

**THE ASSOCIATION BETWEEN ADHERENCE TO THE CANADIAN 24-HOUR
MOVEMENT GUIDELINES AND FRAILITY, AND MORTALITY: A CROSS
SECTIONAL AND PROSPECTIVE ANALYSIS OF THE NATIONAL HEALTH
AND NUTRITION EXAMINATION SURVEY**

by

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BSc Kinesiology w/ Honours, University of New Brunswick, 2021

**A Thesis Submitted in Partial Fulfillment
of the Requirements for the Degree of**

Master of Science in Kinesiology
in the Graduate Academic Unit of Kinesiology

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This thesis is accepted by the
Dean of Graduate Studies

THE UNIVERSITY OF NEW BRUNSWICK

August, 2022

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ABSTRACT

The Canadian 24-Hour Movement Guidelines (24H-MG) give recommendations for physical activity, sedentary time, and sleep. While following the 24H-MG prevents many chronic conditions, the association between meeting these guidelines and frailty, or mortality when considering frailty levels, is unknown. Therefore, the study objective was to investigate the cross sectional and prospective association between adherence to the 24H-MG and frailty and mortality. Participants (n=2739) from the National Health and Nutrition Examination Survey were included. Linear and cox regressions adjusted for known co-variates quantified the relationship between exposure and primary outcome variables. The results show that increased adherence to the 24H-MG is associated with lower frailty levels in adults 20-64 and 65+, with recreational screen time and MVPA showing the strongest association. No prospective association was observed between adherence to the complete 24H-MG and mortality, but adherence to the MVPA guideline in the 65+ age group was associated with lower mortality.

DEDICATION

I dedicate this thesis to my family. First, my parents who were always there to offer advice, encouragement, and love. Second, my siblings who have always been my best friends. Finally, my wife, Emmeline, who somehow always knows what I need, loves me perfectly, and has been my number one fan and supporter!

ACKNOWLEDGEMENT

I would like to begin by recognizing the New Brunswick Health Research Foundation and the University of New Brunswick for providing funding for me to finish my thesis. Next, I would like to acknowledge my family and friends who have supported me in numerous ways, allowing me to pursue my goals! Third, I would like to recognize my undergrad professors, many of whom inspired me not only academically but also encouraged me to become a better person and opened my eyes to paradigms and ideas that have shaped the way I think and interact with the world. Fourth, I would like to acknowledge everyone at the CELLAB who have offered me help, advice and friendship. Fifth, I would like to acknowledge my advisor committee of Doctor Danielle Bouchard and Doctor Jeff Hebert for their invaluable contributions to my thesis. Finally, I would like to acknowledge my supervisor, Doctor Martin Sénéchal for being a mentor and friend, providing me opportunities that will shape my life, and always being there to offer advice.

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List of Symbols, Nomenclature or Abbreviations

24H-MG = 24 Hour Movement Guidelines

FI = Frailty Index

FRAIL Index = Fatigue, Resistance, Ambulation, Illness, Loss of Weight Index

IL-6 = Interleukin-6

LPA = Light Physical Activity

MVPA = Moderate to Vigorous Physical Exercise

NHANES = National Health and Nutrition Examination Survey

PA = Physical Activity

RST = Recreational Screen Time

TNF- α = Tumor Necrosis Factor Alpha

Chapter 1: Introduction

The proportion of seniors (adults aged 65+) is increasing globally (World Health Organization, 2015, pp. 43–45). In Canada, the proportion of seniors is expected to increase from 18% to 25% between 2020 and 2058 (Statistics Canada, 2020). This presents a difficult challenge because seniors have a high prevalence of co-morbidity and disability and consume a significant proportion of societal resources (Canadian Institute for Health Information, 2011, p. 1). In 2018, the average senior cost the Canadian health care system \$11,599, 3.7 times as much as their younger peers (aged 15-64) (Canadian Institute for Health Information, 2020, p. 8).

Nevertheless, not everyone ages the same; successful agers maintain exceptional health late into their life while others experience significant health deterioration and onset of disability from a young age (Lowsky et al., 2014). To help define how successfully someone is aging, the concept of frailty was developed. Frailty is an age-related state in which decline across multiple body systems leads to decreased physiologic reserve and an increased risk of disease, disability, and death (Clegg et al., 2013; Dent, Martin, et al., 2019). Frail individuals do not have the intrinsic capacity to deal with stressors, and so for them minimal stress can often lead to severe impairment (Angulo et al., 2020; Rodríguez-Mañas et al., 2013). Frailty can be identified across the lifespan, but frailty prevalence does increase with chronological age (Kehler et al., 2017).

While these facts are generally agreed on, there is little consensus on what is the best way to define and quantify frailty (Dent et al., 2016). Many models have emerged, the two main ones being Fried's Phenotype Model (Fried et al., 2001) and Rockwood's

Accumulation of Deficits model (Rockwood & Mitnitski, 2007). While each of these models has their own pros and cons, and criterion for defining frailty, they generally agree that individuals progress from a robust, to a pre-frail or vulnerable state, and finally to a frail state (Dent et al., 2016).

Understanding how to prevent and even reverse frailty progression is extremely important as frail individuals are more at risk for various health conditions (Dent, Martin, et al., 2019) and use more healthcare resources (Chi et al., 2021) than their robust peers. Various pharmaceutical, dietary and lifestyle interventions have been tested with the goal of delaying frailty progression (Dent, Morley, et al., 2019). Physical activity and exercise have emerged as one of the keys to frailty management (Angulo et al., 2020; Gwyther et al., 2018; Negm et al., 2019).

In 2020, the Canadian 24-Hour Movement Guidelines (24H-MG) was released for adults aged 18-64 and adults aged 65+ (Ross et al., 2020). These guidelines encouraged individuals to consider their movement behavior through the entire day, rather than just the 150 minutes of moderate to vigorous physical activity (MVPA) and two sessions of strength training per week as recommended by the previous guidelines (Ross et al., 2020; Tremblay, Warburton, et al., 2011). The new guidelines give specific recommendations regarding increasing physical activity, reducing sedentary time and getting a proper amount of sleep (Ross et al., 2020).

Following these guidelines promotes health and quality of life and reduces the risk of diseases such as diabetes and cardiovascular disease (Ross et al., 2020). However, it is unknown whether following the guidelines prevents frailty.

Frailty research conducted in the past has looked at the individual behaviors included in the guidelines and how they impact frailty. For example, isotemporal substitution models have shown that reallocating time spent sedentary to time spent in MVPA or light physical activity (LPA) is associated with reduced frailty (Godin et al., 2020). Performing resistance training also appears to help prevent and reverse frailty (Coelho-Júnior et al., 2021; Talar et al., 2021). Getting a proper amount of sleep prevents frailty (Pourmotabbed et al., 2020). However, to date no study has looked at how the combination of all these behaviors influences frailty.

Therefore, the goal of this thesis was to identify whether adherence to the full composition of the new Canadian 24H-MG is associated with frailty. In addition, we investigated whether adherence to each individual component of the 24H-MG is associated with frailty. We also investigated the relationship between following the guidelines and mortality while considering frailty. It was hypothesized that adhering to the full Canadian 24H-MG and adhering to the individual components of the Canadian 24H-MG will be associated with decreased frailty and mortality.

Chapter 2: Literature Review

2.1 What is Frailty?

2.1.1 Aging

Aging is often associated with frailty, disability, and dependent living in older adults (Sarkisian et al., 2002). However, aging starts at birth and continues until death (Bouchard, 2020, p. 4). During the early stage of aging dependency on others declines. However, pathological aging later in life leads to a decline in independence and the onset of frailty (Bouchard, 2020, p. 4). This U-shaped relationship between dependency and aging is depicted in Figure 1.

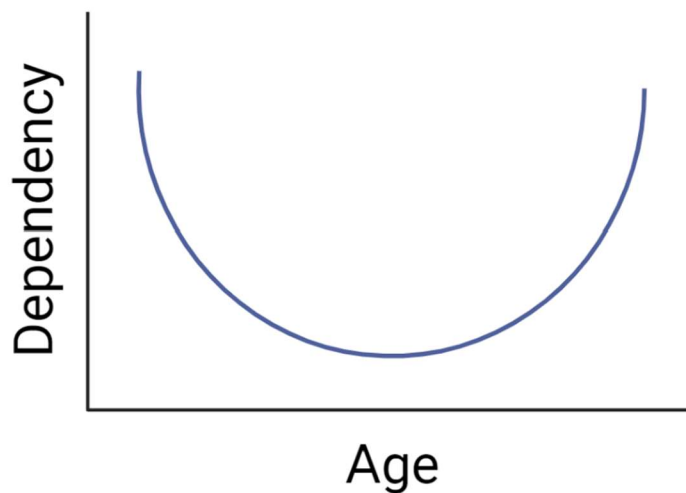


Figure 1: U-shaped relationship between dependency and aging. Created using BioRender.

Adapted from Bouchard (2020, p. 4)

Aging later in life can be viewed as a progressive, generalized impairment of function, resulting in an increased vulnerability to environmental challenge and a growing risk of death and disease (Kirkwood, 2005). Aging is often measured using chronological

age. However, chronological age may not properly reflect biological aging (also called functional age) as the speed and process of decline seen with aging varies between individuals (Belsky et al., 2015). Successful agers maintain exceptional health late into life, while others experience significant decline in mental and physical function from a young age (Lowsky et al., 2014).

According to the World Health Organization, the proportion of older adults is increasing worldwide (World Health Organization, 2015, pp. 43–45). In Canada, the proportion of adults aged 65+ is expected to increase from 18% in 2020 to 25% by 2058 (Statistics Canada, 2020). Since aging in individuals above the age of 65 years is accompanied by a decrease in mental and physical functions, the aging process represents an important challenge for Canadians (Statistics Canada, 2020).

Advancements in modern medicine have increased lifespan at a rate that is outpacing the concurrent increase in healthspan (Crimmins, 2015). In fact, 76% of Canadian seniors report having one or more chronic conditions (Canadian Institute for Health Information, 2011, pp. 3–4) and the average Canadian is expected to live roughly 10.5 years with some level of disability (Government of Canada, 2013, p. 8). In 2018, the average senior cost the Canadian health care system \$11,599 per year whereas the average individuals aged 15-65 only cost \$3,131 per year (Canadian Institute for Health Information, 2020, p. 8). Finding ways to maintain health span and independence throughout the aging process will benefit individuals and society.

2.1.2 Frailty

Frailty is an age-related health state in which decline across multiple body systems leads to reduced physiological reserve and consequently increased risk of disease,

disability, and death (Clegg et al., 2013; Dent, Martin, et al., 2019). Thus, frail individuals have difficulty mustering the intrinsic capacity to deal with stressors they could previously overcome, meaning that minimal stress can lead to severe impairment (Angulo et al., 2020; Rodríguez-Mañas et al., 2013). While these facts are generally agreed upon, there is currently a large debate around how to best define and quantify frailty (Dent et al., 2016). Figure 2 illustrates the progression of aging and lists some of the proposed frailty models.

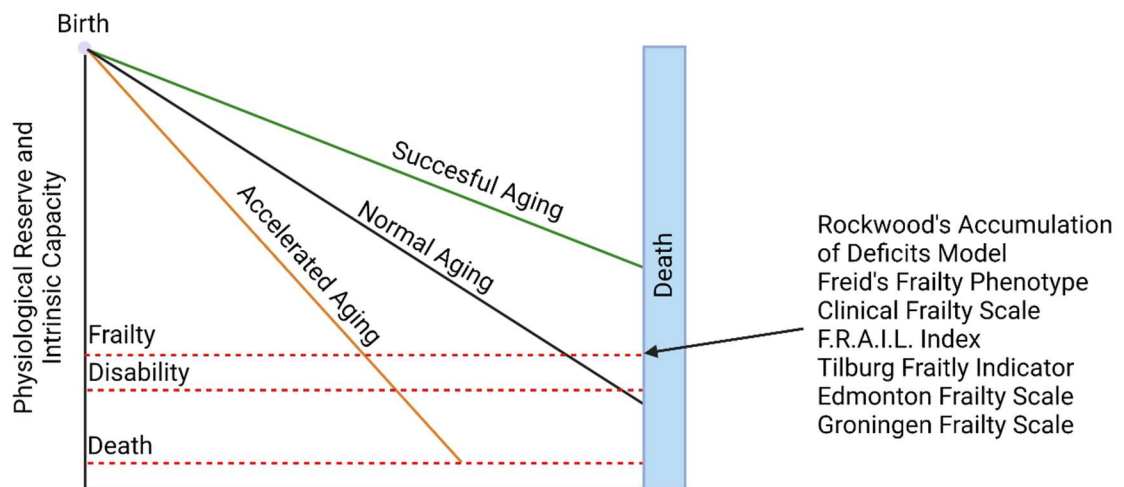


Figure 2: The progression of aging that results in reduced physiological reserve and intrinsic capacity, eventually leading to a state of frailty which can then lead to disability and death. The different lines represent the progress of accelerated, usual, and successful/healthy aging. To the right is several different models used to identify individuals who meet the cut-off point of frailty.

Adapted from Angulo et al., (2020). Created using BioRender

Over the years, many models have been proposed to define and quantify frailty, each with their own pros and cons (Dent et al., 2016). Currently, two main frailty models are used: The Frailty Phenotype and The Accumulation of Deficits Model (Richards et al.,

2018). Fried's Frailty Phenotype defines frailty using five criteria: shrinking (unintentional weight loss), weakness, poor endurance and energy, slowness, and low physical activity levels (Fried et al., 2001). This model was used to create a frailty screening tool that scores individuals from 0 to 5—0 traits = robust (or healthy), 1-2 traits = prefrail and 3-5 traits = frail—based on the number of phenotype criteria they meet (Fried et al., 2001). The Frailty Phenotype has been shown to predict incident falls, worsening mobility, disability, hospitalization, and death (Fried et al., 2001).

Rockwood's Accumulation of Deficits Model argues that as the number of deficits present in an individual increases, frailty increases (Rockwood & Mitnitski, 2007). Deficits include symptoms, signs, disabilities, diseases, and laboratory measurements that accumulate with age (Rockwood & Mitnitski, 2007). This model forms the basis of the Frailty Index (FI), which quantifies frailty based on the proportion of present deficits relative to the number of traits measured (Rockwood & Mitnitski, 2007). FIs are useful because they are a flexible and adaptable to any study that identifies potential deficits as defined above (Rockwood & Mitnitski, 2007). Anytime a FI is mentioned in this paper it can be assumed that the Accumulations of Deficit Model is being used to quantify frailty.

A FI is created using the following methodology: when a deficit trait is identified it is given a score of 1, while a non-deficit trait is scored as 0. The number of deficits is then tabulated and divided by the total number of traits measured. For example, if a 40 item Comprehensive Geriatric Assessment is performed, and the individual is identified to have 12 deficits, their FI score would be $12/40$ or 0.3 (Rockwood & Mitnitski, 2007). FI scores increase with age and higher FI scores have been correlated with death, institutionalization, health service use, and further deficit accumulation (Rockwood & Mitnitski, 2007). FI

scores should be viewed as a continuous variable, although some studies have used set cut-off points to define different level of frailty for comparison purposes (Kehler et al., 2017; Kehler & Theou, 2019).

Additional models and screening tools have been developed that can be used to define and quantify frailty (Dent et al., 2016; Richards et al., 2018). Individual tests have also been used to screen for frailty, including walking speed and grip strength (Dent et al., 2016; Woo et al., 2016). Other tests such as the Edmonton Frailty Scale (Rolfson et al., 2006); Fatigue, Resistance, Ambulation, Illness, Loss of Weight (FRAIL) Index (Morley et al., 2012); Tilburg Frailty Indicator (Gobbens et al., 2010a); Groningen Frailty Indicator (Peters et al., 2012); and others have all been shown to have validity and reliability when identifying frailty (Dent et al., 2016). A list of the different Frailty models can be found in Table 1.

2.2 The Prevalence of Frailty

Frailty prevalence increases with chronological age, although frailty has been observed in individuals as young as 18 years of age (Collard et al., 2012; Kehler et al., 2017; O’Caoimh et al., 2021). Estimations of the prevalence of frailty also changes based on the frailty definition used (Kehler et al., 2017; O’Caoimh et al., 2021).

One systematic review and meta-analysis pooled data from adults aged ≥ 50 years in 62 countries and found that frailty prevalence using a physical frailty measure versus a FI was 12% and 24%, respectively (O’Caoimh et al., 2021). Prevalence of pre-frailty was 46% when using a physical frailty measure and 49% when using a FI (O’Caoimh et al.,

Table 1: A list of frailty models and definitions.

Model	Definition
Frailty Phenotype (Fried et al., 2001)	The Frailty Phenotype defines frailty using five criteria: shrinking (unintentional weight loss), weakness, poor endurance and energy, slowness, and low physical activity levels. This model has been used to create a frailty screening tool that scores individuals from 0 to 5—0 = robust, 1-2 = pre-frail, and 3-5 = frail—based on the number of phenotype criteria they meet.
Accumulation of Deficits (Rockwood & Mitnitski, 2007)	The Accumulation of Deficits Model argues that the more things an individual has wrong with them (deficits), the frailer they are. This model has been used to create a Frailty Index, which quantifies frailty using a continuous variable based on the proportion of deficits present in an individual relative to the number of traits measured.
Clinical Frailty Scale (Rockwood et al., 2005)	The Clinical Frailty Scale uses a physician’s judgement to classify individual’s frailty levels on a scale of 1-9, with 1 meaning very well (highly active and healthy), and 9 meaning terminally ill (expected to die in the next 6 months). Individuals are classified as FRAIL if they score ≥ 5 .
Fatigue, Resistance, Ambulation, Illness, Loss of Weight (FRAIL) Index (Morley et al., 2012)	The FRAIL Index model looks at Frailty based on 5 components: fatigue, strength deficits (resistance), mobility deficits (ambulation), presence of illness, and loss of weight. The advantage of this scale is it is completely based off self-reported questionnaires and can be used remotely. For scoring, 0 = robust, 1-2 = pre-frail, and 3-5 = frail.

Edmonton Frailty Scale (Rolfson et al., 2006)	The Edmonton Frailty Scale defines frailty based on 9 domains: cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, and functional performance. It brings in several possible contributors to frailty, such as cognition, social support, and polypharmacy not already considered by the models above. Individuals are scored out of 17 points. An increase in score represents an increase in frailty.
Tilburg Frailty Indicator (Gobbens et al., 2010a)	The Tilburg Frailty Indicator is a 15-question self-administered questionnaire focused around 3 domains: physical components (health, weight loss walking, balance, hearing, vision, gripping and tiredness); psychological factors (memory, feeling down, anxiety and coping); and social elements (living alone, social isolation and social support). A score of ≥ 5 is considered frail.
Groningen Frailty Indicator (Peters et al., 2012)	The Groningen Frailty Index is a 15-item frailty screening tool available as a self-report or professional version. It measures frailty based on 4 domains: physical (mobility functions, multiple health problems, physical fatigue, vision, hearing); cognitive (cognitive dysfunction); social (emotional isolation); and psychological (depressed mood and feeling of anxiety). A score of ≥ 4 is considered moderate to severely frailty.

2021). Women were more likely to be frail, and frailty prevalence increased with age (O’Caoimh et al., 2021).

Data from the Canadian Health Measure study were analyzed to identify the prevalence of frailty among the Canadian population using both a FI and Fried’s Phenotype

Model in adults aged 18-79 (Kehler et al., 2017). They found the overall prevalence of frailty to be 8.6% and 6.6% when using a FI and Fried’s Phenotype model, respectively. Frailty prevalence increased with age from 5.3% in the 18-34 age group to 7.8% in the 65+ age group when using Fried’s Phenotype Model and from 1.8% in the 18-34 group to 20.2% in the 65+ age group when using a FI (Kehler et al., 2017). Figure 2 displays the prevalence of frailty from this study according to age group and frailty model (Kehler et al., 2017).

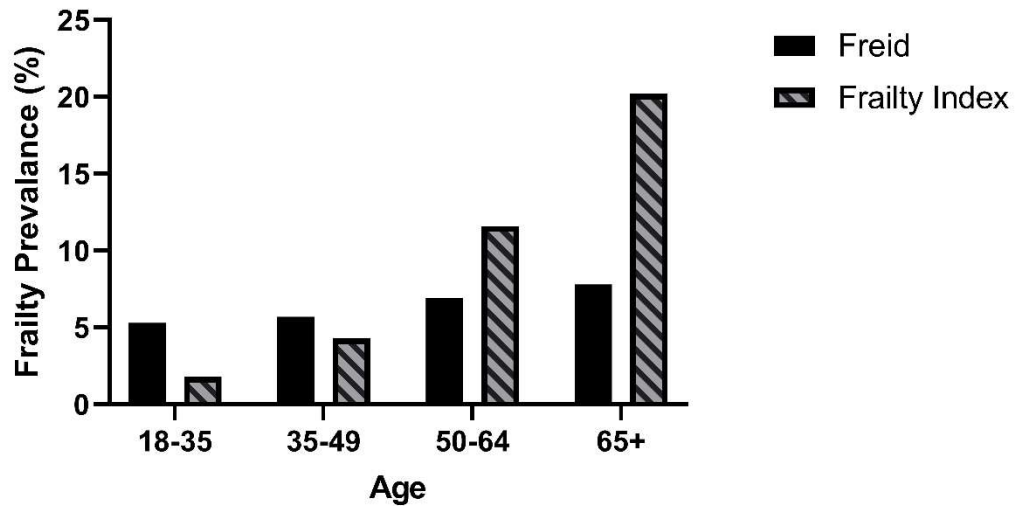


Figure 3: Proportion of Frail Canadians in different age cohorts and defined using Fried’s Phenotype model and Rockwood’s Frailty Index

Adapted from Kehler et al., (2017)

The differences in frailty prevalence found in a Canadian population (Kehler et al., 2017) versus the above-mentioned systematic review of global frailty prevalence (O’Caoimh et al., 2021) can be explained by several reasons. First, the difference in tools used to quantify physical frailty: Kehler et al. (2017) only used Fried’s Frailty Phenotype whereas O’Caoimh et al. (2021) used multiple physical frailty measures. Second, while

FIs have similar predictive ability, they are also flexible with respect to the criteria included in the index, which could potentially impact frailty prevalence. In addition, there is no universal cut-off for frailty when using an FI, which could also impact the prevalence of frailty in a population.

2.3 The Consequences of Frailty

Frailty impacts individuals living with frailty and society (Andrew et al., 2018). Frailty increases one's risk of unmet care needs, falls and fractures, hospitalization, lowered quality of life, functional decline, worsening mobility, disability, and mortality (Dent, Martin, et al., 2019; Kojima, 2017; Spiers et al., 2021; Walston et al., 2018). Following surgery, individuals living with frailty are more likely to experience complications, be re-admitted to the hospital, be discharged to a long-term care home, or die (Richards et al., 2018). Individuals living with frailty are more likely to have obesity; have a higher waist circumference, low HDL-cholesterol concentrations, and hypertension; and experience, or die from, cardiovascular disease (Afilalo et al., 2009; Ramsay et al., 2015). Frail cancer patients have an increased risk of chemotherapy intolerance, postoperative complications, and mortality (Handforth et al., 2015). Individuals living with frailty are more likely to be depressed (Vaughan et al., 2015); feel lonely and socially isolated (Hoogendijk et al., 2016); have lower life satisfaction (St John et al., 2013); and contemplate suicide (Bickford et al., 2021).

Frailty also creates a large burden on society and the health care system. Caregivers of the frail elderly can experience significant financial, physical, and psychosocial burdens (Garlo et al., 2010; Ringer et al., 2017; Schulz & Sherwood, 2008; Zarit et al., 1980). A

systematic review showed that frailty measured using various tools is associated with a higher usage of health care resources (Chi et al., 2021; Kojima, 2019). One study found that individuals living with pre-frailty and frailty cost the healthcare system 30% and 75% more per year, respectively, than non-frail individuals (Salinas-Rodríguez et al., 2019). Therefore, managing frailty can have widespread benefits to individuals, their support networks and society.

2.4 What Causes Frailty?

The pathophysiology of frailty is not clearly elucidated or understood (Soysal et al., 2016). It has been proposed that pathological aging is caused by chronic and systematic, low-grade inflammation (Franceschi et al., 2000; Xia et al., 2016). Inflammation itself is adaptive, and acute inflammation is a necessary part of the immune response (Varela et al., 2018). However, chronic, systematic, low-grade inflammation is pathological and may contribute to the onset of frailty (Sergio, 2008) and the development of various diseases (Xia et al., 2016). Chronic inflammation may result from imbalances in the immune system that elevate pro-inflammatory markers and decreased anti-inflammatory markers (Xia et al., 2016). Indeed, pro-inflammatory markers such as Interleukin-6 (IL-6), Tumor Necrosis Factor Alpha (TNF- α) and C-reactive Proteins (CRP) are elevated in individuals living with frailty (Soysal et al., 2016; Vatic et al., 2020). Systematic inflammation may also contribute to sarcopenia, a condition that contributes to and often precedes physical frailty (Nascimento et al., 2019; Wilson et al., 2017).

The Oxi-Inflammaging Theory postulates that pathological aging is caused by both chronic inflammation and oxidative damage (De la Fuente & Miquel, 2009). Oxidative

damage is caused by reactive oxygen species and free radicals and affects various bodily systems such as the neural, endocrine, and immune system, leading to a disruption of homeostasis, and contributing to pathological aging and frailty (De la Fuente & Miquel, 2009). Increased biomarkers of oxidative stress and decreased antioxidants have been observed in individuals living with frailty (Álvarez-Satta et al., 2020).

The Inflammaging-Inactivity Paradigm begins to bring in lifestyle determinants of aging into the discussion (Flynn et al., 2019). Exercise reduces inflammation in older adults (Liberman et al., 2017) and has a positive effect on many of the diseases affecting by inflammaging (Flynn et al., 2019). In addition, while exercise increases oxidative stress, the health benefits associated with exercise exceeds the detrimental effect of exercise induced oxidative stress on the body (de Gonzalo-Calvo et al., 2013; Gomes et al., 2017)

Lifestyle choices such as smoking and improper diet contribute to frailty (Brinkman et al., 2018; Lorenzo-López et al., 2017; Woo et al., 2010). In addition, depression (Soysal et al., 2017), polypharmacy (Gutiérrez-Valencia et al., 2018), socioeconomic status (Gobbens et al., 2010b; Haapanen et al., 2018; Woo et al., 2010), living location (Woo et al., 2010), and multimorbidity (Gobbens et al., 2010b) have all been shown to be associated with frailty. One systematic review looked at frailty trajectories and found that a diagnosis of Alzheimer's disease, reduced cognition, location of residence, being female, older age, being in recovery from injury, diabetes, financial strain and being a migrant were all risk factors of frailty, while higher education, cultural engagement, higher wealth, being male, higher social support and higher physical activity protected against frailty (Welstead et al., 2020).

2.5 How is frailty treated and prevented?

The importance of understanding how to prevent and treat frailty is becoming increasingly relevant as the proportion of older adults rises globally (Dent, Martin, et al., 2019; Dent, Morley, et al., 2019). Many interventions have been designed to prevent, reverse, or delay frailty progression with varying degrees of success and ease of implementation (Travers et al., 2019). Several methods used to treat frailty include exercise, nutritional, pharmaceutical, or combined method interventions (Dent, Morley, et al., 2019; Walston et al., 2018).

Physical activity interventions are an effective way to treat and prevent frailty (Angulo et al., 2020; Gwyther et al., 2018; Negm et al., 2019, Racey et al., 2021). Exercise interventions for older adults often include aerobic, resistance, balance, power, or flexibility exercises or some combination of these exercises (Angulo et al., 2020; Nascimento et al., 2019; Walston et al., 2018). A recent systematic review found that resistance training improved upper and lower limb muscular strength; physical function; and body composition in frail and pre-frail individuals and should be considered a highly effective tool in preventing the negative effects of frailty (Talar et al., 2021). Other various forms of exercise such as walking (Cesari et al., 2015), exercising with horses (Aranda-García et al., 2015), Tai Chi (Wolf et al., 1996) and multicomponent exercise interventions (Chodzko-Zajko et al., 2009; Nascimento et al., 2019; Tarazona-Santabalbina et al., 2016) have been shown to prevent frailty and mitigate the adverse effects associated with frailty.

Proper nutrition plays a crucial role in the prevention and treatment of frailty (Feart, 2019). Proper macronutrient (specifically protein) and micronutrient (Vit. D, E, C and Folate) intake is associated with lower frailty (Bartali et al., 2006; Lorenzo-López et al.,

2017). Following the Mediterranean Diet has been shown to reduce the incidence of frailty by as much as 64% (Kojima et al., 2018). In addition, high protein consumption has been shown to be protective against frailty and protein supplementation may play an important role in frailty management, and functional capacity and health maintenance (Artaza-Artabe et al., 2016).

There appears to be a complex, bi-directional relationship between frailty and polypharmacy; polypharmacy may contribute to frailty, but the multifaceted needs of frailty may also require multiple medications to treat (Gutiérrez-Valencia et al., 2018). Managing polypharmacy and deprescribing unnecessary medications may be an effective tool to prevent and manage frailty (Morley et al., 2013). At the same time, additional prescriptions to treat the underlying conditions that contribute to frailty may be needed in some cases (Pahor et al., 2018). Therefore, proper prescription and deprescription of medicine is needed to properly manage frailty (Dent, Martin, et al., 2019).

However, proper management of frailty requires a personal and multicomponent approach that incorporates all the methods above (Dent, Martin, et al., 2019; Walston et al., 2018). For example, one systematic review found that interventions consisting of both resistance training and protein supplementation were the best at delaying and reversing frailty progression (Travers et al., 2019). Multidisciplinary, personalized interventions involving a team of clinicians have been shown to be the superior treatment method when working with frail patients (Cameron et al., 2013). Therefore, understand how movement behaviors over a 24-hour day influence frailty may be important to its prevention and management.

2.6 Canadian 24 Hour Movement Guidelines

In 2020, Canada completed its set of 24H-MG by releasing guidelines for adults aged 18-64 and adults aged 65+ to compliment previously released guidelines for children aged 0-4 and children aged 5-17 (Ross et al., 2020; Tremblay et al., 2016, 2017). These guidelines introduced the first ever comprehensive recommendations for 24-Hour movement behavior for adults. The previous physical activity guidelines for adults recommended ≥ 150 minutes of MVPA in 10-minute bouts; ≥ 2 resistance training sessions per week; and balance training for older adults with balance impairment (Tremblay, Warburton, et al., 2011). The new guidelines built on the old guidelines by removing the stipulation that MVPA should be performed in 10-minute bouts and adding additional guidelines: ≤ 8 hours sedentary time per day; several hours of LPA per day; ≤ 3 hours recreational screen time per day; and 7-9 hours of sleep for adults aged 20-64 and 7-8 hours for adults aged 65+ (Ross et al., 2020).

To create these guidelines, a committee was organized that met several times from 2018-2020 to discuss the current research (Ross et al., 2020). This committee also completed two systematic reviews and four umbrella reviews to understand the current literature around healthy movement behavior (Ross et al., 2020). The two systematic reviews looked at current literature on sleep duration and consistency (Chaput, Dutil, Featherstone, Ross, Giangregorio, Saunders, Janssen, Poitras, Kho, Ross-White, Zankar, et al., 2020), and integrated movement behavior (Janssen et al., 2020). The four umbrella reviews looked at strength and resistance training (El-Kotob et al., 2020); balance and functional training (McLaughlin et al., 2020); total sedentary time and the relationship between patterns of sedentary time (Saunders et al., 2020); and sleep duration (Chaput,

Dutil, Featherstone, Ross, Giangregorio, Saunders, Janssen, Poitras, Kho, Ross-White, & Carrier, 2020). In addition, the MVPA guideline component was created based on evidence from the United States' 2018 Physical Activity Guidelines Advisory Committee Scientific Report (Physical Activity Guidelines Advisory Committee, 2018; Ross et al., 2020).

Based on these reviews, guidelines were created using a systematic process that involved input from both the committee, as well as consultation of various stakeholders and the public (Ross et al., 2020). A knowledge translation committee was also formed to advise the creation of materials that would allow for easy understanding of the guidelines by the lay public (Ross et al., 2020; Tomasone et al., 2020).

The evidence from these reviews showed that the composition of movement throughout the day is associated with reduced risk of mortality and improved adiposity, glucose and insulin control, lipids and lipoproteins concentrations, blood pressure, C-reactive protein concentration and resting heart rate (Janssen et al., 2020). In addition, following the individual guideline components has been shown to reduce depression, anxiety, blood pressure, weight gain, dementia, falls, certain types of cancer, type 2 diabetes, stroke, cardiovascular disease incidence and mortality and all-cause mortality and improve muscle strength, physical fitness, sleep, and cognitive function (Chaput, Dutil, Featherstone, Ross, Giangregorio, Saunders, Janssen, Poitras, Kho, Ross-White, & Carrier, 2020; Chaput, Dutil, Featherstone, Ross, Giangregorio, Saunders, Janssen, Poitras, Kho, Ross-White, Zankar, et al., 2020; El-Kotob et al., 2020; Physical Activity Guidelines Advisory Committee, 2018; Saunders et al., 2020). To improve health, time spend sedentary should be replaced with time in physical activity and sleep, with priority going to spending more time in MVPA (Janssen et al., 2020).

Table 2: 24-Hour Movement Guidelines and Their Associated Health Benefits

Guideline Component	Specific Guidelines	Health Benefits
Moderate to vigorous physical activity (Physical Activity Guidelines Advisory Committee, 2018)	≥150 Minutes of moderate to vigorous activity per week	<ul style="list-style-type: none"> • Improved sleep, executive functions, perceived quality of life and physical function • Reduced risk of depression, anxiety, blood pressure, weight gain, dementia, falls, certain types of cancer, type 2 diabetes, stroke, cardiovascular disease incidence and mortality, and all-cause mortality
Light physical activity (Physical Activity Guidelines Advisory Committee, 2018)	Several hours of light physical activity	<ul style="list-style-type: none"> • Replacing sedentary time with light physical activity reduces the risk of cardiovascular disease, type 2 diabetes, and all-cause mortality
Resistance training (El-Kotob et al., 2020)	<ul style="list-style-type: none"> • ≥2 sessions of muscle strengthening exercises per week targeting major muscle groups 	<ul style="list-style-type: none"> • Reduced risk of high blood pressure, cardiovascular disease, and all-cause mortality • Improved muscle strength • Improved physical functioning in older adults
Balance and functional training (McLaughlin et al., 2020)	<ul style="list-style-type: none"> • Perform physical activity that challenges balance (Adults 65+) 	<ul style="list-style-type: none"> • Reduced risk of falls and fall-related fractures • Improved physical function and physical activity levels.

<p>Sedentary time and recreational screen time (Saunders et al., 2020)</p>	<ul style="list-style-type: none"> • ≤ 8 hours of sedentary time per day • Break up long periods of sitting as often as possible • ≤ 3 hours of recreational screen time 	<ul style="list-style-type: none"> • Reduced risk of depression, disability, low physical activity levels, and cognitive problems • Improved body composition, markers of cardiometabolic risk and health related quality of life
<p>Sleep (Chaput, Dutil, Featherstone, Ross, Giangregorio, Saunders, Janssen, Poitras, Kho, Ross-White, & Carrier, 2020; Chaput, Dutil, Featherstone, Ross, Giangregorio, Saunders, Janssen, Poitras, Kho, Ross-White, Zankar, et al., 2020)</p>	<ul style="list-style-type: none"> • 7-9 hours (adults 18-64) and 7-8 hours (adults 65+) of high-quality sleep per night. • Consistent Sleep and Wake Schedule 	<ul style="list-style-type: none"> • Decreased risk of mortality, cardiovascular disease, type 2 diabetes, cognitive disorder, falls, accidents, injuries, obesity, hypertension, and osteoporosis. • Increased cognitive function

2.7 Individual Components of the 24-Hour Movement Guidelines and Frailty

To date, no studies has investigated the association between the full composition of 24H-MG and frailty. However, the association between each of the individual guideline components, and the combination of some of the guideline components, and frailty has been investigated. For example, performing MVPA and resistance training; reducing sedentary time; and getting a proper amount of sleep individually help prevent frailty (Blodgett et al., 2015a; Coelho-Júnior et al., 2021 Kehler, Hay, et al., 2018; Pourmotabbed et al., 2020). The next section will investigate the current available research surrounding each guideline component and frailty.

2.7.1 Sedentary Behavior and Frailty

Sedentary behavior is defined as any behavior that involves little physical movement performed in a sitting or reclined position with an energy expenditure below 1.5 Mets (Tremblay, LeBlanc, et al., 2011). Time spend in sedentary behavior (often called sedentary time) is difficult to accurately quantify but is often measured using accelerometers (Atkin et al., 2012). It is important to note that accelerometers cannot distinguish between standing still and sitting or reclining, so their quantifications of sedentary time may not accurately reflect true time spent in sedentary behavior.

A recent systematic review that included 16 studies found that both cross sectional and longitudinal evidence demonstrated that increased sedentary time was associated with worsening frailty (Kehler, Hay, et al., 2018). For example, Song et al. (2015) found that each additional hour spent sedentary led to a 36% increase in the prevalence of frailty after

two years of follow up, even after adjusting for time spent in MVPA. However, to date, no randomized control trial investigating the reduction in sedentary time and its impact on frailty exists. Therefore, most of the available data on sedentary time and frailty comes from epidemiological data (Kehler & Theou, 2019).

Longitudinal evidence shows that higher or increasing sedentary time increases one's risk of frailty (Susanto et al., 2018). Inversely, other studies have shown that as frailty increases, total sedentary time, and prolonged bouts of sedentary time both increase (da Silva et al., 2019; Kehler & Theou, 2019). This is of great importance because increased sedentary time leads to higher mortality in individuals living with frailty (Kehler & Theou, 2019; Theou et al., 2017). Substituting sedentary time with LPA or MVPA may decrease the risk of developing frailty and mortality (Godin et al., 2020; Kehler, et al., 2018).

In addition, Kehler, Clara, et al. (2018) investigated how patterns of sedentary time impacted Frailty. They discovered that every bout of sedentary time > 30 minutes increased one's risk of developing frailty. They also discovered that while the total number of breaks from sedentary time did not appear to prevent frailty, taking longer and more physically intense breaks (calculated using accelerometers counts per minute) did appear to prevent frailty.

In summary, increased sedentary time leads to increased risk of frailty (Kehler, Hay, et al., 2018). Sedentary time should be broken up with long and physically intense breaks to prevent frailty (Kehler, Clara, et al., 2018)

2.7.2 Recreational Screen time and Frailty

García-Esquinas et al., (2017) broke participants up by tertial based on how much TV they watched and found that those in the highest third of TV viewing were 47% more likely to be frail compared with those in the lowest third of TV watching. Other sedentary behaviors such as computer usage, commuting, sun-bathing, reading, or listening to music where not significantly associated with frailty. Soler-Vila et al., (2016) also found that high amounts of TV viewing increased the risk of frailty, but only for women. In summary, increased tv viewing increases the risk of frailty.

2.7.3 Moderate to Vigorous Physical Activity and Frailty

Using various frailty models, cross-sectional data showed that individuals who perform MVPA are less likely to be frail (Blodgett et al., 2015a; Chen et al., 2020; Mañas et al., 2018; Rodríguez-Gómez et al., 2020). This appears independent of the bout length, MVPA patterns (Kehler et al., 2018), or sex (Kehler et al., 2020). Individuals living with frailty spend less time performing MVPA than their pre-frail and robust peers (Kikuchi et al., 2021).

Isotemporal substitution models have shown that replacing 41 minutes of sedentary time with an equivalent amount of MVPA is associated with a clinically significant difference lower FI score of 0.03 ((Godin et. al., 2020; Eendebak et al., 2018)). Longitudinal analysis has shown that individuals performing vigorous physical activity at baseline (Rogers et al., 2017) or accumulating ≥ 5000 steps per day (Yuki et al., 2019) are less likely to develop frailty after an average follow up of 10 and 7 years respectively.

In summary, performing MVPA is important to frailty prevention, independent of bout length, MVPA patterns or sex.

2.7.4 Light Physical Activity and Frailty

Isotemporal substitution models show that replacing sedentary time with 113 minutes of LPA is associated with a clinically significantly different lower FI score (FI = 0.03) (Godin et al., 2020). Another study found that replacing sedentary time with LPA decreased frailty, but only in those living with co-morbidities (Mañas et al., 2018). However, longitudinal studies have found that LPA performed at baseline did not reduce the trajectory of frailty progression (Rogers et al., 2017; Yuki et al., 2019). Therefore, there is conflicting evidence on whether performing LPA reduces frailty.

2.7.5 Sleep and Frailty

A recent systematic review and meta-analysis found that getting < 6 hours of sleep a night or > 8 hours of sleep a night was associated with a 13% and 21% increase in the odds of developing frailty, respectively (Pourmotabbed et al., 2020). However, the association between sleep duration and frailty was not confirmed by others (Balomenos et al., 2021; Ensrud et al., 2012). In one large cross-sectional study using three different measures of frailty, sleep duration was associated with frailty in men only (Balomenos et al., 2021). However, in a longitudinal study that looked only at men, sleep duration was not associated with decreased progression of frailty or risk of mortality (Ensrud et al., 2012). However, these data need to be interpreted with caution since only very short sleep duration was investigated (<5 hours).

Negative perceived sleep quality appears to exacerbate frailty (Ensrud et al., 2012; Nóbrega et al., 2014; Shih et al., 2020; Wai & Yu, 2020) and has been suggested as a potential frailty criterion (Balomenos et al., 2021). Sleep latency may also contribute to frailty (Nóbrega et al., 2014; Pourmotabbed et al., 2020). Other sleep-related issues that may influence frailty include daytime drowsiness, sleep disorder breathing, and sleep-wake patterns (Balomenos et al., 2021; Ensrud et al., 2012; Pourmotabbed et al., 2020).

In conclusion, there is conflicting evidence on whether sleep timing influences frailty. However, the latest systematic review does show a relationship between sleep timing and frailty. Various measures of sleep quality may also influence frailty.

2.7.6 Resistance Training and Frailty

Resistance training is a highly effective frailty prevention tool (Coelho-Júnior et al., 2021; Talar et al., 2021). In fact, systematic reviews have shown that resistance training combined with protein supplementation may be the most effective way to treat and prevent frailty (Racey et al., 2021; Travers et al., 2019). Progressive resistance training is recommended as part of a frailty treatment plan (Dent, Morley, et al., 2019) and has even been shown to reverse frailty in a randomized control trial (Luger et al., 2016). Resistance training has been shown to have a positive impact in frail and pre-frail individuals on muscle strength and power; various functional outcomes such as gait speed, sit to stand performance, falls incidence and balance; body composition including reduced fat mass and increased muscle mass; and cognition (Haider et al., 2019; Liao et al., 2019; Lopez et al., 2018; Nagai et al., 2018; Talar et al., 2021). In conclusion, the evidence suggests that resistance training is an important frailty prevention tool.

2.8 Individual Components of the 24-H Movement Guidelines, Mortality, and Frailty

Risk of mortality increases as frailty increases (Dent, Martin, et al., 2019; Rockwood & Mitnitski, 2007; Spiers et al., 2021). Therefore, it is not only important to understand how adhering to the Canadian 24H-MG impacts frailty, but also how it can protect against mortality in individuals who are already living with varying degrees of frailty. This section will quickly explore the current research around how adhering to the various components of the guidelines impacts mortality in those living with different levels of frailty.

2.8.1 Sedentary Time, Frailty and Mortality

In the general population, high levels of sedentary time is associated with greater risk of mortality (Physical Activity Guidelines Advisory Committee, 2018). However, it is unclear if this relationship holds true for adults aged 60+ (Mañas et al., 2017). Regarding frailty, one study found that greater amounts of sedentary time was associated with increased risk of mortality in individuals with a FI score >0.1 but not in those with a FI ≤ 0.1 (Theou et al., 2017). Spending more time in recreational screen time has also been shown to increase the risk of mortality (Stamatakis et al., 2011). However, the relationship between recreational screen time and mortality across levels of frailty has not been investigated.

2.8.2 Physical Activity, Frailty and Mortality

Being physically active reduces the risk of mortality (Physical Activity Guidelines Advisory Committee, 2018). One study found that physically active individuals had a lower risk of mortality whether they were robust, pre-frail or frail (as measured by the FRAIL scale) when compared to in-active individuals (Higuera-Fresnillo et al., 2018). Another study found that physical activity reduced the risk of mortality in individuals diagnosed with frailty (defined using cognitive frailty) (Esteban-Cornejo et al., 2019).

Godin et al., (2020) used isotemporal substitution models to investigate the impact that replacing sedentary time with physical activity has on mortality. They defined frailty using a frailty index and classified individuals as robust ($FI \leq 0.1$), vulnerable ($0.1 < FI \leq 0.2$), mildly frail ($0.2 < FI \leq 0.3$) or moderately-severely frail ($FI > 0.3$). They found that replacing one hour of sedentary time with MVPA led to a decreased risk of mortality in vulnerable and mildly individuals living with frailty, but not in robust or moderately-severely individuals living with frailty. In addition, replacing one hour of sedentary time with LPA was associated with reduced mortality in mildly frail or moderately-severely individuals living with frailty but not in robust or vulnerable individuals.

In conclusion, physical activity has been shown to reduce risk of mortality. However, different studies have shown different relationships between physical activity and mortality when controlling for frailty status.

2.8.3 Sleep, Frailty and Mortality

A recent systematic review found that getting less than seven or more than eight hours of sleep a night is associated with an increased risk of mortality in the general

population (Chaput, Dutil, Featherstone, Ross, Giangregorio, Saunders, Janssen, Poitras, Kho, Ross-White, & Carrier, 2020). One study found that long sleep duration (>8 hours), but not short sleep duration (<6 hours), was associated with increased risk of mortality even when controlling for frailty (W. J. Lee et al., 2017). Another study similarly adjusted for frailty status and found that sleeping ≥ 10 hours a night was associated with worse mortality than <10 hours a night. (J. S. W. Lee et al., 2014). However, a 2021 study found that the length of sleep was not significantly associated with mortality when adjusting for frailty status but did find that quality of sleep did appear to influence mortality, even when adjusting for frailty status (Guida et al., 2021). A previous study found similar results, but only investigated men (Ensrud et al., 2012). In conclusion, sleep appears to be associated with mortality, but conflicting results have been identified when investigating the relationship between sleep, frailty and mortality.

2.8.4. 24-Hour Movement Behavior, Frailty and Mortality

At least two studies have found that the composition of physical activity, sleep and sedentary time throughout the entire 24 Hour day influences mortality (Clarke & Janssen, 2021; McGregor et al., 2019). Both found that the most important movement behavior was MVPA and that risk of mortality increased if time spent in MVPA was allocated to other behaviors such as sleep, LPA or sedentary time (Clarke & Janssen, 2021; McGregor et al., 2019). However, neither study considered frailty in their statistical models.

2.9 Knowledge Gap

From the current literature review, it is obvious that frailty is a world-wide health issue (O’Caoimh et al., 2021). Various interventions have been designed to prevent and

reverse frailty (Dent, Morley, et al., 2019; Walston et al., 2018). Although research has shown that many of the behaviors included in the 24H-MG are relevant to preventing frailty including time spent in physical activity (Godin et al., 2020), sedentary time (Kehler, Hay, et al., 2018), and sleep (Pourmotabbed et al., 2020), it is unclear what role the Canadian 24H-MG could play in preventing frailty. Consequently, the current literature review highlighted major limitations. First, most of these studies have not combined the 24H-MG components to investigate the association with frailty, and none have looked at how full 24-hour movement behavior impacts frailty. Second, although the relationship between mortality, frailty and individual movement behaviors covered by the 24H-MG have been investigated, none have looked at how the full composition of the 24H-MG influences mortality when considering frailty. Third, most of the study investigating frailty and these individuals' component were limited to older populations. This thesis will first, fill the gap in the current literature by identifying whether the individual's component and the full 24H-MG are associated with frailty levels in adults and older adults. In addition, it will investigate whether the individual's component and the full 24H-MG are associated mortality in individuals of different frailty levels.

2.10 Objective and Hypothesis

There were two objectives in this study. The first objective used a cross sectional design, while the second objective used a prospective design.

Objective 1: To investigate the cross-sectional association between meeting the complete 24H-MG, adherence to the individual components of the 24H-MG, and frailty levels in adults and older adults. It is hypothesized that both meeting the complete 24H-MG and

adherence to the individual components of the 24H-MG will be associated with lower frailty levels in adults and older adults.

Objective 2: To investigate the prospective association between meeting the complete 24H-MG, adherence to the individual components of the 24H-MG, and mortality in adults and older adults. It is hypothesized that both meeting the complete 24H-MG and adherence to the individual components of the 24H-MG, will reduce the risk of mortality when controlling for frailty status.

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Chapter 3 Article

THE ASSOCIATION BETWEEN ADHERENCE TO THE CANADIAN 24-HOUR MOVEMENT GUIDELINES AND FRAILTY, AND MORTALITY: A CROSS SECTIONAL AND PROSPECTIVE ANALYSIS OF THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

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Student's Contribution: Daniel Meister created the database, ran all statistical analyses, and prepared the manuscript

Conflict of Interest: None from all authors

Funding: This research received funding from the New Brunswick Health Research Foundation

ABSTRACT

Background: Studies have investigated the association between adherence to the Canadian 24-Hour Movement Guidelines (24H-MG) and chronic diseases in adults and older adults. However, its association with frailty, and all-cause mortality when adjusting for frailty, has not been investigated.

Objective: The primary objective of this study was to investigate the association between adherence to the Canadian 24H-MG, the individual components of the Canadian 24H-MG, and frailty. The secondary objective was to investigate the association between adherence to the Canadian 24H-MG, the individual components of the Canadian 24H-MG, and all-cause mortality while adjusting for frailty levels and covariates.

Methods: This study consists of both a cross-sectional and longitudinal analysis (average 10 years follow up) of 2739 individuals (age = 50.6 ± 18.1 years; male = 1370 (50.0%)) from the 2005-2006 cycle of the National Health and Nutrition Examination Survey (NHANES). The primary outcome measures were frailty and all-cause mortality. Frailty was quantified using the accumulation of deficits model (46-item frailty index), while all-cause mortality was reported as months from time of participant examination. The primary exposure variable was the combined and individual 24H-MG components according to established thresholds for adults and older adults. All analysis were stratified in two age group (young: 20-64 and older adults 65+ years).

Results: Only 16 (0.6%) individuals met all the 24H-MG components. Linear regression revealed that meeting the complete Canadian 24H-MG guidelines was associated with reduce frailty in individuals aged 20-64 ($\beta = -0.439$ (95% C.I. = -0.551;-

0.328); $p < 0.001$) and 65+ ($\beta = -0.322$ (95% C.I. = -0.490:-0.154); $p < 0.001$). In addition, meeting each guideline component was associated with lower frailty ($p < 0.05$). Meeting the MVPA guideline component had the strongest association with frailty in the 20-64 age group ($\beta = -0.144$ (95% C.I. = -0.183:-0.106); $P = 0.001$), while meeting the recreational screen time guideline component had the greatest association with frailty in the 65+ age group ($\beta = -0.131$ (95% C.I. = -0.181:-0.081); $P < 0.001$). Cox regression revealed that apart from meeting 3 guideline components in the 65+ group (HR = 0.40 (95% C.I. = 0.22 – 0.712); $P = 0.002$), there was not significantly associated with reduced mortality. Of the individual guideline components, only meeting the MVPA guideline component in the 65+ group was associated with reduced risk of mortality (HR = 0.48 (95% C.I. = 0.25-0.93); $P = 0.029$).

Conclusion: Very few individuals (less than 1%) adhere to the complete version of Canadian 24-HMG. Adherence to the Canadian 24H-MG may be protective against frailty. For frailty prevention a special emphasis should be put on increasing MVPA and decreasing recreational screen time. However, adherence to the complete 24H-MG does not protect against premature mortality when controlling for frailty status.

INTRODUCTION

In 2020, the new 24-Hour Movement Guidelines (24H-MG) for adults aged 20-65 and adults aged 65 years or older (Ross et al., 2020) were introduced to the public to compliment previously released guidelines for children and youth (aged 5-17) (Tremblay et al., 2016), and the early years (aged 0-4) (Tremblay et al., 2017). These new guidelines were implemented based on the evidence that other type of movement than moderate-to-vigorous physical activity (MVPA) including sleep (Yin et al., 2017), and sedentary behavior (Biswas et al., 2015), are associated with morbidity and mortality in adults. Therefore, considering movement over a full 24-hour period (McGregor et al., 2019) appears to be relevant when investigating movement and health, as opposed to focusing on MVPA, which generally represents < 5% of the total day (Chaput et al., 2014). Various studies have investigated the association between adherence to a comprehensive, 24-hour movement assessment and several outcomes, such as obesity (MacLeod et al., 2020), global cognition in children (Walsh et al., 2018), and premature mortality (Clarke & Janssen, 2021; McGregor et al., 2019). However, to the best of our knowledge, no research has been conducted to investigate the relationship between adherence to the 24H-MG and frailty, or whether adherence to the 24H-MG influences mortality when accounting for frailty status-

Frailty is an age-related health state of reduced physiologic reserve across multiple body systems which leads to reduced intrinsic capacity to deal with stressors (Clegg et al., 2013; Dent et al., 2019; Morley et al., 2013). Thus, individuals living with frailty are at an increased risk of disease, disability, and premature mortality (Fried et al., 2004). Although the complete 24H-MG have not been studied in relation to frailty, studies suggest that its

individual components are associated with frailty. For example, even individuals who meet less than 50% of the weekly MVPA recommendation have been shown to have lower frailty compared to individuals who do not do any MVPA (Kehler, Clara, et al., 2018). Sleeping less than 6 hours a night or sleeping more than 8 hours a night is associated with a 13% and 21% increase in risk of frailty, respectively (Pourmotabbed et al., 2020). In addition, increased sedentary behavior has been shown to increase one's risk of being frail (Kehler, Clara, et al., 2018; Kehler, Hay, et al., 2018), and evidence suggests that replacing sedentary time with 113 minutes of light physical activity (LPA) or 41 minutes of MVPA can reduce frailty by a clinically significant amount (Godin et al., 2020). Sedentary time (Theou et al., 2017), physically active levels (Higuera-Fresnillo et al., 2018), and sleeping time (Lee et al., 2017) have also all been shown to influence mortality when considering frailty status. However, there is no study yet that has investigated the association between the comprehensive 24H-MG and frailty or the 24H-MG and mortality when controlling for frailty status.

Consequently, the first objective of this study was to investigate the cross-sectional association between adherence to the new Canadian 24H-MG, its individual components and frailty in adults and older adults. It is hypothesized that adherence to the combined 24H-MG, and the individual components of the 24H-MG, will be associated with lower frailty levels. The secondary objective is to investigate the prospective association between adherence to the complete Canadian 24H-MG, its individual components, and mortality when accounting for frailty status. It is hypothesized that adherence to the complete Canadian 24H-MG and adherence to its individual components will be associated with reduced mortality regardless of frailty status.

METHODS

Study Design

Data from the 2005-2006 National Health and Nutrition Examination Survey (NHANES) cycles were used. These cycles were chosen because they are the only cycle that contains accelerometer data for PA, screen time, strength training, and sleep data. NHANES is a cross-sectional designed survey. However, by using the National Death Index, we were able to perform a prospective study looking at the longitudinal association between meeting the 24H-MG and mortality. Participants were included in our study if they meet the minimum age requirement (20 years), had at least 4 days of valid accelerometer data, had enough data to construct a valid frailty index (FI) and had no missing covariate data. We included adults above 20 so that the relationship between adherence to the 24H-MG and frailty across the adult lifespan could be quantified. Frailty increases in prevalence with age, but has been identified in both younger and older adults (Kehler et al., 2017)

Originally, the 2005-2006 NHANES Data Base contained 10384 records. Of those, 4040 were missing accelerometer data, and an additional 1450 did not have at least 4 days of valid accelerometer data. Of the 4894 remaining individuals an additional 1882 did not meet the age requirements (≥ 20) leaving 3012 remaining individuals. An additional 7 individuals were missing movement guideline data (sleep and recreational screen time use), 177 were missing data related to confounding variables (alcohol use and education level), 1 was missing mortality data and 88 were missing enough data to construct a FI. Therefore, the final sample size of the current study was 2739 individuals (Figure 1). NHANES was approved by the National Center of Health Statistics Institutional Review Board and each

participant provided written consent. Details on how NHANES was created can be found on their website (*NHANES 2005-2006 Overview*, n.d.)

Primary Exposure Variables

Physical Activity (PA) and sedentary time: PA and sedentary time were quantified using accelerometer data. Participants wore an accelerometer fixed to an elastic customized to each participant's waist circumference on their right hip. Uniaxial ActiGraph AM-7164 accelerometers were used, and intensity readings were summed over each 1-minute epoch in counts per minute. Participants were instructed to wear the accelerometer during all waking hours for seven consecutive days and to remove it at night and during water-based activities (e.g., bathing, swimming) (*NHANES 2005-2006: Physical Activity Monitor Data Documentation, Codebook, and Frequencies*, n.d.). The data were considered valid if the accelerometer had been worn for a minimum of four days, with a minimum average wear time of 10 hours per day (Troiano et al., 2008). Non-wear time was identified by at least 60 consecutive minutes of counts between 0 and 100 (Troiano et al., 2008). Sedentary time, MVPA and LPA, were identified using age and sex specific count per minute cut-points (Troiano et al., 2008).

Adherence to three of the guideline components were quantified using this data. First, the MVPA guideline component aligns with the adult Canadian PA guideline recommendation of ≥ 150 minutes of MVPA per week²³. Second, the 24H-MG further stipulate that individual should perform several hours of structured and unstructured LPA, but do not provide a specific recommendation for the number of hours. Therefore, time in LPA was quantified, and quartiles for the study sample were computed stratified by age

categories (20-39, 40-59, 60+). The highest quartile was used as the criterion for reaching this guideline. Third, the guidelines recommend ≤ 8 hours per day spend sedentary as measured by accelerometer data represented meeting this guideline.

Resistance Training: Two questions were asked in NHANES regarding resistance training. First, participants were asked “Over the past 30 days, did {you/SP} do any physical activities specifically designed to strengthen {your/his/her} muscles such as lifting weights, push-ups or sit-ups? Include all such activities even if you have mentioned them before.” If they responded yes to this question then respondents were prompted with the following question: “[Over the past 30 days], how often did {you/SP} do these physical activities? [Activities designed to strengthen {your/his/her} muscles such as lifting weights, push-ups or sit-ups]” (*NHANES 2005-2006*, n.d.). The answers to this second questions were divided by 30 and multiplied by seven to quantify number of bouts of resistance training performed per week, while those who answered “no” to the first question were assumed to not perform any resistance training. The 24H-MG recommend that individuals should perform ≥ 2 sessions of resistance training per week.

Sleep: Sleep was self-reported using the following question “The next set of questions is about your sleeping habits. How much sleep {do you/does SP} usually get at night on weekdays or workdays?”, with answers ranging from 1-11 hours/night (*NHANES 2005-2006: Sleep Disorders Data Documentation, Codebook, and Frequencies*, n.d.). The 24H-MG recommend sleeping between 7 and 9 hours for adults aged 20-64, and 7 and 8 hours for adults aged 65+ (Ross et al., 2020). Participants sleeping the recommended hours

within their age category met the sleep guideline, whereas participants sleeping either more or less hours per night did not.

Recreational screen time: Recreational screen time was also self-reported. Participants were asked the question “Over the past 30 days, on average about how many hours per day did {you/SP} sit and watch TV or videos? Would you say...” with answers being Less than 1 hour, 1 hour, 2 hours, 3 hours, 4 hours, or 5 hours or more (*NHANES 2005-2006*, n.d.). NHANES participants were also asked how much time they spent using the computer. We only used data from the TV viewing question because it was impossible to separate recreational and productive screen time in the computer usage question. For recreational screen time, participants were found to meet this guideline component if they reported watching ≤ 3 hours of TV per day.

The 24H-MG: The new 24H-MG for adults 20-64 and 65+ from the Canadian Society for Exercise Physiology (Ross et al., 2020) were adapted to create a comprehensive movement assessment. The guidelines include recommendations for PA, sitting time, and sleep. Based on the guidelines, a single dichotomous variable was created for each of the 6 components (MVPA, LPA, sedentary time, recreational screen time, sleep, and resistance training). For each guideline component, a 1 was given to the individuals when meeting the guideline for this criterion and 0 was given for not meeting the guideline. To investigate the association between the combined 24H-MG and frailty, everyone’s dichotomous variable of individual guideline was combined into a composite score: the total 24H-MG. Scores ranged from 0-6; zero represents not meeting any of the guideline components and six represents meeting the complete 24H-MG. For all regression models, those meeting

five or six of the guidelines were combined into one group due to the small number of individuals who met all the guidelines (n=16).

Co-variates: Variables adjusted for include age, sex, ethnicity, education level, and smoking and alcohol usage, all of which have been shown to influence frailty in past studies (Jazbar et al., 2021; Kojima et al., 2015; Majid et al., 2020) All these variables were self-reported through in person household interviews. Exactly which questions were asked can be obtained on the NHANES website (*NHANES Questionnaires, Datasets, and Related Documentation*, n.d.). Age in years was computed based on date of birth, with individuals ≥ 85 years of age being combined into a single category to maintain confidentiality (*NHANES 2005-2006 Demographics Data Documentation, Codebook and Frequency*, n.d.). Ethnicity was categorized for our study as either Non-Hispanic White, Non-Hispanic Black, Mexican American, or other (*NHANES 2005-2006 Demographics Data Documentation, Codebook and Frequency*, n.d.). Education level was categorized for our study as either less than grade 11; high school diploma or some college or AA degree; or college graduate or above (*NHANES 2005-2006 Demographics Data Documentation, Codebook and Frequency*, n.d.). For smoking status, participants were first asked “{Have you/Has SP} smoked at least 100 cigarettes in {your/his/her} entire life?” If they responded yes, they were then prompted to answer the question “{Do you/Does SP} now smoke cigarettes?” (*NHANES 2005-2006: Smoking - Cigarette Use Data Documentation, Codebook, and Frequencies*, n.d.). We categorized the participants as non-smokers if they had smoked less than 100 cigarettes in their lifetime, past smokers if they had smoked more than 100 cigarettes in lifetime but had since quit, and current smokers if they had smoked more than 100 cigarettes in lifetime and were still smoking. For alcohol consumption, we

used three survey questions to classify individuals as either non/light drinkers (0-1 drinks/day), moderate drinkers (2 drinks/day) and heavy drinkers (>2 drinks/day). The first survey question asked was “In any one year, {have you/has SP} had at least 12 drinks of any type of alcoholic beverage?” The second survey question asked was “In {your/SP's} entire life, {have you/has he/ has she} had at least 12 drinks of any type of alcoholic beverage?” The third question asked was “In the past 12 months, on those days that {you/SP} drank alcoholic beverages, on the average, how many drinks did {you/he/she} have?”. Details can be found on the NHANES website (*NHANES 2005-2006-Alcohol Use Data Documentation, Codebook and Frequency*, n.d.).

Primary Outcome

Frailty: Frailty levels were defined using The Accumulation of Health Deficits Model (Rockwood & Mitnitski, 2007). This model has been operationalized to create a FI which quantifies frailty by dividing the number of deficits observed by the total number of potential deficits measured (Rockwood & Mitnitski, 2007). In the current study, we used a modified version of the 46-item deficit model developed and validated for NHANES by Blodgett et al. (2015a), which included a combination of self-reported and objectively measured data spread through 5 main categories: comorbidities, functions, signs and symptoms, laboratory values, and others self-reported information (Blodgett et al., 2015a). Individuals who had a minimum of 80 % of the 46-item were included in the analysis. As an example, if someone had 19 of the 46 items measured being identified as deficits, their FI score would be 19/46 or 0.442. Therefore, FI range from 0 to 1. Past studies have used

cut-offs of 0 - <0.1 to represent robust; 0.1 - <0.2 to represent vulnerable, 0.2 - <0.3 to represent mildly frail and >0.3 to represent moderately to severely frail.

Mortality: Mortality-Death Certificate records from the National Death Index (NDI) were linked with records from the NHANES database. These records provide information regarding the cause of death, as well as the time to death recorded in months from the day the participant's examination occurred with a total follow up time of 10 years. For this study, we focused on all-cause mortality. Months to death was converted to years to death by dividing months to death by 12. The data was obtained from the NHANES website where additional documentation regarding the dataset can be found (*NCHS Data Linkage - Mortality Data - Public-Use Files*, n.d.).

Statistical Analysis

Descriptive data was reported using mean \pm standard deviation (SD) for continuous variables and n (%) for categorical variables. A t-test and chi-squared test were used to compare the age and sex differences, respectively, between the included and excluded samples.

For the linear regression, a box-cox transformation was applied to the data so that it met the normality assumption. Multiple linear regression was used to investigate the association between adherence to the 24H-MG and frailty, and to investigate the association between adherence to each of the individual guideline components and frailty. Linear regression results are reported as β -values with standard error. Cox proportional hazard models were then created to estimate the risk of all-causes mortality based on the composite score of the complete 24H-MG, as well as meeting the individual guideline components.

Cox proportional hazard results will be reported as hazard ratios with 95% confidence intervals. All models were adjusted for age, sex, ethnicity, education level, cigarette, and alcohol usage. An unadjusted cox regression model, and model adjusted for all co-variates and frailty was also run. Since an interaction term was found to be significant for age ($p < 0.05$), all regression models were ran by age group (20-64 and 65+ yrs). Data management and statistical analysis were performed using RStudio software version 4.1.2. An alpha level of 0.05 was used for all analyses. Statistics accounted for sample weights to enhance external validity of our results.

RESULTS

Our sample consisted of 2739 individuals with an average age of 50.6 ± 18.1 years, 1370 (50.0%) of whom identified as male. Information on participant ethnicity, education levels, and smoking and alcohol are described in Table 1. The average FI of our sample was 0.122 ± 0.104 . On average, our sample met 2.63 ± 1.29 guideline components. We compared participant excluded to participant kept in the current analysis and found that excluded participants were significantly younger (45.58 ± 19.9 vs. 50.6 ± 18.1 years) and less proportionately male (45.4% vs 50%).

Table 2 describes how many individuals were meeting each individual guideline components, as well as how many guideline components individuals were following. The recreational screen time guideline component was the most followed ($n = 2106$ (76.9%)), while the strength training guideline component was the least followed ($n = 512$ (18.7%)). 111 (4.1%) individuals did not meet any of the movement guidelines and 16 (0.6%) met the complete 24H-MG. The most common number of guideline components followed was 3 ($n = 725$ (26.5%))

The results of the linear regression analysis (Table 3) showed that meeting at least one of the guideline components in the 20-64 group ($\beta = -0.144$ (95% C.I. = -0.252 ; -0.035); $P = 0.009$) and 2 in the 65+ group lead to a significant reduction in FI score ($\beta = -0.111$ (95% C.I. = -0.193 ; -0.029); $P = 0.008$). Meeting each of the individual guideline components also lead to a significant decrease in FI, except for the sleep guidelines in the 65+ group ($\beta = -0.035$ (95% C.I. = -0.083 ; 0.012); $P = 0.094$). Meeting the MVPA guideline component had the strongest association with decreased FI in the 20-64 age group ($\beta = -$

0.144 (95% C.I. = -0.183:-0.106; P = <0.001), while meeting the recreational screen time guideline component had the strongest association with FI in the 65+ age group ($\beta = -0.131$ (95% C.I. = -0.181:-0.081); P = <0.001).

In the 20-64 age group, unadjusted Cox Regression showed that meeting 2, 3, or 4 guideline components and meeting the MVPA and recreational screen time guideline components was associated with reduced risk of mortality. However, once the model was adjusted for known co-variates, no association was observed between adherence to the guidelines or the individual guideline components and mortality. This lack of association remained once frailty was added to the model (figure 3). Frailty was significantly associated with mortality (for every 0.01 increase HR = 1.05 (95% C.I. = 1.04 – 1.07) P = <0.001)

In the 65 + age group, unadjusted Cox Regression showed that meeting 2, 3, 4, or 5-6 of the guideline components and meeting the MVPA, recreational screen time, sedentary time and resistance training guideline components was significantly associated with reduced frailty. When adjusting for known co-variates, only meeting 2 (HR = 0.60 (95% C.I. = 0.38 -0.93) P = 0.022) or 3 guidelines (HR = 0.32 (95% C.I. = 0.18 – 0.58) P = <0.001), and meeting the MVPA (0.45 (95% C.I. = 0.22 – 0.91) P= 0.025) and recreational screen time guideline (HR = 0.67 (95% C.I. = 0.51 – 0.90) P = 0.007) components individually was associated with reduced risk of mortality. Once the model was further adjusted for frailty, only meeting 3 guideline components (HR = 0.40 (95% C.I. = 0.22 – 0.71); P = 0.002) was associated with reduced mortality when looking at the complete guidelines. Of the individual guidelines, only meeting the MVPA guideline

component (HR = 0.48 (95% CI = 0.25-0.93); P = 0.02) was associated with reduced risk of mortality. Frailty was also associated with increased risk of mortality (for every 0.01 increase HR = 1.04 (95% C.I. = 1.03 -1.05) P = <0.001).

DISCUSSION

The current study provides relevant results for the management and the treatment of frailty in adults and older adults. First, we found that in adults and older adults meeting at least one or two components of the 24H-MG was protective against frailty. Second, the MVPA and recreational screen time guideline component were the most associated with decreased frailty in younger adults compared to recreational screen time and light PA in older adults. Third, only older adults meeting 3 3 guideline components had a lower risk of premature all-cause mortality, with following the MVPA guideline component being the strongest predictor of all-cause mortality in adults 65+. These results are important because they provide insight into how the 24H-MG can be leveraged for the management and treatment of frailty, and prevention of mortality in adults of different frailty score.

Our linear regression results showed that adhering to at least one guideline component in the 20-64 age group and at least two guideline components in the 65+ group was associated with a significant reduction in FI score and there was a dose response relationship between the number of guideline components met and reduction in FI score. This adds to the growing body of evidence that behavior over the 24-hour day is important to health (Clarke & Janssen, 2021; MacLeod et al., 2020; McGregor et al., 2019; Walsh et al., 2018). These results also support past studies that have found that replacing sedentary time with LPA and MVPA helps prevent frailty (Blodgett et al., 2015b; Chen et al., 2020; Mañas et al., 2018; Rodríguez-Gómez et al., 2020). This study is unique since 1) is the first study looking at the complete 24H-MG and its association with frailty in a large sample of young adults and older adults, and 2) it includes behavior such as recreational screen time,

sleep and strength training that have not been considered in other studies of movement behavior and frailty. Overall, our data are important since they help better understanding the relationship between the 24H-MG and frailty on the whole spectrum of age affected by frailty.

Except for the sleep guideline components in the 65+ group, adherence to each individual guideline component in both the 20-64 and 65+ age group was also associated with lower FI score. Of the individual guideline components, meeting the MVPA guideline component in the 20-64 age group and the recreational screen time guideline component in the 65+ age group was associated with the greatest decrease in FI score. This supports past studies that found that performing MVPA prevents frailty (Godin et al., 2020) in both males and females (Kehler et al., 2020) and when considering both bout and sporadic MVPA (Kehler, Clara, et al., 2018). Our study adds to these results by showing that performing MVPA is associated with lower FI score in both a younger (20-64) and older (65+) sample, as past studies have only considered older adults (50+).

Our results also agree with past studies that found that increased sedentary time is associated with increased frailty (Kehler, Hay, et al., 2018) and that recreational screen time may be more dangerous than other sedentary behavior when considering frailty prevention (García-Esquinas et al., 2017). These results are relevant because they demonstrate that clinicians who are using the 24H-MG to prevent frailty should specifically emphasize the danger of recreational screen viewing when counseling against excessive sedentary time.

Meeting the sleep length guideline component was shown to prevent frailty in the 20-64 age group. This confirms results from a systematic review that found that both long and short sleep duration was predictive of frailty (Pourmottabed et al., 2020). Nevertheless, other studies have found no association between sleep duration and frailty (Ensrud et al., 2012), which align with our lack of association observed in individuals aged 65+. In the systematic review by Pourmottabed et al (2020) they used the cut offs of < 6 hours of sleep a night or > 8 hours of sleep a night to investigate the relationship between sleep duration and frailty. They found that long sleep duration increased frailty risk by more (21%) than short sleep duration (13%). It is possible that the range of sleep duration included in the 24H-MG for adults 65+ (7-8 hours) is too narrow and sleep durations such as 6 hours may still be enough to prevent frailty. In addition, the 24H-MG contain the recommendation that sleep timing should be consistent. This could not be measured in our study as it was not recorded in NHANES. Nevertheless, sleep timing and different extremes of sleep duration should be considered in future studies to better understand how they can help preventing frailty.

In both the 20-64 and 65+ age group in our study, meeting the resistance training guideline component was associated with reduced frailty. International clinical practice guidelines released in 2019 recommend progressive resistance training as part of a frailty management plan (Dent et al., 2019). However, to the best of our knowledge, past studies investigating the relationship between combined movement behavior and frailty have not included resistance training (Godin et al., 2020; Kehler et al., 2020). Therefore, our research adds to the scientific literature by including resistance training in our analysis and demonstrates that performing resistance training as recommended by the 24H-MG is

sufficient to lower frailty. To better understand frailty prevention, future studies should investigate the optimal number of sessions of resistance training per week needed to prevent frailty.

A secondary finding of our study is that there was no clear relationship between adherence to the 24H-MG and risk of all-cause mortality when controlling for frailty status. Only meeting three guideline components in the 65+ group was associated with reduced mortality. To the best of our knowledge, this is the first study that has investigated the relationship between 24H-MG and mortality while controlling for frailty status. Two other studies have looked at the relationship between 24H-MG and mortality (Clarke & Janssen, 2021; McGregor et al., 2019). While both found that daily movement composition is related to mortality, neither controlled for frailty status, a known predictor of mortality (Kojima et al., 2018). These studies also did not consider recreational screen time or strength training, which are important predictors of mortality (Ross et al., 2020).

Of our individual guideline components, only the MVPA guideline component in the 65+ group was significantly associated with reduced frailty. A past study investigating mortality, frailty and movement behavior found that replacing sedentary time with 38 minutes or 18 minutes per day of MVPA in vulnerable and mildly frail individuals respectively reduced risk of mortality by 50%, but replacing sedentary time with MVPA did not impact mortality in non-frail or moderately-severely frail individuals (Godin et al., 2020). Interestingly, our 20-64 age group had an average FI of 0.094 (non-frail) while our 65+ age group had a FI of 0.202 (mildly frail) meaning that the average FI and association between MVPA and risk of mortality are similar between the two studies. However, the

study also found that replacing sedentary time with LPA reduced risk of mortality in mildly and moderately-severely frail individuals (Godin et al., 2020), which was not supported by our study as LPA was not associated with mortality. This difference could be explained by the way that LPA was quantified in the two studies. In our study, we identified whether individuals had met the LPA guideline component based on quantiles, whereas Godin et al. (2020) used isothermal substitution models to investigate how replacing sedentary time with LPA impacted frailty. Once clear recommendations are determined on how much LPA an individual should accumulate, the relationship between meeting this guideline, frailty and mortality should be revisited.

Several limitations of this study need to be discussed. First, recreational screen time, strength training, and sleep time were both self-reported and might have influenced the association observed. Second, accelerometers cannot quantify water activities, movement performed when sitting (e.g.: biking), or upper body movement; cannot distinguish between quiet standing and sitting; and do not properly assess activity at very low and very high intensities. In addition, accelerometers were not given to NHANES participants in a wheelchair, which should be considered in frail populations who often have mobility issues. Third, high amounts of LPA were determined using an arbitrary value based on quartiles due to the lack of clear cut-points and research. While these limitations may have affected the results of our study, its strengths include a large sample size, statistical analyses performed using survey weights and adjusted for potential confounding variables, and the use of accelerometer data, which is more valid than commonly used PA questionnaires.

In conclusion, the individual components of the 24H-MG are associated with lower frailty and therefore should be used to inform the prevention and treatment of frailty in adults and older adults. Increasing MVPA and reducing recreational screen time appears to have the greatest influence on frailty and should be emphasized for frailty management. Overall, there was not a clear relationship between mortality and following the complete 24H-MG when adjusting for frailty status.

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Table 3: General Characteristics of the Study Sample

Age (years)	50.6 ± 18.1
Male n (%)	1370 (50.0%)
Ethnicity	
Non-Hispanic white n (%)	1445 (52.7%)
Non-Hispanic black n (%)	560 (20.4%)
Mexican American n (%)	560 (20.4%)
Other	174 (6.3%)
Education	
Grade 11 or Below n (%)	691 (25.2%)
High School Diploma or Some College or AA Degree n (%)	1460 (53.3%)
College Graduate/Above n (%)	588 (21.47%)
Smoking Status	
Current Smoker n (%)	522 (19.1%)
Past Smoker n (%)	774 (28.3%)
Non-Smoker n (%)	1442 (52.7%)
Alcohol Use	
Heavy Drinker n (%)	629 (23.0%)
Moderate Drinker n (%)	503 (18.4%)
Light/Non-Drinker n (%)	1607 (58.7%)
Frailty	
Frailty Index mean (range 0-1)	0.122 ± 0.104
Movement Guidelines	
Guideline components followed	2.63 ± 1.29

Data are presented as mean ± SD for continuous variable and n (%) for categorical variables.

Table 4: Number of individuals meeting movement guidelines

	Number of People n (%)
Individual Guidelines	
MVPA Guideline	998 (36.4%)
Light Physical Activity Guideline	688 (25.1%)
Sedentary Time Guideline	1286 (47.0%)
Recreational Screen Time Guideline	2106 (76.9%)
Sleep Guideline	1617 (59.0%)
Strength Training Guideline	512 (18.7%)
# of Guidelines Met	
0 Guidelines	111 (4.1%)
1 Guideline	456 (16.7%)
2 Guidelines	713 (26.0%)
3 Guidelines	725 (26.5%)
4 Guidelines	536 (19.6%)
5 Guidelines	182 (6.6%)
6 Guidelines	16 (0.6%)

Data are presented as n (%) for categorical variables.

Table 5: Linear regression analysis looking at the relationship between adherence to the Canadian 24-Hour Movement Guidelines, it's individual components and frailty.

	Adults Aged 20-64			Adults Aged 65+				
	β -Value	95% CI	P-value	β -Value	95%CI	P-value		
Individual Guidelines								
MVPA Guideline	-0.144	-0.183	-0.106	< 0.001	-0.093	-0.174	-0.012	0.002
Light Physical Activity Guideline	-0.090	-0.131	-0.050	< 0.001	-0.109	-0.165	-0.053	< 0.001
Sedentary Time Guideline	-0.070	-0.108	-0.032	< 0.001	-0.051	-0.104	0.001	0.021
RST Guideline	-0.138	-0.191	-0.086	< 0.001	-0.131	-0.181	-0.081	< 0.001
Sleep Guideline	-0.041	-0.078	-0.004	0.013	-0.035	-0.083	0.012	0.094
Strength Training Guideline	-0.040	-0.087	0.007	0.038	-0.099	-0.157	-0.041	< 0.001
# of Guideline Components Met								
1 Guideline Component	-0.144	-0.252	-0.035	0.009	-0.026	-0.105	0.054	0.534
2 Guideline Components	-0.309	-0.412	-0.206	< 0.001	-0.111	-0.193	-0.029	0.008
3 Guideline Components	-0.344	-0.445	-0.244	< 0.001	-0.162	-0.248	-0.076	< 0.001
4 Guideline Components	-0.373	-0.476	-0.270	< 0.001	-0.242	-0.336	-0.148	< 0.001
5-6 Guideline Components	-0.439	-0.551	-0.328	< 0.001	-0.322	-0.490	-0.154	< 0.001

All models are adjusted for age, sex, education, race, smoking status, and alcohol use. MVPA = moderate to vigorous Physical Activity; RST = Recreational Screen Time.

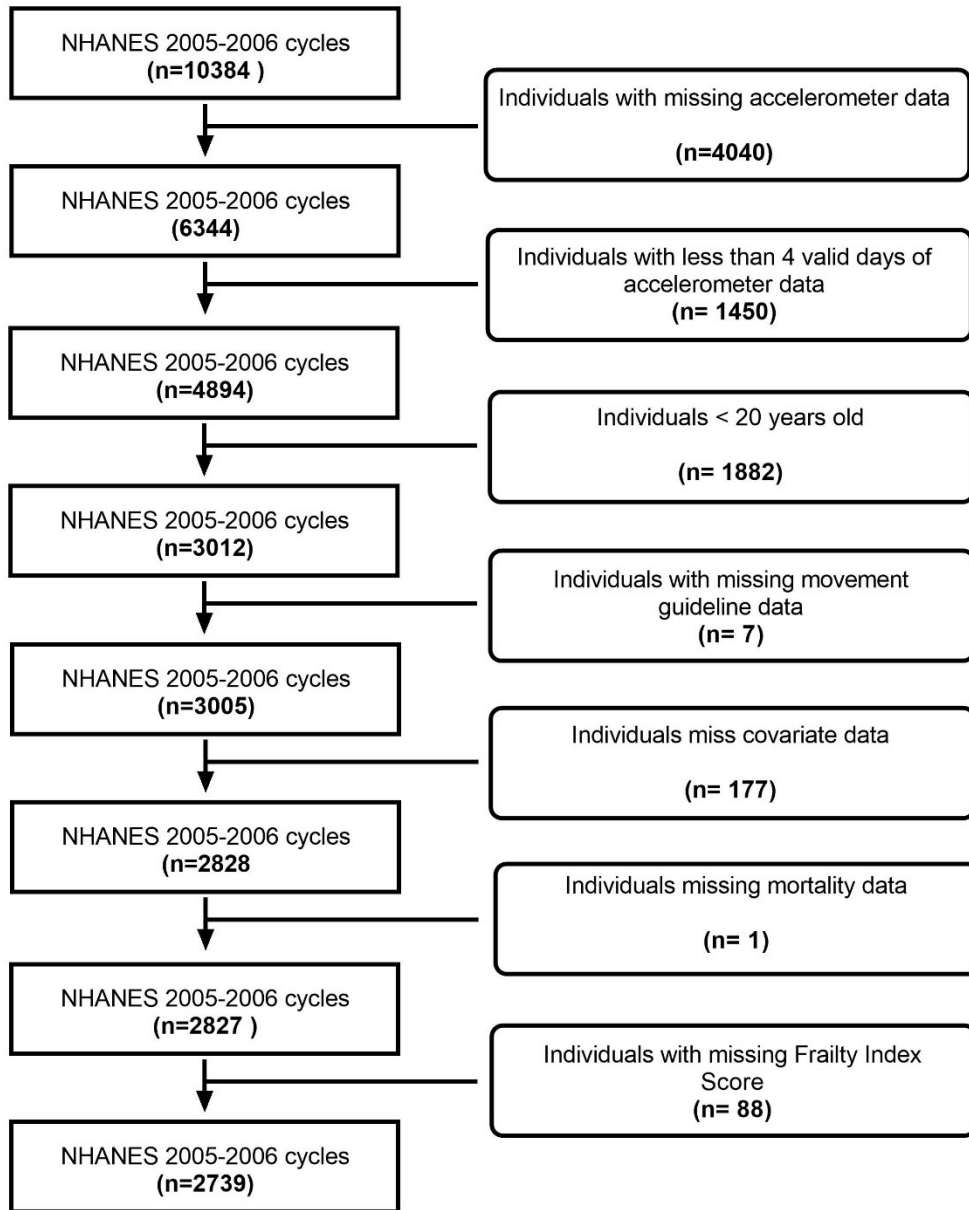
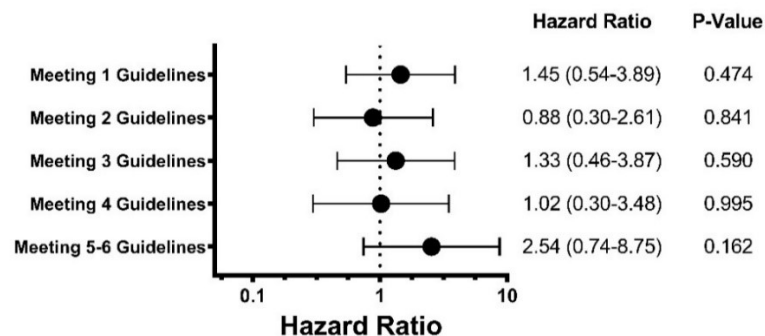
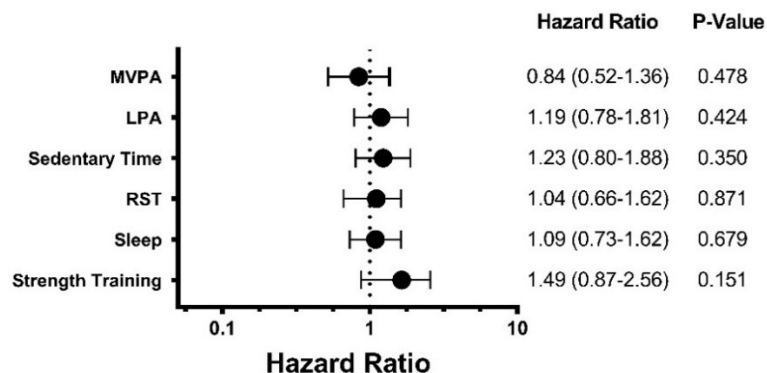


Figure 4: Final sample flow chart

Individual Guidelines

Complete Guidelines

Aged 20-64



Aged 65+

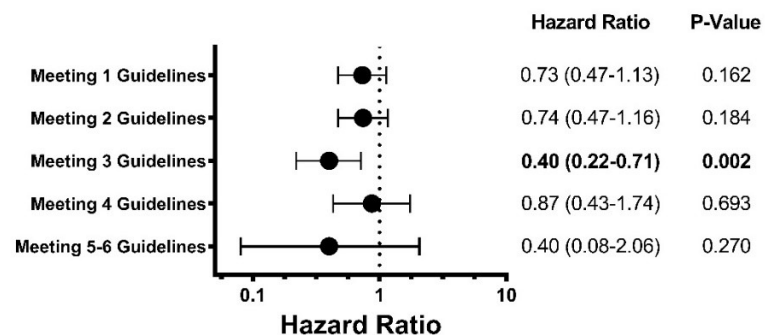
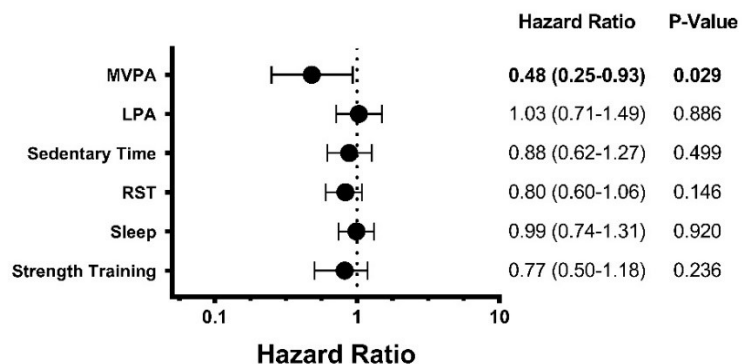


Figure 5: Cox Regression results looking at the relationship between adherence to the Canadian 24-Hour Movement Guidelines, individual guidelines components and mortality when adjusting for frailty status. MVPA = Moderate to Vigorous Physical Activity; LPA = Light Physical Activity; and RST = Recreational Screen Time.

Appendix

Table 6: The 46-Items included in our frailty index

Self-Reported Items	Lab Items
1. Angina/ angina pectoris	1. Pulse rate (60-99 bpm)
2. Heart attack	2. Blood pressure- systolic (90-140 mmHg)
3. Coronary heart disease	3. Pulse pressure (30-60 mmHg)
4. Stroke	4. Glycohemoglobin levels ($\leq 5.70\%$)
5. Thyroid condition	5. Mean cell volume (80-96 fL)
6. Cancer	6. Platelet count SI (150-450 unit 1000 cells/uL)
7. Arthritis	7. Glucose, serum (3.9-6.1 mmol/L)
8. High blood pressure	8. Sodium (136-142 mmol/L)
9. Diabetes mellitus	9. Blood urea nitrogen (3-20 mg/dL)
10. Weak/failing kidneys	10. Bicarbonate (≤ 28 mmol/L)
11. Confusion or inability to remember things	11. Total cholesterol (≤ 6.47 mmol/L)
12. Difficulty managing money	12. Red cell distribution width ($\leq 14.6\%$)
13. Difficulty stooping, crouching, kneeling	13. Lactate dehydrogenase (≤ 190 U/L)
14. Difficulty lifting or carrying	14. Triglyceride (< 1.67 mmol/L)
15. Difficulty preparing meals	15. Alkaline phosphatase (≤ 115 U/L)
16. Difficulty walking between rooms on same floor	16. Creatinine (Men: 60-110, Women: 45-90 $\mu\text{mol/L}$)
17. Difficulty standing up from armless chair	17. Hemoglobin (Men: 13.5-18, Women: 12-16 g/dL)
18. Difficulty getting in and out of bed	18. Uric acid (Men: 240-510, Women: 160-430 $\mu\text{mol/L}$)
19. Difficulty using fork and knife	19. Total calcium (2-2.5 mmol/L)
20. Difficulty dressing yourself difficulty	
21. Difficulty grasping/holding small objects	
22. Difficulty attending social event	
23. Self-reported health	
24. Frequency of healthcare use	
25. Health compared to 1 year ago	
26. Overnight hospital stays	
27. Medications	

Curriculum Vitae

Candidate's full name: Daniel Meister

Universities attended (with dates and degrees obtained):

- 1) University of New Brunswick (2017-2021) Bachelor of Science in Kinesiology w/ Honours;

Publications:

- 1) Keshavarz M., Sénéchal M, Dombrowski SU, Meister D & Bouchard, D.R. Examining the role of sex on the benefits of muscle-strengthening activities for people living with obesity. (Health Science Reports, 2022)

Conference Presentations:

- 1) Oral Conference Presentation: "D. Meister, S. Kehler, D. Bouchard, J. Boudreau, M. Sénéchal, Effect of Adherence to the Canadian 24-Hour Movement Guidelines on Premature Mortality in Individuals Living With Different Levels of Frailty. Atlantic Provinces Exercise Scientists and Socio-Culturalists (APES+) Conference. March, 2021"
- 2) Poster Conference Presentation: "D. Meister, S. Kehler , D.R. Bouchard, J. Boudreau, M. Sénéchal. The Association between Adherence to the Canadian 24-Hour Movement Guidelines and Frailty: A Cross Sectional Study. New Brunswick Health Research Foundation (NBHRF) Health Research Week. November 15-19, 2022"