

Estimating Falls Risk from the Association between Gait Velocity and Cognitive Task
Performance under Dual Tasking

by

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B.Sc. University of Tehran, 2015
M.Sc. Science and Research University , 2019

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of
Master of Science

In the

School of Exercise Science, Physical and Health Education

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University of Victoria

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Estimating Fall Risk from a Combination of Gait and Cognition Metrics

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Supervisory Committee

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Abstract

BACKGROUND: Age-related deterioration in the nervous system results in the decline of motor and cognitive abilities, which both have been identified as contributing to fall risk in older adults. Dual-task gait, which involves walking while performing a secondary cognitive task, is a common way to assess the interactions between cognitive and motor function. Previous work has established associations between the cost of the cognitive load on gait parameters (e.g., velocity) and fall risk in older adults. However, to date, no study has explored the potential value of combining a direct measure of performance on the cognitive component of the dual-task with the gait measures in fall risk prediction modeling.

RESEARCH QUESTIONS: Does including measures of performance on the cognitive task in dual-task walking with the gait velocity measures enhance the capacity to predict fall risk. Is this predictive capacity different in models employing dual-task gait velocity versus models including the cost of the cognitive load on gait velocity?

METHODS: Thirty-two community-dwelling older adults (76 years \pm 3.44) were classified as fallers (n = 17) and non-fallers (n = 15) based on self-report of having at least one fall in the past 12 months. They completed single-task and dual-task walking on a pressure-sensing electronic walkway system. A progressively enhanced series of logistic regression models were performed commencing with gait velocity during the dual-task (Loaded Gait Velocity, LGV) as the covariate in predicting fall risk. This model was subsequently augmented by adding a measure of cognitive performance covariate and then further augmented with the addition of the interaction variable

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between the LGV and the cognitive performance variables. This stepped series of modelling was then repeated with the dual-task cost gait velocity (DTC_{GV} , difference in gait velocity between single and dual-task).

RESULTS: With the addition of the cognitive measures (CM) and the interaction variables between the GV and CM variables, in both the LGV and DTC_{GV} models, the Nagelkerke's R square increased as did the models' respective sensitivity. Notably, the model including the LGV, CM and the interaction variables achieved 88.2% sensitivity, 80% specificity, with an overall classification accuracy of 84.4%.

DISCUSSION: This study is the first to show that the ability to identify fallers and non-fallers is enhanced by using both gait and cognition measures as well as interaction variables between gait and cognition measures. Further, our findings suggest that the added value of the cognitive measures is best realized with LGV rather than DTC_{GV} . It reasons that because DTC already encompasses the cost of the cognitive load on the motor performance (gait velocity), combining it with cognitive metrics does not enhance its predictive capacity. This work suggests there is clinical utility of including cognitive performance measures in fall risk modeling as well as it provides further evidence of the interplay between cognitive and motor function in fall risk.

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List of Abbreviations

AD - Alzheimer's Disease

AAI - Attention Allocation Index

CM - Cognitive Measures

CNS - Central Nervous System

CV - Coefficient of Variation

DS - Difference Scores

DT - Dual Task

DTC - Dual Task Cost

DTC_{GV} - Dual Task Cost on Gait Velocity

DTE - Dual Task Effect

GV - Gait Velocity

LGV - Loaded Gait Velocity

MCI - Mild Cognitive Impairment

MMSE - Mini Mental State Examination

MoCA - Montreal Cognitive Assessment Scale

NC - Number of Counts

PAR-Q - Physical Activity Readiness Questionnaire

PD - Parkinson's Disease

POC - Performance-resource operating characteristic

PTC - Percentage of True Counts

ST - Single task

ULGV - Unloaded Gait Velocity

Acknowledgments

I would like to thank my patient and supportive supervisors, Dr. Sandra Hundza and Dr. Marc Klimstra, for helping with this research project. Dear Sandra, I appreciate your kindness and your dedication to show me the highest values of humanity. Dear Marc, I learned from you that responsibly facing challenges is the way to grow. I am so glad I have got to know you both.

I would also like to thank Catherine Depond for her motherly love and support.

Dedication

I want to dedicate this thesis work to my partner, Arvin, who has been a constant source of encouragement.

Chapter 1: Introduction

1.1 General Statement of the Problem

There will be continued growth in the proportion of older adults within the Canadian population over the next 2 decades (National Advisory Council on Aging, 1999). Aging is often accompanied by a decline in mobility and cognitive function, which are consequences of the age-related changes in the nervous system. The nervous system changes include, for example, the loss in volume of gray matter and changes in quality and quantity of white matter in specific brain regions, an associated reduced number of neurons and neural connections and decreased neurotransmitters (Rosano et al., 2005; Howieson et al., 1998), declines in neuromuscular function (Doherty, 2003) and increase in sarcopenia (the loss of muscle mass and strength, and reduction in muscle contraction speed that result in less power of lower limb). Age-related changes in the central nervous system (CNS) also result in a reduced ability to process and integrate multiple sensory inputs which results in impaired balance, increased postural sway, and slower walking speed (Zecevic et al., 2006). These changes are considered as main factors that contribute to reduced mobility and fall risk in older adults (M. Montero-Odasso et al., 2015). As people age, the relationship between mobility and cognitive decline grows (Montero-Odasso et al., 2006); such that lower gait velocity and cognitive impairment often co-occur in the same elderly individual (Rosano et al., 2005; Allan et al., 2005) and this co-occurrence contributes to the increased falls risk in this group (Tinetti et al., 1988).

A fall is commonly defined in the literature as “inadvertently coming to rest on the ground, floor or other lower level, excluding intentional change in position to rest in furniture, wall or other objects” (Unit & Clinical, 2007). It is estimated that one-third of the community-dwelling older

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adults (aged 65 years and over) experience at least 1 fall every year (Public Health Agency of Canada, 2014), making falls the most common cause of injury among older adults (Tinetti, 2003). Falls often result in serious consequences, including head injuries, bone fractures (e.g., hip fractures), hospitalization (Public Health Agency of Canada, 2014), admission to a nursing home, chronic pain, reduced quality of life, and increased risk of death (Canadian Institute for Health Information; Stel et al., 2004). About 25% of older people who endure a hip fracture, for example, from a fall, pass away within a year of the fall-related injury (Cho et al., 2016). Falls in older adults also result in significant financial costs to the individuals and the healthcare systems (Public Health Agency of Canada, 2014).

Identifying those at risk of falls is of critical importance and fall risk assessment often includes evaluating walking while executing a secondary task (i.e., dual-task) to investigate cognition and gait interactions. “Stop Walking While Talking” was a primary study that revealed that the inability to continue a conversation during walking could be considered as a sign of future falls in elderly individuals (Lundin-Olsson et al., 1975). Alterations in gait function are magnified under dual-task in older adults (Yogev-Seligmann et al., 2008). When doing both motor and cognitive tasks simultaneously, there appears to be interference and competing demands on reduced shared neural resources (Ivanoff, 2005; Yogev-Seligmann et al., 2008). Previous studies defined the effect of dual-task testing on gait performance, demonstrating associations between reducing gait speed and executive dysfunction. Dual-task assessments play a unique role in revealing the brain’s capacity to share resources between walking and an attention demanding task (Muir et al., 2012); this has the potential for clinicians and researchers to identify those who are at higher falls risk and onset of dementia, allowing for the provision of timely interventions. Yamada et al. predicted that if the difference in performance between single task and dual-task (dual-task

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cost or difference scores) was more than 18%, the person is at risk of falls. Additionally, the onset of gait pattern changes may present up to 10 years before the clinical presentation of cognitive decline in older adults that later convert to MCI (Chou et al., 2019). Very few studies have investigated cognitive metrics, and those that used only the cognitive task as their outcome measure and did not include the impact of cognitive load on the motor task (Olivier Beauchet et al., 2007). For example, Beauchet and colleagues evaluated only the rate of backward counting while walking and its association with fall risk. To date, dual-task gait fall risk assessments have not incorporated both the performance on both the gait and cognitive tasks in determining fall risk. Therefore, their combined predictive value in determining fall risk has not yet been evaluated.

1.2 Significance

This study proposed to determine if combining performance on the cognitive component of the dual-task along with traditional gait metrics (e.g., gait velocity) would enhance the sensitivity and specificity in identifying fallers. This research has the potential to improve the capacity to more accurately identify those at risk of falls as well as monitor change in fall risk status, both of which could facilitate timelier, targeted interventions to decelerate decline, prevent falls and mitigate the potential associated negative health and societal outcomes.

1.3 Research Questions

Does combining performance on the cognitive component of the dual-task along with traditional gait velocity metrics (i.e., either dual-task gait velocity or dual-task cost on gait velocity) enhance the classification of fall risk?

1.4 Limitations

The power of this study is limited by its sample size, 32 older adults. However, this sample size is consistent with previous similar older adult studies (Filar-Mierzwa et al., 2017; Wrisley & Kumar, 2010; Josephs et al., 2016; Keskin et al., 2008). The sample includes volunteers from community-dwelling older adults (i.e., age greater than 70 years) who live in Victoria, British Columbia, Canada. So, the results should not be generalized to populations from other regions of Canada or the world or other age groups. The study was further limited because it examined the potential capacity of only one gait metric (gait velocity) and the combinations of that with cognition metrics; thus, this work should not be regarded as an exhaustive study of the possible gait and cognitive metrics that could measure falls risk.

Chapter 2: Literature Review

2.1 Significance of Falls

Falling, one of the geriatric syndromes, affects about one-third of older adults per year (Tinetti, 2003). Major falls are associated with head injuries, bone fractures, and deaths (Tinetti, 2003). In Canada, between 2008 to 2009, over 73,000 injury-related hospitalizations are recorded to be from adults (over 65) falling (Stinchcombe et al., 2014). More than 90% of hip fractures arise from falls (Goldacre et al., 2002). About one-fourth of older adults who sustained a hip fracture die within six months after the falling incidence (Abdelhafiz & Austin, 2003), and near one-fourth of the survivors discharge to a nursing home, often staying for more than a year or even for the rest of their lives (March et al., 1999). Life expectancy in hip fracture survivors is up to 15 years less than the same-aged people (von Friesendorff et al., 2016). Hence, although all fallings in older adults do not end their lives, it often results in a meaningful decline in their overall quality of life. For example, overcautious fear of future falls, known as post-fall anxiety syndrome, could be one of these non-fatal consequences of falling. This syndrome increases self-restriction of activities and leads older adults to become more dependent and immobile (March et al., 1999) and further augments fall risk (Bloch et al., 2014). Additionally, the medical expenses associated with falls in older adults are substantial, with high costs for both the patients and healthcare systems (Public Health Agency of Canada, 2014).

2.2 Fall Risk Factors in Older Adults

Due to the high worldwide prevalence of falling, in the last two decades more researchers have focused on fall prevention strategies, which has included identifying fall risk factors (Stewart

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Williams et al., 2015). In assessments of fall risk factors, a fall is defined as “inadvertently coming to rest on the ground, floor or other lower level, excluding intentional change in position to rest in furniture, wall or other objects” (Unit & Clinical, 2007). Falls can result from multiple factors. The level of physical activity (O. Beauchet et al., 2009), the number of medications (specifically psychoactive drugs such as benzodiazepines, antidepressants, or neuroleptics) (Taylor et al., 2014; Allali et al., 2017; Winblad et al., 2004; Launay et al., 2013) sleep problems (Brassington et al., 2000), autonomic dysfunction (Allan et al., 2007), poor vision (Callisaya et al., 2014), anxiety, depression (Taylor et al., 2014), dangerous behaviors, lower muscle strength (Avlund et al., 1994), impaired balance, mobility and cognitive decline (e.g., memory, attention), and other comorbidities (e.g., neurosensory and neuro-motor changes) are all examples of fall risk factors. The strongest indicator of risk of future falls is the existence of a history of falls (Hollman et al., 2007). Cognitive decline and gait dysfunction are often used as predictors of fall risk; accordingly, both will be reviewed in more depth below as fall risk indicators.

2.3 Cognitive Impairment

Cognition is a complicated concept that includes several domains. Mild to advanced cognitive impairment is evident in more than one-fifth of older adults over 85 years old (Lopez et al., 2003). Cognitive decline or dementia could be an independent risk factor for falling (Van Iersel et al., 2004). The falling rate is between twofold and threefold among older adults with dementia, compared to their cognitively intact peers (Shaw, 2002). Measurements of health care costs have shown that cognitively impaired fallers are more likely to need institutional care, resulting in higher health care expenses for this group (Public Health Agency of Canada, 2014).

Formerly, scholars studied falls and dementia independently, which might explain the gap in our knowledge about the cognition-motor interactions and their influences on falls (M. Montero-Odasso & Speechley, 2018). They focused on the influence of gait function on fall risk, focusing less on cognitive decline (Muir et al., 2012). As a result, cognition has gained lower attention in fall prevention plans. In 1978 Bernard Isaacs stated that this could be a shallow judgment to attribute falls in older adults only to muscular or articular impairments and their effects on walking and balance. Rather, our central neural systems function is responsible primarily for falls in older individuals (Isaacs, 1978; Montero-Odasso et al., 2015). After the publication of Bernard Isaacs innovative article, the relationship between cognitive impairment and falls risk was further supported by subsequent studies (Muir et al., 2012), which have provided evidence that falls and cognitive impairment are interdependent in older adults (Muir et al., 2012). When eventually researchers started to investigate falls risk factors in older adults suffering from cognitive decline (Salvà et al., 2012) Allan et al., 2009), they did not distinguish the levels of cognitive capacity (Horikawa et al., 2005) in their subjects. Mild cognitive impairment (MCI) sits on the continuum between cognitively healthy aging and early dementia (R. C. Petersen, 2004). Petersen (Petersen, 1999) states that MCI is a status in which people complain about their memory while showing no mobility disorder in their daily life. Cognitive capacity drops between 6% to 10% annually among MCI patients, while it is 1% or 2% in cognitively healthy older adults (Lehrner et al., 2005). With the progression of MCI, individuals gradually develop other dementias like Alzheimer's Disease (AD) (R. C. Petersen, 2004). The risk of developing AD among MCI patients is 10 to 15 times more than healthy older adults (Ronald C. Petersen et al., 2001). In a study in 2017, it was found that falls prevalence is 50% in AD patients, 64% in non-AD cognitively impaired patients, and 25% in cognitively healthy older adults (Allali et al., 2017).

A deeper investigation into the reasons that cognitive impairment increases the risk of falling, shows that most of the risk factors are associated with aging and are often accompanied by changes in the nervous system (M. Montero-Odasso et al., 2015). These changes include reductions in grey matter volume (Resnick et al., 2003) and in quality and quantity of white matter, associated in part with a reduced number of neurons and neural connections and decreased neurotransmitters (Howieson et al., 1998; Rosano et al., 2005; Seidler et al., 2010). Some brain regions, such as temporal areas and the entorhinal cortices, are more vulnerable in AD individuals (Sakurai et al., 2019). Progression in the deterioration of white matter in diseases like AD, Parkinson's Disease (PD), and the subcortical infarcts, which are conditions where cognition is often impaired, have shown links to increase risk of falling (Callisaya et al., 2014, 2015). In order to identify which regional brain volumes are impacted in cognitively impaired patients, Sakurai and Montero-Odasso et al. used 3T magnetic resonance imaging (Sakurai et al., 2019). They found that volume reduction in the left entorhinal cortex is independently associated with differences in walking patterns between single-task of only walking and dual-tasks of walking while doing a cognitive task.

Oral interviews and specific tests have been used to help define the severity of cognitive impairment in older adults. One of these tests is Mini-Mental State Examination (MMSE) (Allali et al., 2017), scaled between 0 to 30. It is reported that the cut-off of 24 represents MCI (Enzensberger et al., 1997). In MCI subjects with a higher level of education, MMSE score is reported 26 (Gillain et al., 2009). In mild dementia (mild stage of AD) MMSE score in all the patients is 20 or more (Susan W Muir et al., 2012). In the studies that reported MMSE scores for cognitively healthy participants, this score was (28.8 ± 1.1) (Gillain et al., 2009; Lee & Park, 2018; Susan W Muir et al., 2012). Montreal Cognitive Assessment Scale (MoCA) is another test that is

also scaled between 0 to 30; similar to MMSE, a higher MoCA score indicates better performance. MoCA is a valid tool that helps clinicians diagnose MCI in older adults (Nasreddine et al., 2005; M. Montero-Odasso, Casas, et al., 2009). If a participant gets a score less than 26 in MoCA, but more than 26 in MMSE, they will be categorized under the MCI group (Nasreddine et al., 2005).

2.4 Gait and Cognitive Impairment in Older Adults

Changes in the walking paradigm (or gait dynamics) are among the most common causes of falls (McCrum et al., 2017). Normal and rhythmic gait depends on many components such as joints mobility (particularly in the lower body), muscle activation timing and forces, sensory inputs (e.g., normal vision), and vestibular system's condition (Nutt et al., 1993). For some time, it was considered that walking was merely an automatic motor task. This view was rejected due to its inconsistency with the practical evidence (Simon & Giladi, 2005); cognitive status also affects posture and gait stability (Woollacott & Shumway-cook, 2002). Both motor and cognitive capability are required for normal walking. In general, motor tasks correspondingly require additional cognitive resources and the motor and cognitive demands are reliant on specific and many shared cortical areas (Li & Lindenberger, 2002). Simultaneously performing cognitive and motor tasks engage lateral frontal cortices, which overlap with other regions such as the ventrolateral and dorsolateral prefrontal cortices and premotor cortices (Annweiler et al., 2013; Holtzer et al., 2011; Mirelman et al., 2014). The brain's capacity to process information becomes restricted with age, so the two tasks that are being performed at the same time interfere and compete for reduced neural resources resulting in postural instability, balance problems, slower walking speed, and eventually increased fall risk (Van Iersel et al., 2004; Yogev-Seligmann et al., 2008). Accordingly, deficits in attention or motor function are independently associated with the

risk of falling (Simon & Giladi, 2005; M. Montero-Odasso et al., 2012). When the person is walking, they need to pay attention to the environment. They also need to avoid postural perturbations that would lead to slide or fall (Yogev-Seligmann et al., 2008). Moreover, dual-tasking, such as walking while thinking, is a common behavior among human beings. That is why older people may stop walking when confronted with an attention-demanding cognitive task such as calculating (Allali et al., 2017). As people age, the relationship between mobility and cognitive impairment is found to be increased (Montero-Odasso et al., 2006). In an experiment, swing time variability increased in older people when walking while performing an attention-demanding cognitive task but did not change in younger adults (Springer et al., 2006). Lower gait velocity has been demonstrated to be an applicable preclinical marker of new falls (M. Montero-Odasso et al., 2005). Deficiencies in specific cognitive domains are associated with slow gait velocity. This fact indicates that maintaining normal gait performance depends on those specific cognitive domains (Montero-Odasso, Casas, et al., 2009; Montero-Odasso, Bergman, et al., 2009).

To investigate the interactions between cognition, gait, and falls risk, researchers observe individuals walking while executing a secondary task that requires attention, a dual-task. They assess modifications in subjects walking while performing the dual-task from the reference conditions when they were only doing the single motor task (e.g., walking) (Woollacott & Shumway-cook, 2002). Primary research showed that one of the markers of future fallers is that the subjects at higher risk of falls could be disturbed easily and cannot hold their conversations while walking (Lundin-Olsson et al., 1975). During gait assessments, researchers identify gait changes under cognitive load called the “dual-task cost” or “difference scores” such as decreasing walking speed (M. Montero-Odasso, Bergman, et al., 2009; M. Montero-Odasso et al., 2012). These gait changes reveal subtle brain impairment (M. Montero-Odasso, Bergman, et al., 2009).

They are related to the increased engagement in cortical attention processes while walking (M. Montero-Odasso et al., 2012). Older adults who show greater dual-task costs during gait evaluations are at higher risk of falling (O. Beauchet et al., 2009). Likewise, AD and PD patients also show higher dual-task costs (Sheridan et al., 2003) and are at higher risk of falls. A better understanding of the relations between early gait disturbance during a dual walking task and early cognitive decline or dementia using quantitative changes in gait parameters such as reduction in gait velocity and stride length among older adults may improve the identification of those at risk of falls (M. Montero-Odasso et al., 2012; Yamada et al., 2011).

A benefit of dual-task assessments is that the brain's capacity to share cognitive resources between motor task and an attention-demanding task gets revealed (Muir et al., 2012), allowing timely identification of people who are at higher falls risk to facilitate early targeted interventions which may decelerate the progression of dementia and decrease fall risk. In a longitudinal study of 1038 individuals who had relatively intact gait, Yamada et al. showed that if the dual-task cost in walking gait velocity was more than 18%, they are at a higher risk of falls than others whose dual-task costs were less than this number (Yamada et al., 2011). In addition to fall risk, the dual-task paradigm could be a potential clinical motor marker for early detection of older adults with MCI at higher risk of progression (M. M. Montero-Odasso et al., 2017). For example, early mobility decline in older adults was found to precede the onset of clinically confirmed cognitive deterioration (Van Iersel et al., 2004).

2.5 Gait Parameters used in Dual-Task Assessments

Gait is a complicated neuro-motor task that has many measurable parameters that could be measured stride-to-stride or over time (Hausdorff, 2007). These parameters are classified into

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spatial and temporal groups (Hamacher et al., 2011). Spatial parameters are generally any parameters that can be defined as a distance covered between two steps or strides (Bertoli et al., 2018). Commonly used spatial parameters are: stride length, step length, and step width in dual-task investigations. Commonly used temporal parameters are: stride time, step time, stance time, swing time, and double support time (Bertoli et al., 2018). Gait measures also could be combinations of different spatial and temporal parameters and as a result are highly correlated to their component parameters. For example, gait velocity is correlated to stride length. Studying gait parameters gives insight into the integrity of the neuro-motor system (Maki, 1997; Hamacher et al., 2011). As noted, one of the indicators for fall risk is changes in walking gait dynamics. For instance, reduction in gait velocity is associated with functional loss, as noted in numerous studies (Abellan Van Kan et al., 2009). A two-year prospective study showed that gait velocity could predict falls in older adults (Herman et al., 2010). Also, slower gait velocity (Howieson et al., 1998) and increased stance time (Hsieh & Cho, 2012) are reported to be associated with faster development of cognitive decline and dementia in older adults. After gait velocity, step or stride regularity, coefficient of variation of stride time, and coefficient of variation of step length are among the most commonly used measures. The coefficient of variation is calculated as $CV = ([\text{standard deviation of the parameter} / \text{mean value of the parameter}] \times 100)$. Hausdorff et al., 2001 found that one of the strong markers for fall risk is the increased gait variability while performing dual-task. Modarresi et al., 2019 explored gait characteristics associated with falls in dementia, including AD. Their findings showed that step length variability is a parameter that is associated with recurring falls in older adults with dementia. Another parameter that can potentially provide the predictive utility of fall risk is step width (Smith et al., 2017). Though, this parameter is not easy to measure in comparison to the parameters such as step length (Sanchez et al., 2019).

Although gait characteristics could represent cognition and motor integration and fall risk, this is not true for all gait measures. Some gait measures such as mean values of swing time and single support time are not reported to be different between fallers and non-fallers (Allali et al., 2017). Gait parameters can be related to demographic parameters; for example, gait velocity and stride length are gender-dependent and greater in men (Inoue et al., 2017).

Gait parameters can be collected utilizing an electronic walkway system, GAITRite. The data obtained from this system has high concurrent validity for both spatial and temporal gait parameters. For most of the parameters that this system can measure, correlation coefficients exceed 0.93 (McDonough et al., 2001). This system is highly test-retest reliable. For parameters such as gait velocity, cadence, stride length, and single and double support times, reliability coefficients exceed 0.85 (McDonough et al., 2001). Footswitch sensors (Bahureksa et al., 2016), Locomotrix (Centaure Metrix, Evry, Essonne, France) (Gillain et al., 2009), DynaPort MiniMod (McRoberts BV, The Hague, The Netherlands), motion capture cameras, and other movement tracking devices (Lee & Park, 2018) could also be used to collect gait parameters.

2.6 Dual Tasks Assessments

As mentioned before, when someone performs a dual-task, the demands on their central nervous system increases because both the cognitive and motor task require neural processing (Markman & Brendl, 2005). The change in cognitive demands with dual tasking depends on the dual-task's type and its level of complexity. Some researchers investigated the effect of the type and complexity of the cognitive component of the dual-task on gait characteristics. They compared the effects of two or more different cognitive tasks on specific gait parameters, as well as assessing

the dual-tasks costs to the gait parameters under each cognition test (M. Montero-Odasso et al., 2012).

Dual-task taxonomies are guidelines that help to choose the most appropriate cognitive test relative to the research question and the regions of the brain of interest. The cognitive tasks are clustered into four main groups: mental tracking, verbal fluency, working memory, and verbal memory (Al-Yahya et al., 2011). Mental tracking tasks refer to tasks that require holding information in the mind while performing a mental process (Lezak et. al., 2004). For testing mental tracking, backward counting from 30 to 378 by ones to sevens is the most commonly used task (Olivier Beauchet et al., 2011, 2014; Gschwind et al., 2017; Martínez-Ramírez et al., 2016). However, although backward counting is categorized as a mental tracking challenge in some studies (Lezak, M.D. et al., Neuropsychological assessment. 2004: Oxford University Press, USA), this task is also categorized as a working memory challenge (Hunter et al., 2018). Working memory refers to a task of holding information mentally for later processing. In verbal fluency, naming animals is the most commonly used task (Gschwind et al., 2017; Martínez-Ramírez et al., 2016), and in verbal memory, short story recall was one of the cognitive tasks that were used (Bahureksa et al., 2016).

In 2015 a review of the literature on interferences between cognitive and motor tasks, McIsaac et al. built a framework for dual-tasks (McIsaac et al., 2015) based on the performance measurement methods. Performance-resource operating characteristic (POC) known as between task trade-off, attention allocation index (AAI), known as within task trade-off, and dual-task effect (DTE) were their measurement methods. Their taxonomy assisted in determining the level of task complexity. Simple tasks included single motor tasks such as drinking a cup of water, single cognitive tasks such as reciting the alphabet, dual motor-motor tasks such as drinking a cup of

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water while writing a note with the other hand, and dual motor-cognitive tasks such as quickly pointing to a target while counting to 100. Hard tasks included single motor tasks such as walking with forearm crutches, single cognitive tasks such as paced auditory serial addition task, dual motor-motor tasks such as cycling on a college campus while juggling, and dual motor-cognitive tasks such as juggling while subtracting serial 7s.

Based on a systemic literature review of dual-task costs when the motor task was walking, Wollesen et al. tried to build another “taxonomy of cognitive tasks to evaluate cognitive-motor interference on spatiotemporal gait parameters in older people” (Wollesen et al., 2019) including adults with a minimum age of 60. Because of the large diversity in types of cognitive tasks and gait parameters (gait velocity, step length, cadence, stride length, etc.) among papers, they could not conclude which clinical test was the most appropriate for detecting the interference between cognition and the motor task of walking.

Using the same cognitive tasks, some researchers investigated the effects of dual-tasking on patients suffering from a specific cognitive impairment such as MCI or AD (Bahureksa et al., 2016; Gillain et al., 2009). They compared the results of their tests between different groups. One of the findings was that under dual-tasking, cognitively healthy older adults prioritize cognitive tasks over motor tasks (Corp et al., 2018). “Cognition-first” (Corp et al., 2018) is a pattern that is also seen in cognitively impaired older adults (Lee & Park, 2018). Prioritization of cognition over gait in dual-tasking justifies the high risk of falls in elderly individuals.

Chapter 3: Manuscript

3.1 Introduction

The most common causes of injury among older adults are falls (Tinetti, 2003). Every year, it is estimated 1 in 3 community-dwelling older adults (aged 65 years and over) experience at least one fall (Public Health Agency of Canada, 2014) often resulting in serious injury, hospitalization (Public Health Agency of Canada, 2014), admission to a nursing home, reduced quality of life, and increased risk of death (Canadian Institute for Health Information, 2010; Stel et al., 2004). About 25 percent of older people who sustain a hip fracture, for example, from a fall, pass away within a year of the fall-related injury (Cho et al., 2016). Falls in older adults also result in significant financial costs to the individuals and the healthcare systems (Public Health Agency of Canada, 2014).

The cause of falls is generally multifactorial in nature, involving mobility and cognitive decline (e.g., memory, attention), impaired balance, dizziness, polypharmacy (Rubenstein, 2006), visual disorders, depression, and anxiety (Taylor et al., 2014). The concomitant decline in mobility, balance, and cognitive function is associated with the age-related deterioration in sensori-motor-cognitive systems leading to increased fall risk (Gardner et al., 2016). More specifically, these nervous system changes include for example, the loss in volume of gray matter and changes in quality and quantity of white matter in several brain regions, associated in part with a reduced number of neurons and neural connections and decreased neurotransmitters (Seidler et al., 2010). Frontal are reported to be the regions involved when young adults performed a cognitive task while doing a motor task (Mirelman et al., 2014). Evidence suggests that motor control is more attentionally demanding for older adults, requiring additional cognitive resources and increasing

the codependence on certain cortical areas (Li & Lindenberger, 2002). As a result, when doing both motor and cognitive tasks simultaneously, in older adults there appears to be interference and competing demands on reduced shared neural resources (Ivanoff, 2005; Yogev-Seligmann et al., 2008). Sakurai and colleagues (2019) found that left entorhinal cortex volume reduction is independently associated with differences in gait patterns between only walking (Single-task, ST) walking while doing an attentional, cognitive task (Dual-task, DT) in older adults with MCI. In older adults, alterations in gait function are magnified under DT conditions when compared to young adults (Yogev-Seligmann et al., 2008). Thus, dual-task assessments play a unique role in revealing the nervous system's capacity to share resources between walking and an attention-demanding task (Muir et al., 2012); this has the potential for clinicians and researchers to identify those who are at higher falls risk.

To date, most studies employing dual-task gait assessments to determine fall risk have evaluated the impact of the cognitive task on the gait performance. Yamada et al. predicted that if the difference in performance between the ST and DT was more than 18%, the person is at risk of falls. Our previous work showed that difference in performance between the ST and DT for stride length, width, and time as well as variability stride width and velocity, were key indicators of fall history (Commandeur et al., 2018). Limited dual-task gait assessments studies have evaluated performance on the cognitive task and these studies did not include gait performance (Olivier Beauchet et al., 2007). For example, Beauchet and colleagues evaluated the speed of backward counting while walking and its association with fall risk, but did not include gait performance metrics (Olivier Beauchet et al., 2007).

The potential predictive value of including the performance on both the cognitive and gait tasks during a dual-task gait assessment in identifying fall risk has not yet been evaluated. To that

end, this study proposed to determine if combining performance on the cognitive component with the gait velocity in dual-task walking enhances the identification of fall risk in models including dual-task gait velocity as well as models including the cost of the cognitive load on gait velocity.

3.2 Methods

3.2.1 Participants

Thirty-four community-dwelling older adults volunteered to participate in this study. The participants were interviewed and classified into 2 groups of fallers ($n = 17$) and non-fallers ($n = 17$) based on a self-report of falling in the past 12 months. Inclusion criteria contained a score of 24 or above on the Mini-Mental Status Examination (MMSE) (Enzensberger et al., 1997), fluency in English speaking, and independent walking ability. The exclusion criteria contained a diagnosis of dementia, recent major illnesses, or a history of a metabolic, cardiovascular, musculoskeletal, neurological or sensory impairments that may impact their ability for full participation. Participants were screened with the Physical Activity Readiness Questionnaire (PAR-Q); physician approval was obtained if the subjects answered 'yes' to any of the questions. All participants provided written informed consent, and the study was conducted in accordance University of Victoria Human Research Ethics Board.

3.2.2 Protocol

Participants performed 20 walking passes (i.e., there and back 10 times) at a self-selected normal walking speed along 6.4 meters instrumented electronic walkway system GAITRite® (CIR Systems INC, Sparta, NJ) using a sampling rate of 120 Hz. To avoid the impact of acceleration and deceleration on GV, participants walked 1.5 m prior to and 1.5 m beyond the end of the mat.

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Ten of the passes were STs with no cognitive load, while the other 10 passes were DT where the participants counted backward aloud, subtracting serial 7s from a randomly-generated 3-digit number between 300 to 599. The initial randomized number was given to the participants by the examiner. The participants were asked to concentrate on accurately subtracting serial 7's throughout the time they were walking. The order of the conditions was randomized, and the examiners were blinded to the participants' fall history. Counting backward by serial 7s was chosen as a cognitive load based on its superior ability to predict fall risk over other cognitive tasks (Bahureksa et al., 2016). While subjects were performing the DT, the examiners recorded their voices as an audio file using a lapel Bluetooth microphone. The participants were wearing a safety belt and were closely spotted for balance during testing. Before each condition, participants walked 3 passes for procedure familiarization.

3.2.3 Gait and Cognitive Metrics

Mean GV was recorded during the STs (unloaded gait velocity, ULGV) and DTs (loaded gait velocity, LGV) GV was chosen because it encompasses time and length metrics and has been indicated in the literature as a predictor of motor and cognitive decline (M. Montero-Odasso et al., 2012). The dual-task cost (DTC) was also calculated for GV (Equation 1).

$$\text{Equation 1: } DTC_{GV} = ST_{GV} - DT_{GV}$$

Using Adobe Audition 2020, the audio files were processed, extracting the cognitive performance variables comprising the number of counts (NC) and the percentage of true counts (PTC) based on the last number the subject counted. Two of the participants were removed from the dataset due to low level of accuracy in their backward counting by serial 7's (i.e. less than 30% correct numbers) as this was believed to represent reduced focus on the cognitive task. Therefore,

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thirty-two subjects (76 years \pm 3.44) including 17 fallers and 15 non-fallers remained in the dataset for statistical data analysis.

3.2.4 Statistical Data Analysis

All variables were centralized by subtracting the respective means. A progressively enhanced series of logistic regression models were performed commencing with gait velocity during the dual-task (Loaded Gait Velocity, LGV) as the covariate in predicting fall risk. This model was subsequently augmented by adding cognitive performance covariate. The analysis was further augmented with the addition of interaction variables made between the gait variable and each cognitive measure (CM). In the LGV model, the interaction variables were made by multiplying the product (LGV and NC) and (LGV and PTC).

This stepped modelling was then repeated with the dual-task cost gait velocity (DTC_{GV} - difference in gait velocity between single- and dual-task). Therefore in the (DTC_{GV} model the interaction variables were made the product of (DTC_{GV} and NC) and (DTC_{GV} and PTC).

In order to see how well the models explain the criterion variable (fall risk), Nagelkerke's R squares, the significance of variables and the sensitivity, specificity, and the overall classification accuracy for each model were documented. For all statistical analysis, (SPSS v. 26®) was used. The Hosmer-Lemeshow test was also conducted to assess the goodness of fit in all logistic regression models.

3.3 Results

3.3.1 Sample Characteristics

No significant differences were observed between the fallers and non-fallers for participant descriptive characteristics as outlined in Table 1.

Table 1. Participants Characteristics for fallers and non-fallers

Characteristic	Non-fallers (n = 15) females (n = 7), males (n = 8)	Fallers (n = 17) females (n = 13), males (n = 4)	P-value
Age (yrs)	M = 75.27, SD = 3.53	M = 76.69, SD = 3.32	0.26
Height (cm)	M = 167.80, SD = 8.47	M = 166.31, SD = 8.51	0.63
Leg length (cm)	M = 91.82, SD = 5.59	M = 90.19, SD = 5.30	0.42
Weight (kg)	M = 87.34, SD = 32.93	M = 76.79, SD = 16.35	0.29
MMSE	M = 28.55, SD = 0.93	M = 28.19, SD = 1.64	0.48

Abbreviations: n = number of samples, yrs = years, cm = centimeters, kg = kilograms, M = mean, SD = standard deviation, MMSE = mini mental status examination.

3.3.2 LGV and DTC_{GV} and Cognitive Measures

Mean values and standard deviations for GV under ST (ULGV), LGV, DTC_{GV}, and CMs for fallers and non-fallers are summarized in Table 2. For both LGV and DTC_{GV} models the Nagelkerke’s R square increased with the addition of the CM and the interaction variables between the GV and CM variables as outlined in Table 3. Nagelkerke’s R squares were consistently higher for the LGV models. For both LGV and DTC_{GV} models the sensitivity for correctly classifying fallers increased with the addition of the CM and the interaction variables between the GV and

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CM variables as outlined in Table 4. Across the 3 levels of analysis, sensitivity, specificity, and the overall classification accuracy were greater for LGV regression models with the highest sensitivity of 88.2% (correctly classified fallers), highest specificity of 86.7% (correctly classified non-fallers), and the highest overall accuracy of 87.5% on the 3rd level of analysis as shown in Table 4.

Table 2. Gait and cognitive metrics for fallers and non-fallers

Variable	Mean		SD	
	fallers	non-fallers	fallers	non-fallers
NC	79	72	45.84	43.23
PTC	72.2	76.1	15.32	16.62
ULGV (cm/s)	134.91	145.15	21.54	18.81
LGV (cm/s)	95.9	120.74	33.47	28.62
DTC _{GV} (cm/s)	39.01	24.41	30.03	22.33

Abbreviations: NC = number of counts, PTC = percentage of true counts, ULGV = unloaded gait velocity, LGV = loaded gait velocity, DTC_{GV} = dual-task cost for gait velocity, SD = standard deviation.

Table 3. Nagelkerk's R square for DTC_{GV} and LGV approaches for each level of analysis.

	LGV	DTC _{GV}
Gait	0.196	0.101
Gait & cognitive measures	0.281	0.127
Gait, cognitive & interaction measures	0.493	0.182

Table 4. Sensitivity, specificity, and overall accuracy for DTC_{GV} and LGV approaches for each level of analysis.

	LGV			DTC_{GV}		
	Sensitivity	Specificity	Overall accuracy	Sensitivity	Specificity	Overall accuracy
Gait	70.6	80.0	75.0	64.7	66.7	65.6
Gait & cognitive measures	76.5	66.7	71.9	64.7	53.3	59.4
Gait, cognitive & interaction measures	88.2	86.7	87.5	76.5	46.7	62.5

Note: Sensitivity, specificity, and overall accuracy are reported as a percentage.

The goodness of fit for the models was supported by the Hosmer-Lemeshow test (Table 5). Tables 6 and 7 display the variables in the regression models' equations for LGV and DTC_{GV} respectively for all 3 levels. LGV variable consistently reached significance as did the interaction variable for $PTC * GV$.

Table 5. Hosmer and Lemeshow test results

	LGV			DTC_{GV}		
	Chi-Square	df	Sig.	Chi-Square	df	Sig.
Gait	12.499	8	0.130	6.022	8	0.645
Gait & cognitive measures	5.459	8	0.708	6.733	8	0.566
Gait, cognitive & interaction variables	10.121	8	0.257	6.700	8	0.569

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Table 6. Results of Binary Logistic Regressions at an alpha level of $p < 0.05$ for LGV for each level of analysis.

	Variable	B	S.E	Wald	df	Sig	Exp(B)	95% CI	
								Lower	Upper
Gait	LGV	-0.028	0.014	3.865	1	0.049	0.972	0.945	1.000
	Constant	0.196	0.392	0.271	1	0.617	1.217		
Gait & cognitive measures	LGV	-0.045	0.021	4.694	1	0.030	0.956	0.918	0.996
	NC	-0.019	0.015	1.609	1	0.205	0.981	0.952	1.011
	PTC	-0.009	0.027	0.112	1	0.738	0.991	0.940	1.045
	Constant	0.164	0.402	0.166	1	0.683	1.178		
Gait, cognitive & interaction variables	LGV	-0.065	0.030	4.683	1	0.030	0.937	0.884	0.994
	NC	-0.009	0.025	0.120	1	0.730	0.991	0.944	1.042
	PTC	0.038	0.044	0.736	1	0.391	1.038	0.953	1.131
	LGV * NC	0.000	0.000	1.392	1	0.238	1.000	1.000	1.001
	LGV * PTC	-0.004	0.002	4.453	1	0.035	0.996	0.992	1.000
	Constant	0.582	0.653	0.792	1	0.373	1.789		

Abbreviations: PTC = percentage of true counts, NC = number of counts, SE = standard error, CI = confidence interval. Bold variables are significant predictors of fall status.

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Table 7. Results of Binary Logistic Regressions at an alpha level of $p < 0.05$ for DTC_{GV} for each level of analysis.

	Variable	B	S.E	Wald	df	Sig	Exp(B)	95% CI	
								Lower	Upper
Gait	DTC_{GV}	0.023	0.016	2.124	1	0.145	1.023	0.992	1.056
	Constant	0.155	0.371	0.173	1	0.677	1.167		
Gait & cognitive variable	DTC_{GV}	0.028	0.019	2.241	1	0.134	1.028	0.991	1.067
	NC	-0.007	0.012	0.341	1	0.559	0.993	0.971	1.016
	PTC	-0.007	0.028	0.069	1	0.793	0.993	0.940	1.048
	Constant	0.142	0.374	0.144	1	0.704	1.153		
Gait, cognitive & interaction variables	DTC_{GV}	0.023	0.022	1.113	1	0.291	1.023	0.980	1.068
	NC	-0.007	0.018	0.149	1	0.700	0.993	0.958	1.029
	PTC	-0.010	0.029	0.120	1	0.729	0.990	0.935	1.048
	$DTC_{GV} * NC$	0.000	0.000	0.000	1	0.987	1.000	0.999	1.001
	$DTC_{GV} * PTC$	0.001	0.001	1.051	1	0.305	1.001	0.996	1.004
	Constant	0.188	0.473	0.158	1	0.691	1.207		

3.4 Discussion

To the best of our knowledge, this study is the first to use a combination of gait and cognition measures in fall risk modeling among community-dwelling older adults. This work clearly demonstrates the relative added value of incorporating CMs for both LGV and DTC_{GV} models in identifying fallers and non-fallers. Further, this study highlights the interdependence between cognition and mobility and their impact on fall risk in older adults (Montero-Odasso et al., 2006; M. Montero-Odasso et al., 2012).

This study evaluated GV under ST and DT gait conditions which is a common way to assess the interrelation between cognition and mobility (Muir et al., 2012). Dual-task gait testing is also a means of assessing the capacity of the age-reduced neural resources to support a cognitive task during gait. For instance, in a cohort of older adults with mild cognitive impairment, higher DTC_{GV} in counting backward and subtracting serial 7s conditions were associated with a smaller volume of the left entorhinal cortex (Sakurai et al., 2019). Similar to previous studies, when the participants were asked to subtract by serial 7s during walking, their working memory was challenged providing sufficient cognitive load to have a pronounced impact on walking performance (Bahureksa et al., 2016). While working near the limitation of one's cognitive ability (Hunter et al., 2018), there appears to be competing demands on the reduced shared neural resources resulting in interference and reduced performance on either the motor task, the cognitive task, or both (Yogev-Seligmann et al., 2008). Consistent with previous findings, our investigation demonstrates the utility of both LGV and DTC_{GV} for identifying fall risk in older adults (Muir-Hunter & Wittwer, 2016). However, the novel contribution of the current study involves the incorporation of cognitive performance metrics along with motor performance metrics as well as

interaction variables between them to be used in the investigations of fall risk in older adults during DT gait. Though a few past studies have considered CMs, these investigations have still not sufficiently benefited from using both cognitive and motor metrics in their analysis (Olivier Beauchet et al., 2007).

The addition of the CMs and subsequently the CM * GV interaction variables, progressively increased the Nagelkerk's R square in both the LGV and DTC_{GV} models. For the LGV and DTC_{GV} model, the R² value increased by 2.5 and 1.8 times, respectively, suggesting that the addition of the CM and the interaction variables improved the capacity of the models to explain the variation in fall classification. The potential importance of cognitive performance and the interplay between cognition and mobility is further demonstrated in the improved sensitivity of fall risk classification for both the LGV and DTC_{GV} models. The addition of the CMs and the CM * GV interaction variables improved fall risk sensitivity by 25% in the LGV model and 18% in the DTC_{GV} model. Lastly, the addition of the CMs and subsequent addition of the CM * GV interaction variables in the LGV regression model provided an enhanced model with 2 significant variables comprising the LGV variable as well as the LGV * PTC interaction variable. In sum, the addition of the cognitive performance variables improved the model accuracy for both the LGV and the DTC_{GV} models demonstrating the strong interplay between motor and cognition function during DT gait. Further, this study clearly establishes the potential value of incorporating cognitive performance in the modeling to predict fall risk. Although it might add complexity in clinical or research settings to gather cognitive data as part of a basic older adult gait assessment, this work shows that the improved fall risk predictive capacity gained with its inclusion, justifies incurring this added complexity.

Our results also demonstrate an interplay between the mobility and the cognitive variables that is different in the LGV model than in the DTC_{GV} model. Despite the focus of the literature on DTC in different gait measures under cognitive load (Sakurai et al., 2019), our results demonstrated that LGV in DT gait testing in conjunction with the cognitive performance measures provides a strong classification of fallers versus non-fallers relative to DTC_{GV} models. Specifically, a larger Nagelkerk's R square was seen in the LGV model over the DTC_{GV} model in this sample of older adults. Further, for the DTC_{GV} model, though the sensitivity of the model was increased, the specificity was decreased lowering the overall model accuracy. This is in stark contrast to the increases in sensitivity, specificity and overall model accuracy seen in LGV modelling. In fact, the LGV model with CMs and the interaction variables provided predictive capacity with 88.2% sensitivity, 86.7% specificity and an overall model performance of 87.5%. Lastly, the appearance of 2 significant variables in the LGV model while there was no significant variable in the DTC_{GV} model, provides additional evidence of the strength of the LGV model over DTC_{GV} . It could be reasoned that the DTC already incorporates the cognitive performance into the motor performance and therefore combining it with CMs does not enhance its predictive capacity. In contrast, it is not surprising that the LGV's predictive capacity improves when combined with CMs variable, since it does not have cognitive cost explicitly incorporated. Gait velocity incorporates both spatial and temporal gait parameters and is relatively easy to collect. Further our findings support the predictive capacity of gait velocity of fall risk and therefore gait velocity is a key gait metric that should be included in geriatric clinical or research assessments. Gait velocity provides an effective biomarker of one's overall function and therefore may also have potential capacity to be used as an indicator of those at higher risk of impending adverse health events (M. Montero-Odasso et al., 2005).

Interestingly, in contrast with some previous work, the DTC_{GV} model in the current study had lower sensitivity and specificity than the LGV model. This does not negate the proven utility of the DTC in older adults' studies. In the current investigation GV or DTC_{GV} were used as solo gait parameters in each regression model. In contrast previous work included many different gait measures such as stride length, stride width, stride time and also stride velocity for both loaded and dual-task cost gait conditions (Commandeur et al., 2018). Further in other work that included gait velocity, step length, stride length, step time, stride time, and double support time, DTC also was shown to be a noteworthy measure (M. Montero-Odasso, Casas, et al., 2009),.

Lastly, this work reaffirms that the difference in GV with and without cognitive load (DTC_{GV}) is greater in those at risk of falls (Table 2) (Hollman et al., 2007). In this study, GV dropped under DT conditions by 28.9% and 16.8% for both fallers and non-fallers respectively. The larger drop in GV in the faller group supports the nature of our primary grouping. This is also in keeping with previous studies, which reported that if the DTC for GV was 20% or higher, the elderly subject is at greater risk for falling (Hollman et al., 2007). Other studies showed that DTC_{GV} for 20% or higher is also an indicator of risk for progression of dementia (M. M. Montero-Odasso et. al., 2017).

3.5 Summary

Distinct from previous dual-task gait studies, which included only the gait measures to predict fall risk and identify fallers, we established the potential importance of including CMs as well. In the current study, the regression model providing the highest sensitivity, specificity and overall accuracy consisted of LGV, NC and PTC as well as the interaction variables (LGV * NC and LGV * PTC). Our work demonstrates that these cognitive and interaction measures have

potential clinical utility in identifying those at risk of falls. Further, this work highlights the interplay between cognitive and motor function and therefore suggests the potential utility of combined cognitive- and motor-based interventions that may prevent/delay the onset of fall risk.

Our work also demonstrated that the utility of including cognition measures is best highlighted in LGV models rather than DTC_{GV} model. Yet, when gait measures are used in isolation (i.e., without cognition metrics) DTC gait measures are recommended as they better represent losses in motor functionality under cognitive load (Annweiler et al., 2013; Nordin et al., 2010).

3.6 Future Directions

This research presents a strong classification model for detecting older adults at risk of falls using a combination of GV and cognitive performance and interaction variables. The inclusion of cognitive performance metrics in this type of modelling should be expanded to explore other gait measures proven to be associated with falls or cognitive impairment (e.g., step length variability). Further, this work should be repeated with larger more diverse sample of community-dwelling older adults. Specifically, it would be useful to better understand the relationships between gait performance and fall risk prediction among those individuals with different levels of cognitive function. Potentially the associations in the modelling could be greater for different clinical populations. Further longitudinal studies are necessary to evaluate the utility of models with a combination of cognitive and gait variables in identifying the upcoming incidence of falls in a current non-faller cohort.

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