hazard ratios for multiple falls were similar to two other studies that found an association between multiple falls and I/ADL difficulty.[14,16] This study specifically looked at the risk of I/ADL difficulty for older adults post-fall with MCI. Participants with MCI had a significant risk of IADL difficulty after one fall, but not participants with intact cognition or dementia.

Based on trajectory models for those participants who fell, about 20% of participants had increased difficulty with I/ADLs post an initial fall with difficulties with more I/ADLs over time. A study looking at trajectories after a serious fall injury, found that 64% of participants had little to no improvement in I/ADLs 12 months post-fall injury.[18] Those results in addition to the results of this study add to the evidence that falls can have a long-lasting impact on older adult's independence. While participants with difficulties in more I/ADLs prior to a fall were more likely to have difficulties with I/ADLs, post-fall, the number of difficulties increased post-fall. Additionally, individuals with specific characteristics, such as older age, female gender, greater neighborhood deprivation, more falls, medically treated falls, and polypharmacy were more likely to have more difficulty following a fall. In the trajectory models, significantly more participants who were in the increasing difficulty post-fall trajectories, had MCI, compared to participants in the no change/ gradual increase in difficulty trajectories. The trajectory model results indicate participants with MCI were more likely to have difficulty with I/ADLs, which is similar to other findings in the literature.[24,25] The characteristics of those participants at higher risk of negative outcomes post-fall range from not-modifiable (age, gender) to more-modifiable (polypharmacy, future falls). Identifying individuals who may be more at-risk post-fall, based on these characteristics, can help medical professionals, community organizations, and public health professionals provide targeted interventions to mitigate loss of independence post-fall.

This study had multiple strengths. The study population was relatively large, and the study was longer in duration, and had more measures than other studies identified that assessed the association between falls and I/ADLs. It was the only study found to include participants with MCI and evaluate specifically if MCI modifies the impact of falls on I/ADLs. NDI was included in this study, a variable that is associated with both increased fall risk and I/ADL impairment.[34-36] The design of GEMS also allowed for the inclusion of multiple covariates of interest including polypharmacy and prior hospitalizations, both of which address the health status of participants, important risk factors for falls[1,7,40] and difficulty with I/ADLs.[41,42] The percentage of participants with difficulties with ADLs at baseline is similar to that of a large scale study done in the United States with a comparable mean age of participants.[11]

Our analysis was limited by missing data on falls, NDI, and age for time axis. The study would have benefitted from more frequent measures of falls to reduce any potential recall bias. Additionally, the frequency of measurement of MCI changed during the study period, potentially missing changes in cognitive status in the first half of the study, when it was measured only one time in about four years, compared to annually in the second half of the study.

Conclusions

We found that a single fall was associated with an increased risk of difficulty with ADLs, and multiple falls were associated with an increased risk of difficulty with IADLs. More falls were associated with a higher risk of I/ADL difficulty and participants with MCI had increased risk of difficulty with IADLs after just one fall. About 20% of participants had increasing I/ADL difficulty post a first fall that persisted and worsened over time. There are significant differences in some of the characteristics of participants who had increasing difficulty with I/ADLs. Importantly, some of these characteristics such as polypharmacy, repeated falling, and NDI are potentially modifiable or appropriate for targeted intervention. Older adults are at risk of losing independence after a fall, and it is crucial that interventions are provided to address these modifiable characteristics to prevent further difficulty with I/ADLs.

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Chapter 5: Discussion

This dissertation aimed to further understand associations between potential predictors of falls and outcomes post-fall in understudied populations, with novel measurements and methods, for utilization in improving the health and well-being of older adults at both the individual and population levels. This research focused on associations between gait speed and falls, to help determine if and under what circumstances gait speed could be used as a screening tool for fall risk. The relationship between falls and difficulty with ADLs and IADLs was assessed to better comprehend the magnitude of the risk of I/ADL impairment post-fall and its trajectory, in addition to identifying which older adults are at higher risk post-fall for ongoing and increasing difficulty with I/ADLs. Both the analyses of gait speed and fall risk, and falls and difficulty with I/ADLs, focused on older adults with MCI. Older adults with MCI have a higher fall risk[1] and a higher risk of difficulty with I/ADLs,[2,3] and are an understudied population with few specific guidelines on assessing and managing fall risk.[4,5] Given the high rates of falls among older adults,[6-8] it is imperative to identify a variety of ways to easily screen for fall risk and to understand how to better intervene, once a fall has occurred and the consequences of not doing so.

Gait Speed and Falls

We found an association between continuous gait speed and falls. This provides evidence that the relationship between gait speed and fall risk is a continuum, with each decrease in gait speed resulting in an increased risk of falls. This differs from the common practice of using gait speed thresholds to identify older adults with higher fall risk. Viewing each decline in gait speed as increasing risk of falls may help in earlier identification of people at greater risk of falling.

To further explore the relationship between gait speed and fall risk, we assessed change in gait speed and falls. Both change in gait speed and percent change in gait speed are associated with increased risk of falls. The effect size for change and percent change were similar; therefore, percent change, a more complicated calculation, does not necessarily need to be utilized, and simply change in gait speed can be used. Finding an association between change in gait speed and fall risk is significant because it potentially identifies older adults at the beginning of a trajectory of increased fall risk and allows for earlier intervention to prevent falls. These results also add to evidence that gait speed is a useful measurement to collect at an annual clinic visit or fall clinic to track changes over time. For someone starting with a faster gait speed, change in gait speed could detect increased fall risk before a gait speed threshold is reached and before a fall occurs, allowing for timely fall prevention. Identifying older adults at increased fall risk before falls occur is essential for multiple reasons, especially given the increased risk for falls with each additional fall,[9] and the risk of difficulty with I/ADLs associated with one fall and increased risk with each subsequent fall. A variety of interventions exist that successfully prevent falls, but fewer options are associated with successfully decreasing recurrent falls, once falls start.[10]

Gait speed, Falls, and Mild cognitive impairment

We hypothesized that the association between gait speed and falls would differ for people with and without MCI. The reasoning behind this was the specific risk factors associated with falls in people with MCI, such as impaired safety awareness and difficulty negotiating obstacles, and the concern that gait speed in a controlled environment may not adequately capture these risk factors.[5,11] Our results showed an association between gait speed and change in gait speed and fall risk that did not vary by cognitive status. There is emerging research on executive function and gait speed. Impairment in executive function, both a risk factor for falls[12] and one of the cognitive domains used in diagnosing MCI,[13,14] is associated with slower gait speed.[15,16] The impaired executive function that can occur in MCI may cause slowing of gait speed and therefore associated detection of increased fall risk. Several studies have found an association between MCI and slower gait speed.[17,18] While the initial hypothesis was incorrect, the positive outcome is evidence in support of using gait speed as a screening tool for people with MCI. This is important because recommendations have been made to prioritize screening for falls in people with MCI and currently there is a lack of guidelines for screening people with MCI for fall risk.[4]

Falls and Activities of Daily Living and Instrumental Activities of Daily Living

We found a significant association between falls and difficulty with I/ADLs. Experiencing just one fall was associated with increased risk of difficulty with ADLs, and two or more falls were associated with increased risk of difficulty with IADLs. We observed a dose response of higher risk of difficulty with I/ADLs with each increase in number of falls. With trajectory modeling, we found that difficulty with I/ADLs for some participants did not improve post-fall, but instead continued to worsen over time. Without intervention, a portion of older adults who fall are likely going to require assistance, modifications to their home, and/or assistive technology to live independently safely, or may need to move to a different living situation. These changes and modifications can be expensive and burdensome to the older adult who is experiencing a loss of independence.[19] Based on the results of the latent class analysis, older adults with specific characteristics, such as polypharmacy, history of hospitalizations, higher neighborhood deprivation index (NDI), and MCI are more likely to have more difficulty with I/ADLs post-fall. The results for NDI are particularly relevant when thinking about fall prevention and post-fall interventions, as older adults with higher NDI are at greater risk of poorer post-fall outcomes and may be less likely to have the economic resources to pay for the support or other accommodations required to address increasing difficulty with I/ADLs. These results make a strong case for ensuring that fall prevention programs are available in areas with higher NDI.[20]

Future Research

The current research analyzed associations between gait speed and falls. Now that this research has added to the evidence of the relationships between gait speed and falls, the next steps are using these measures to create prediction models. The approach for building prediction models differs from the approach used for understanding associations, in that it involves utilizing the covariates with the best predictive values rather than focusing on adjusting for covariates that are most likely to be confounders and that may be clinically and biologically important. The development of prediction tools will depend on metrics such as AIC/BIC and AUC and ROC. The current data from GEMS can be used to create a prediction model for gait speed and falls, and then ideally, this prediction tool would be applied to a different study population to determine its predictive capabilities. Once establishing that the prediction tool meets pre-specified standards and is useful for predicting fall risk, the prediction tool can be used in a pilot study to test it in clinical practice alongside other fall screening procedures. The purpose of the pilot testing is to determine feasibility and accuracy in a real-world setting, before using gait speed to screen for falls in a larger study population. Using gait speed has the potential to increase screening for fall risk in older adults with the purpose of connecting those with higher fall risk is to evidence-based fall prevention programs.[10,21]

In the analysis of falls and difficulties with I/ADLs, several characteristics associated with trajectories with increasing difficulty stood out as being potentially modifiable. Some of these potentially modifiable risk factors also have a well-established association with fall risk, and are addressed by fall screening tools and prevention programs. Examples of these factors included previous falls/ multiple falls and polypharmacy/ medications use.[6,9,10,22,23] One risk factor which stood out both as being understudied, and appropriate for public health intervention is higher NDI.[20] Determining the availability of fall prevention programs in areas with higher NDI is a subject for further research, as there is limited literature on this topic.[24,25] Additional research would address the impact of fall intervention programs in areas with high NDI on reducing falls and difficulty with I/ADLs post-fall. A pilot study investigating the impact of providing low cost/ no cost I/ADL support post-fall, such as caregiving, home modifications, and/or assistive technology would provide evidence as to whether trajectories of increasing difficulty with I/ADLs could be stabilized or reversed with additional support post-fall. Given the significant difference between study site and post-fall trajectories, and diversity in study sites both in terms of NDI and rurality, access to and the impact of fall prevention programs in rural areas is also an essential area of future research. The limited research on fall prevention in rural areas indicates a need for more access to fall prevention programs outside of metropolitan areas.[26]

Conclusions

Fall prevention is an ongoing and increasing challenge in public health.[27] The results of this research provide further evidence that intervention needs to occur both pre- and post- fall to reduce negative health impacts for older adults. We found significant associations between gait speed and change in gait speed and falls for adults both with and without MCI, and between falls and difficulty with I/ADLs. Our research has added support for the use of gait speed as a potential screening tool and furthered understanding of outcomes for older adults who fall, while providing the groundwork for future research to develop prediction tools and improve health post-fall.

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