

Wearable-based analysis of everyday life performances of individuals with frailty in advanced age

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If it were not for the great variability among individuals, medicine might as well be a science and not an art.

Sir William Osler, 1892

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Abbreviations

ADL	Activities of Daily Living
AMPS	Assessment of Motor and Process Skills
APS	Acceleration per Second
BMR	Basal metabolic rate
CFS	Clinical Frailty Scale
CHS	Cardiovascular Health Study
DALY	Disability-adjusted life years
DEGS1	German Health Interview and Examination Survey for Adults
DIT	Diet induced thermogenesis
EE	Energy expenditure
ENMO	Euclidean Norm Minus One
FI	Frailty Index
FIM	Functional Independence Measurement
IMU	Inertial measurement unit
MAD	Mean Amplitude Deviation
MAX95	95 th Percentile of Acceleration Peaks
MeSH	Medical Subject Headings
MET	Metabolic equivalent of task
MLTQ	Minnesota Leisure Time Questionnaire
MMSE Mini	Mental State Examination
MPA	Mean Peak Acceleration
MVPA	Moderate-to-vigorous physical activity
PA	Physical activity
PCA	principal component analysis
PPS	Peaks per Second
PSMS	Physical self-maintenance scale
RA	Relative Activity
RATIO	Peak Ratio
SHARE	Survey of Health, Aging and Retirement in Europe
SPPB	Short Physical Performance Battery
STD	Peak Standard Deviation
SUM	Weighted Sum of Acceleration per Second
TD	Trial Duration
TUG	Timed up & go
UE	upper extremity

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Abstract

The demographic shift is leading to increased chronic diseases and geriatric syndromes like frailty. Frailty is a multidimensional syndrome indicated by a reduced individual reserve to cope with internal or external stressors, with inconsistent definitions in the literature. Physical frailty, as one of the most famous concepts, often leads to an unfavorable prognosis, with progress frequently measured by the level of independence maintained in the home environment. While widely accepted, physical frailty has limitations (e.g., time consuming) in clinical use. Consequently, efforts are made to simplify frailty assessments by including the assessment of a single physical parameter or the utilization of instrumented methods assessing a person's ability to maintain their autonomy and effectively manage their daily activities, as these activities are deemed more reflective of the inherent functional status of older individuals than less functional activities. Therefore, evaluating complex instrumental activities of daily living (i-ADL), where upper limb function is crucial, may be essential for individuals with frailty. Still, the role of upper limb performance in daily activities in relation to physical frailty has been insufficiently studied. As the capacity to execute a specific activity does not necessarily correlate with active daily engagement, it becomes crucial to evaluate both a person's capability to perform i-ADL tasks and the frequency of their engagement, as this reflects and contributes to the frailty syndrome. Given the common use of self-reported assessments and considering their inherent limitations, further comparing them to actual activity is essential.

The overall aim of this cumulative dissertation was to examine daily life performances of older adults with frailty. Specifically, the thesis explored the impact of the frailty syndrome on two specific i-ADL and further investigated the relationship between daily activity behavior, as an indicator of activity volume, and individuals' self-reported and perceived frailty status.

Three studies were conducted. In study I (pilot-study) and II, we assessed the use of a smartwatch to measure complex ADL performance and its consistency across tasks in relation to frailty. Results supported the use of an upper limb kinematic approach with a wrist-worn device for the assessment of naturally paced ADLs. While trial duration was not effective for assessing ADLs in older individuals and differentiating between levels of frailty, higher frailty levels were associated with slower, more monotonous upper limb movements. Furthermore, there was no task-frailty interaction, and agility and smoothness had the strongest correlations between tasks. Study III explored the relationship between sensor-based daily activity metrics (like walking and upper limb activity) and self-reported frailty in an at-risk cohort. We further analyzed behavioral patterns and validated self-reports using clustering methods to deepen our understanding of this association. The results supported the idea of altered ADL behavior in frailty, revealing discrepancies between self-reported frailty and daily activity levels. Specifically, older women perceived themselves in poorer condition, as evidenced by their upper limb activity profiles.

In conclusion, the assessment of upper limb function in frail elderly suggests that time-based measures, such as trial duration, may not be suitable for differentiating ADL performance in older adults with and without frailty. Nonetheless, certain kinematic parameters appeared to effectively distinguish between

frailty levels during naturally paced ADL tasks. Hence, kinematic parameters collected during upper extremity ADL tasks could offer valuable insights into the motor status of older adults across varying frailty stages. The findings highlight potential biases when examining the relationship between daily activity behavior, which reflects activity volume or engagement, and self-perceived frailty status – a commonly used initial screening method. In particular, older women who were dependent on walking aids tended to rate themselves as frail, even if their upper limb activity levels remained high. In summary, the results of this cumulative dissertation not only demonstrate the possibility to distinguish and evaluate upper limb performances between different levels of frailty by using a wearable-based method, they also could contribute to the discussion about the definition of frailty.

Zusammenfassung

Zusammenfassung

Der demographische Wandel führt neben einer Zunahme chronischer Krankheiten auch zum Anstieg geriatrischer Syndrome wie dem Frailty Syndrom. Frailty ist ein multimodales Syndrom, das durch eine reduzierte individuelle Reserve zur Bewältigung interner oder externer Stressoren gekennzeichnet ist. Bislang besteht kein Konsens über die Definition des Syndroms. Körperliche Frailty, als eines der bekanntesten Konzepte, führt häufig zu einer ungünstigen Prognose, wobei das Fortschreiten oft am Grad der Unabhängigkeit im häuslichen Umfeld gemessen wird. Obwohl weitgehend akzeptiert, hat körperliche Frailty in der klinischen Anwendung ihre Grenzen. Demnach werden Anstrengungen unternommen, die Erfassung von Frailty durch die Erhebung einzelner physischer Parameter oder instrumenteller Methoden zu vereinfachen, die die Fähigkeit einer Person zur Aufrechterhaltung ihrer Autonomie und zur effektiven Bewältigung der täglichen Aktivitäten beurteilen. Diese Aktivitäten spiegeln besonders den inhärenten Funktionsstand der Personen wider. Daher scheint speziell die Bewertung komplexer instrumenteller Aktivitäten des täglichen Lebens (i-ADL), bei denen die Funktion der oberen Extremität entscheidend ist, wesentlich. Dennoch ist die Rolle der oberen Extremität bei den täglichen Aktivitäten von Frailty betroffener Personen unzureichend erforscht. Da die Fähigkeit, eine bestimmte Aktivität auszuführen, nicht zwangsläufig mit einer regelmäßigen Ausführung im täglichen Leben in Zusammenhang steht, ist es wichtig, sowohl die Fähigkeit einer Person zur Durchführung von i-ADL als auch die Häufigkeit ihrer Ausführung im Alltag zu bewerten, denn gerade das Aktivitätslevel der Person spiegelt Frailty und dessen Fortschreiten wider. Angesichts der weit verbreiteten Verwendung von Selbstberichten zur Erfassung von Frailty ist es entscheidend, diese mit der tatsächlichen täglichen Aktivität abzugleichen.

Das übergeordnete Ziel dieser kumulativen Dissertation war es, die Leistungen im alltäglichen Leben älterer Menschen mit und ohne Frailty zu untersuchen. Hierbei wurde speziell die Auswirkung des Frailty Syndroms auf spezifische i-ADL untersucht und weiter die Beziehung zwischen dem Alltagsverhalten als Indikator für das Aktivitätsvolumen und dem selbstberichteten Frailtystatus der Individuen evaluiert. Dabei wurden drei Studien durchgeführt. In Studie I (Pilotstudie) und II wurde der Einsatz einer Smartwatch zur Messung der komplexen ADL-Performanz und deren Konsistenz über Aufgaben hinweg in Bezug auf das Frailtylevel untersucht. Die Ergebnisse befürworten den Gebrauch eines kinematischen Ansatzes für die obere Extremität unter Verwendung eines am Handgelenk getragenen Sensors zur Erfassung von ADL. Während die Versuchsdauer sich als nicht aussagekräftig für die Bewertung von ADL bei älteren Personen zeigte, waren höhere Grade von Frailty mit langsameren, monotoneren Bewegungen der oberen Extremität verbunden. Darüber hinaus gab es keine Interaktion zwischen Aufgabe und Frailtylevel, und Agilität und Bewegungsfluss wiesen die stärksten Korrelationen zwischen den Aufgaben auf. Studie III untersuchte die Beziehung zwischen sensorgestützten täglichen Aktivitätsmetriken (wie Gehen und Aktivität der oberen Extremität) und selbstberichteter Frailty. Weiter wurden Verhaltensmuster analysiert, um das Verständnis dieser Assoziation zu vertiefen. Die Ergebnisse unterstützten die Idee einer veränderten ADL-Performanz und zeigten Diskrepanzen zwischen den Selbstberichten von Frailty und täglichen Aktivitätsniveaus auf.

Insbesondere Frauen schätzten sich in einem schlechteren Zustand ein, entgegen des aufgezeigten Aktivitätsprofils der oberen Extremität.

Mit Blick auf die Ergebnisse der Einzelstudien lässt sich festhalten, dass die Bewertung der Funktion der oberen Extremität bei älteren Personen mit Frailty darauf hindeutet, dass zeitbasierte Metriken wie Versuchsdauer für die Bewertung der ADL-Performanz nicht geeignet sind. Dennoch scheinen sich bestimmte kinematische Parameter, für die in natürlicher Geschwindigkeit ausgeführten ADL-Aufgaben, effektiv zwischen den Frailtystufen zu unterscheiden. Folglich könnten kinematische Parameter, die während der ADL-Aufgaben der oberen Extremität erfasst werden, wertvolle Information über den motorischen Zustand älterer Personen in unterschiedlichen Frailtystufen liefern. Weitere Untersuchungen zur Verbindung zwischen dem täglichem Aktivitätsverhalten, welches das Aktivitätsvolumen oder Engagement widerspiegelt, und dem subjektiv eingeschätzten Frailtystaus – einer gängigen Methode zum initialen Screening, zeigten potenzielle Verzerrungen auf. Insbesondere älteren Frauen, die Gehhilfen verwendeten, tendierten dazu, sich selbst als frail einzuschätzen, auch wenn ihre Aktivitätsniveaus der oberen Extremität ein hohes Level aufwiesen. Zusammenfassend verdeutlichen die Ergebnisse der vorliegenden Dissertation nicht nur die Möglichkeit zur Bewertung der Leistung der oberen Extremität verschiedener Frailtygrade mittels einer tragbaren Methodik, sondern könnten ebenso zur Diskussion über die eigentliche Definition des Frailty-Begriffs beitragen. Chapter 1

General Introduction

Introduction

1. Introduction

The global population is experiencing a significant demographic shift, marked by a growing percentage of elderly individuals. The number of people aged over 65 years is anticipated to rise from 524 million in 2010 to an estimated 1.5 billion by 2050, constituting around 16 % of the world's population (World Health Organization, 2002). The most elderly individuals, along with the most rapidly aging population, are found in less developed nations. From 2010 to 2050, the population of older individuals in these less developed countries is projected to surge by over 250 %, whereas in developed countries, the increase is anticipated to be 71 % (World Health Organization, 2002). At present, Europe is home to 9 of the top 10 countries with over 10 million residents and the largest proportion of elderly individuals, with Germany ranking 3rd at 24 % (World Health Organization, 2002). Further estimates state, that in addition, the oldest old (85 and older) are the fastest growing group (Azzopardi et al., 2016; World Health Organization, 2002). The described developments mainly arise from the considerable advancements in medicine and public health throughout the last 100 years – a notion that is underpinned by the fact that the average life span has almost doubled within that period (World Health Organization, 2002). These advancements are part of a significant shift in global human health that is taking place at varying speeds and through different pathways. This transformation covers several changes worldwide, such as a decrease in high fertility rates, a steady rise in life expectancy, and a shift in the predominant causes of death and illness from infectious and parasitic diseases to noncommunicable diseases and chronic conditions. In early nonindustrial societies, the risk of death was increased across all age groups, and only a minority of individuals reached advanced age. In modern societies, most people survive past middle age, and mortality rates are predominantly concentrated among the elderly population (World Health Organization, 2002). This growth in our elderly population predicts a rise in the burden of diseases, disabilities, and negative events, which will result in significant personal and societal costs (Prince et al., 2015). This significant demographic shift has far-reaching implications for the development and provision of healthcare and social services (Clegg et al., 2013).

The discussion regarding the connection between aging and disease revolves around the question of whether aging should be viewed as normal, natural, and physiological or as a pathological process. When considering this relationship from medical, molecular, social, and historical perspectives, aging might not be strictly categorized as a disease or non-disease. Rather, it includes both age-related diseases and their early-stage manifestations, as well as other pathological changes (Gladyshev & Gladyshev, 2016). In turn, it is very well known that variability is inherently intertwined with the aging process. As such, older adults are not a uniform high-risk group; they possess diverse health statuses and prospects (Ferrucci & Kuchel, 2021; Nguyen et al., 2021). Although this greater heterogeneity is not true for all variables (e.g., laboratory values) it is especially important for e.g., physical performance measures, chronic condition, and the frailty index as a measure of vulnerability regarding stressors (Nguyen et al., 2021). Therefore, this stresses the urge to establish methods that can differentiate those who are most likely to require support services or

encounter health crises. This is essential for effectively and efficiently addressing the impeding challenges (Bandeen-Roche et al., 2023; Morley et al., 2013).

1.1 Thesis outline

This cumulative dissertation is structured into the following primary sections:

The **first chapter** offers a broad overview of the challenges within the specialist area of geriatrics, emphasizing the diversity among older adults. Further, it introduces the concept of the geriatric frailty syndrome, which aims to capture the varied vulnerability present in the elderly population. Additionally, this chapter reviews various approaches for assessing physical frailty, as one of the most famous concepts, and presents instrumented methods for evaluating daily life performance in frail older adults.

The **second chapter** details the central methods and material utilized in the studies included in the dissertation. The initial two studies focus on a kinematic approach assessing activities of daily living, whereas the third study explores daily activity behavior and its relation to self-reported frailty. All three studies emphasize the significance of the upper extremity, as essential aspect of the performance of instrumental activities of daily living using a wrist-worn device.

The **third chapter** presents the primary findings along with the complete version of the three articles that constitute this dissertation.

The **fourth chapter** provides a discussion about the potential relevance of upper limb activity and its transfer to the concept of physical frailty. More precisely, this chapter explores the potential of wearables, specifically those worn on the wrist.

1.2 History and path of geriatrics

The term "geriatrics" was coined by Ignatz Leo Nascher (* 11.10.1863 in Vienna), marking the birth of modern geriatrics. The word itself originates from "geronte" referring to a group of men over 60 years of age who formed the legislative council (gerousia) in Athens (Morley, 2004). At that time, the field of geriatrics steadily increased over the years in the United Kingdom and United States of America. In contrast, the development of geriatrics in Europe has been inconsistent, with programs experiencing periods of growth followed by decline, largely influenced by the leadership at that time. In the early 20th century, Austria was a pioneer in the emerging field of geriatric care. It was the Austrian system that inspired Nascher to coin the term "geriatrics". The teachings of the Austrian geriatric school were codified in 1910 by Dr. Arnold Lorand in his book "Old Age Deferred". According to him the causes of aging were arterio-sclerosis, immune problems leading to increased infections, and abnormalities of the secretions of the ductless glans (Morley, 2004). The initial breakthrough in contemporary geriatrics occurred when the geriatric assessment was organized into a collection of commonly employed screening tools. The launching instrument in the set was formulated in 1955 by Dorothea Barthel, a physical therapist stationed at Montebello Stage Hospital in Baltimore. At this hospital, the Barthel index (Mahoney & Barthel, 1965) was implemented to measure functional capacity of all patients undergoing rehabilitation. Consequently, a series of publications emerged, establishing it as the benchmark for assessing functionality, commonly referred to as the "gold standard" index (Mahoney & Barthel, 1965). After that, a bunch of geriatric assessments were developed such as "Activities of Daily Living" (Katz et al., 1963, 1970), "Instrumental Activities of Daily Living" (Lawton & Brody, 1963), "Mini-Mental Status Examination" (Folstein et al., 1975), "Geriatric Depression Scale" (Yesavage et al., 1982), "Functional Independence Measurement (FIM)" (Dodds et al., 1993) and the "Get Up and Go" (Mathias et al., 1986) assessment (Morley, 2004), with the attempt to quantify aspects such as of activities of daily living (ADL), cognition, and depression.

In recent years, there has been a continual growth in both geriatrics, which focuses on the medical care and treatment of older adults, and gerontology, which explores aging from a multidisciplinary perspective. It is evident that it is primarily characterized by the complexity and variability of cases, which requires a comprehensive assessment of the "current state". To achieve this, it is first necessary to understand the uniqueness of the geriatric patient.

1.2.1 Introduction of the geriatric patient

The typical profile of a geriatric patient, whether male or female, consists of a combination of multiple illnesses (multimorbidity) and advanced age. Additionally, other characteristics include atypical progressions or symptoms of medical conditions, the presence of one or more geriatric syndromes, frequent hospitalizations, and the use of multiple medications, which significantly increase the risk of adverse drug reactions (Ernst et al., 2020). Geriatric syndromes are multifactorial conditions that jeopardize patients' ability to function independently and may require long-term care. They represent the manifestation of coexisting diseases rather than being attributed to a specific disease process. These age-typical problem constellations require a detailed diagnosis because, unlike classical syndrome terms, there is no specific underlying disease process. Examples of well-known geriatric syndromes include immobility, dizziness, malnutrition, and frailty. Typical illnesses among geriatric patients are linked with limitations in activity, participation, and overall life quality (Ernst et al., 2020). Although advancing age appears to correspond with reduced well-being and heightened frailty levels (Collard 2012), the health and functional abilities of older adults fluctuates significantly over time, influenced by genetic, biological, environmental, as well as other physical, psychological, and social factors. Consequently, individuals of the same chronological age might possess varying biological ages (Kojima et al., 2019; Mitnitski et al., 2002). The concept of frailty seeks to clarify these differences among older adults (Collard 2012).

Introduction

1.3 Geriatric frailty syndrome

The demographic shift is not only resulting in a higher occurrence of chronic diseases but is also contributing to the increase of geriatric syndromes like the frailty syndrome. For this dissertation, the frailty syndrome was intentionally selected as the central concept, as it is the most comprehensive, attempting to explain or measure the great variability of geriatric patients. The next chapter will provide an overview of the general idea of frailty. Subsequently, we will concentrate specifically on the physical frailty syndrome ("1.4.2 Physical frailty syndrome"), given its prominence as one of the most well-known concepts. Understanding the implication of frailty is crucial for healthcare professionals and policymakers, as it can help to optimize strategies and resource allocation to meet the evolving needs of an aging population.

1.3.1 History

Frailty is widely recognized as an essential cornerstone of geriatric medicine, representing a significant underlying vulnerability to numerous other geriatric syndromes and negative health outcomes. The term frailty stems from the Latin word "fragilitas", which refers to something weak and susceptible to being easily broken, damaged, or destroyed (Sciacchitano et al., 2024). The origins of frailty can be tracked back to the 1980s, were chronological age, care requirements, and disability were seen synonymously with frailty (Hogan, 2018; Walston et al., 2018). In 1991, the term "frail elderly" was incorporated into the Medical Subject Headings (MeSH) database of the National Library of Medicine. It was defined as "Older adults or aged individuals who are lacking in general strength and are unusually susceptible to disease or to other infirmity" (MeSH). Since then, over the course of the following thirty years, there has been a significant surge in the quantity of biomedical research papers dedicated to this subject matter (Hogan, 2018). According to current understanding, frailty is characterized as an increased susceptibility to stressors resulting from various interconnecting systems. This state leads to a decline in homeostatic reserve, which refers to the body's ability to adapt and respond efficiently to changes, crucial for sustaining overall health, robustness, and resilience (Bergman et al., 2007; Hogan, 2018).

1.3.2 General concept

Although literature constantly evolves the concept, there is still debate about how to define the condition (Dent et al., 2019). Over the last decades, significant global initiatives have focused on achieving a consensus regarding frailty. Frailty is generally seen as multidimensional geriatric syndrome indicated by a reduced capacity (individual reserve) of the aging organism to cope with internal or external stressors such as infections, injuries, and changes in medication (Fried et al., 2001; Morley et al., 2013). It is considered a valuable approach for understanding the diverse range of health conditions among older individuals and for predicting outcomes such as falls, mortality, and the likelihood of institutionalization (Ensrud et al., 2009; Fried et al., 2001; Gill et al., 2006; Hogan, 2018). In recent decades, three significant aspects have solidified in the understanding of frailty. First, frailty encompasses multiple dimensions, involving both physical and psychosocial factors in its evolution. Second, despite its higher occurrence as age advances,

frailty represents an extreme outcome within the spectrum of normal aging. Third, frailty is characterized by dynamism, indicating individuals' ability to transition between varying levels of frailty over time (Hoogendijk et al., 2019; Markle-Reid & Browne, 2003). In this context, transitions towards advanced frailty states are observed more frequently than the reverse, probably due to hysteresis (Gill et al., 2006). There is an ongoing discussion whether frailty should imply functional limitations or be seen as a pre-disability stage. Additionally, there is also increasing emphasis on various frailty subtypes, such as social, nutritional, and cognitive frailty. However, the evidence supporting these subtypes remains limited (Panza et al., 2015). Another recent proposal is the concept of intrinsic capacity, which focuses on the physical and mental abilities of an individual rather than concentrating on losses as assessed by conventional frailty measures (Cesari et al., 2018). Although the World Health Organization supports this concept, it lacks empirical validation (Hoogendijk et al., 2019). Given the ongoing lack of consensus regarding the definition of frailty, it is not surprising that the ICD-10 code "R54 (senility)" remains unelaborated (Ernst et al., 2020) and is quite generally described as age-related physical debility.

1.3.3 Epidemiology

Frailty affects millions of older adults globally. Nevertheless, the precise prevalence of frailty remains uncertain, particularly due to the predominant focus of frailty research on high-income countries (Hoogendijk et al., 2019). A systematic review, incorporating data from 21 cohorts including 61,500 older adults (inclusion criteria 65 years and older) residing in high-income countries, revealed a weighted average estimate of 11 % for frailty. In general, the data underscored significant variations in frailty prevalence among studies, spanning a range from 4 % to 59 % (Collard et al., 2012). However, arranging the studies based on the frailty definition employed significantly narrowed the variation in the results. Among studies using a physical phenotype definition of frailty, the prevalence ranged from 4.0 to 17.0 % (Collard et al., 2012), showing variations by 13.0 percent points.

Similarly in Germany, the prevalence of frailty shows variability across different studies. Buttery and colleagues (2015) conducted a cross-sectional analysis of the first wave of the German Health Interview and Examination Survey for Adults (DEGS1) between 2008 and 2011. Their study involved 1,843 communitydwelling people aged between 65-79 years. They documented an overall frailty prevalence of 2.6 %, with pre-frailty being prevalent in 38.8 % of the participants. Nevertheless, in comparison to results from other German, European, and international studies, the observed prevalence of the DEGS1 study was lower (Buttery et al., 2015). For instance, the SHARE cohort study (wave 2004), which included older individuals of ten European countries, estimated a frailty rate of 12.1 % among people aged over 65 years (Santos-Eggimann et al., 2009).

In general, variations in frailty prevalence might be explained by true variation, country specific differences, different study designs, participant inclusion criteria, as well as heterogeneity of instruments used to operationalize frailty (Buttery et al., 2015; Collard et al., 2012; Syddall et al., 2010; Theou et al., 2015). Although there is uncertainty regarding the exact prevalence of frailty, several consistent trends have been identified in numerous studies (Hoogendijk et al., 2019). Frailty tends to be more common among women than men (across every age group), and its prevalence increases with age (Bandeen-Roche et al., 2015; Gordon et al., 2017; Santos-Eggimann et al., 2009). Additionally, individuals from lower socioeconomic backgrounds, including those with lower educational levels or income, as well as ethnic minorities, tend to have higher rates of frailty (Bandeen-Roche et al., 2015; Hoogendijk et al., 2014). Although data is still limited, the prevalence of frailty seems to be highest in Africa and lowest in Europe (O'Caoimh et al., 2021).

1.3.4 Risk of adverse consequences

As frailty becomes increasing prevalent and exhibits a robust association with various adverse health consequences, its impact on the well-being of elderly individuals and the strained healthcare system becomes evident.

Risk of adverse health outcomes

Frailty poses a significant risk of mortality in older adults, and this risk seems to be dose-responsive with the growing number of components or deficits present (Shamliyan et al., 2013). The association between frailty and mortality holds true even across different settings and subpopulations (Drubbel et al., 2013; Handforth et al., 2015; S. W. Kim et al., 2014; McAdams-Demarco et al., 2015). Frail older adults face an increased risk of adverse health outcomes (Hoogendijk et al., 2019), including disability (Boyd et al., 2005; Ensrud et al., 2009; Kojima, 2017), falls and fractures (Ensrud et al., 2007, 2009), deteriorating mobility (Fried et al., 2001), loneliness (Hoogendijk et al., 2016), diminished quality of life (Kojima, Iliffe, et al., 2016), depression (Soysal et al., 2017), cognitive decline (Robertson et al., 2013), dementia (Kojima, Taniguchi, et al., 2016), hospitalization (Kojima, 2016), and admission to nursing homes (Kojima, 2018). When considering disability-adjusted life years (DALY), they are notably higher in older adults identified as frail (physical frailty: 4.56 DALY) compared to those identified as pre-frail (2.38 DALY) and robust individuals (1.45 DALY) (O'Donovan et al., 2019).

Costs of frailty

Research on health care associated costs related to frailty consistently demonstrate a clear trend of rising expenses as the level of frailty increases. This trend encompasses factors such as increased utilization of health-care services in areas including inpatient care, post-acute care, and outpatient care (Ensrud et al., 2018; Hoogendijk et al., 2019; Kim et al., 2019). This is also reflected in figures for Germany. In a cross-sectional study including 2,598 older participants aged 57-84 years in Saarland, Germany, conducted between 2008 and 2010, the prevalence of frailty (defined as having \geq 3 predefined symptoms) was 8 %. The average total costs over a 3-month period were 3,659 € with 4 or 5 symptoms, 1,616 € for those with 3 symptoms, and 642 € for the non-frail controls. Even after accounting for comorbidities and general socio-demographic characteristics, there remained a significant difference in total costs between frail and non-

frail older adults, amounting to $1,917 \notin$ for those with 4 or 5 symptoms and 680 \notin for those with 3 symptoms (Bock et al., 2016). Specifically, the expenses for residential care rose notably with an increase in the frailty index. For participants with an index ≥ 4 , the cost was $2,104 \notin$, whereas it was only 268 \notin for those who were not frail. Robust participants hardly utilized any nursing care services, leading to an average expenditure of $2 \notin$ in this domain. Conversely, the average cost of nursing care for those with a frailty index of 3 was $262 \notin$, and for those with an index of ≥ 4 , it was $672 \notin$. Furthermore, the average medication expenses consistently increased with the frailty index, varying from $128 \notin$ for robust participants to 400 \notin for those with a frailty index of 4-5. Overall, expenses were more closely linked to frailty and comorbidity rather than age (Bock et al., 2016).

1.3.5 Risk factors, prevention, and intervention

Recognizing the factors that contribute to frailty is crucial for healthcare, but the ground truth remains elusive. Understanding these factors may not only help us to understand frailty better but also lays the foundation for effective public health and prevention plans. This is especially important when we can potentially address these risk factors through specific measures (Hoogendijk et al., 2019). In short, identifying frailty risk factors empowers us to take (pro)active steps, improve well-being and reduce the impact of frailty on individuals and health care systems.

A variety of factors can favor the development or progression of frailty (Hoogendijk et al., 2019). These factors encompass a wide range of aspects and conditions covering sociodemographic (particularly driven by age and female sex), clinical (including multimorbidity and polypharmacy), lifestyle (notably low physical activity), and biological domains (e.g., deficiencies in micronutrients) (see Figure 1).



Figure 1. Factors that increase the likelihood of the onset or progression of frailty (Feng et al., 2017; Hoogendijk et al., 2019).

Fortunately, many of these influential factors, especially clinical and lifestyle factors may be modifiable (Figure 1, marked in green). A good example of this is reduced physical activity. This is seen as one of the major contributors to the onset and progression of frailty (Hoogendijk et al., 2019). Engaging in physical

activity is recognized for preserving or enhancing the functionality of several physiological systems that may be compromised in frailty. These systems include muscle and cardiac function, cognition, the endocrine system (specifically glucose metabolism), and inflammation. Moreover, regular physical activity can postpone the onset of chronic diseases (McPhee et al., 2016). Additional examples of potential modifiable risk factors comprise age-related anorexia, characterized by a general loss of appetite or reduced food intake, deficiencies in various micronutrients, obesity, hormone deficiencies, and other alterations in the endocrine system, and social factors like loneliness (Hoogendijk et al., 2019).

Guidelines for intervention

As of now, there are only few evidence-based and multidisciplinary guidelines designed to identify and manage the condition of frailty (e.g., Dent et al. 2017, 2019). However, specific interventions may have the capacity to interrupt, slow down, or reverse the downward trajectory (Dent et al., 2019).



Figure 2. International clinical practice guidelines (Dent et al., 2019).

Based on the current guideline recommendations for the management and intervention of frailty (Dent et al., 2017, 2019), several approaches can be suggested (see Figure 2). First, initial screening by a rapid frailty instrument of older adults should be performed, followed by a comprehensive assessment of frailty as part of a more comprehensive management plan, if the screening results are positive (Dent et al., 2019). Older adults diagnosed with frailty should be instructed in a progressive, personalized exercise program that contains resistance training. In addition, pharmacological treatment should include the reduction or discontinuation of inappropriate or unnecessary medications. As fatigue is a key aspect of Fried's frailty phenotype (detailed explanation of the construct follows in the next chapter), individuals with frailty should be screened, as addressing reversible causes of fatigue through targeted interventions may improve frailty

outcomes. Lastly, if unintentional weight loss occurs, screening for reversible causes should be performed and protein and calorie supplementation or food fortification should be considered (Dent et al., 2017, 2019). It is important to note that the field of geriatric medicine continuously advances, with ongoing developments in assessment methods, treatment approaches, and technologies. Consequently, it is imperative that evidence-based clinical guidelines for frailty are frequently reviewed and updated to reflect the advancements (Dent et al., 2017). Additional research is required to determine whether assessing frailty and provided targeted treatment will result in benefits for individual patients and the sustainability of the healthcare system (Hoogendijk et al., 2019).

As stated above, the variation in frailty prevalence can be attributed, in part, to the utilization of various measurement instruments. The subsequent chapter serves as an illustration of the array of definitions and instruments associated with frailty.

1.4 Definitions and clinical assessments of the frailty syndrome

The absence of a universal consensus on the definition of frailty has resulted in the creation of multiple instruments for its assessment. As such, numerous tools are available for identifying and classifying frail older adults.

1.4.1 Types and use of frailty instruments

Up to now, there is a plethora of frailty assessments. The literature has introduced several definitions and instruments, such as the FRAIL scale (comprising Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight) by the International Academy of Nutrition and Aging (Abellan van Kan et al., 2008; Abellan Van Kan et al., 2008), the Frailty Instrument for Primary Care within the Survey of Health, Ageing, and Retirement in Europe (SHARE-FI) (Romero-Ortuno et al., 2010), and the Groningen Frailty Indicator (Steverink et al., 2001) (Chen et al., 2014). In 2019, Faller and colleagues conducted a systematic review focusing on tools designated to detect frailty syndrome among older adults. They identified a total of 51 instruments designed for assessing frailty. While the primary domains covered by these instruments were largely physical in nature, it is worth noting that certain tools also encompassed aspects related to psychology, social well-being or rather support, and environmental factors (e.g., housing conditions (De Witte et al., 2013)) (Faller et al., 2019). As previously mentioned, a variety of operational definitions for frailty exist, but most are grounded in one of two conceptual frameworks (Park & Ko, 2021). The initial framework characterizes frailty as a distinct clinical syndrome with its own pathophysiology. It consists of five criteria, based on both clinical tests and questionnaires (frailty phenotype (Bandeen-Roche et al. 2006; Fried et al. 2001)). Those five criteria include aspects of unintentional weight loss, slow walking speed, low grip strength, selfreported exhaustion, and low physical activity (Fried et al., 2001). The second, known as the deficit accumulation model (Frailty Index - FI), assesses vulnerability by aggregating comorbidities, disease conditions, functional and cognitive impairments, and psychological factors (Mitnitski et al., 2001; Rockwood & Mitnitski, 2007). The FI is a continuous scale, ranging from 0 to1 (Rockwood et al., 2005). It can be

derived from questionnaires, clinical test, or extracted from data collected during routine care for screening (Drubbel et al., 2013; Jones et al., 2004). Both these concepts have shown predictive capabilities concerning heightened risk of institutionalization and increased mortality (Fried et al., 2021). The choice of screening tools for frailty may vary depending on the environment and the specific demographics being evaluated (Benzinger et al., 2021).

In 2016, Buta and colleagues published a review about the characterization of the use of frailty instruments (Buta et al., 2016). Altogether, 67 frailty instruments were identified, with nine of them being highly cited (\geq 200 citations). Additionally, they assessed the overall usage and categorized the instruments into eight distinct use cases. These applications include risk assessment for adverse health outcomes (31 %), etiological studies of frailty (22 %), methodology studies (14 %), biomarker studies (12 %), inclusion/exclusion criteria (10 %), estimating prevalence as primary goal (5 %), clinical decision-making (2 %), and intervention targeting (2 %). Observational studies emerged as the most prevalent assessment context (Buta et al., 2016) (see Figure 3).



Figure 3. Illustration of the diversity of frailty instruments, its use, and categories. Own illustration based on (Buta et al., 2016).

The assessment and evaluation of frailty can be conducted through various instruments classified into different categories (see Figure 3). Hence, the assessments can be grouped into subjective (only self-reported items), objective, and mixed categories (Bouillon et al., 2013). In objective performance-based evaluations, measurements such as walking speed focus on objective aspects to determine frailty status (Abellan Van Kan et al., 2009; Clegg et al., 2015; Turner & Clegg, 2014). Subjective self-reports, in turn, include components which are either reported by the participant or reported by a clinician or researcher. Examples for assessments based on self and external evaluation are the Clinical Frailty Scale (CFS) (Rockwood et al., 2005), the FRAIL Scale (Abellan van Kan et al., 2008; Abellan Van Kan et al., 2008) and the Groningen Frailty Indicator (Steverink et al., 2001). The third classification, known as mixed assessments, merges elements from both objective and subjective assessments (Bouillon et al., 2013). An example of a mixed assessment is the Fried frailty phenotype (Fried et al., 2001).

In general, objective performance-based tools have various advantages, including delivering more accurate and valid results and greater sensitivity to changes over time (Hussain et al., 2018). However, assessment methods relying on observation and subjective judgments are generally quick and easy to use (Dishman et al., 2001). These methods can evaluate complex behaviors but lack objectivity and reliability. A specific form of subjective self-assessment is the use of questionnaires, which can be an effective means of reaching lager groups at lower cost (Prince et al., 2008). These questionnaires are widely embraced, impose a relatively low burden on individuals and cause minimal disruption to their usual habits. Nevertheless, selfreport questionnaires are susceptible to various biases, including perceptual and recall errors (Nunes et al., 2015). For example, Bandeen-Roche and colleagues (2023) have shown that subpopulations identified as frail assessed by the original physical frailty score (mixed assessment) compared to a version substituting walking speed and grip strength by self-reported items systematically differ (Bandeen-Roche et al., 2023). However, despite these limitations, self-report questionnaires can be valuable, particularly for intentional screening purposes (Nunes et al., 2015).

A recent survey conducted by Kudelka and colleagues (2024) aimed to evaluate the instruments currently used in the Comprehensive Geriatric Assessment in Germany. The survey emphasizes the significance of standardized evaluations or procedures for assessing the frailty syndrome, which is currently lacking in routine geriatric clinical practice. The selection of assessment tools has an impact on the conduction of clinical trials and studies. The existence of various distinct tools highlights the responsibility to ensure the comparability of collected data across clinical and scientific contexts. This is aimed at minimizing the burden on geriatric patients and promoting the selection of optimal treatment options (Kudelka et al., 2024). Overall, assessments should be concise and straightforward to enhance the likelihood of translation into clinical practice. Therefore, the selection of assessments should align with the specific indicators: screening for the presence or degree of frailty, tracking dynamic changes of frailty, or monitoring therapeutic interventions (Morley et al., 2013).

1.4.2 Physical frailty syndrome

The primary focus of this perspective is on the syndrome of phenotypic frailty, which will be referred to "physical frailty" hereafter. In 2013, the term "physical frailty" was defined by a consensus group consisting of delegates from 6 major international, European, and US societies as follows: "a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death." (Morley et al., 2013). The most widely recognized concept is the physical frailty phenotype according to Fried and colleagues, which was tested in a large cohort study of over 5,300 community-dwelling older adults in the US (Fried et al. 2001; Fried et al. 1991). Based on prior research on frailty, Fried and her colleagues (2001) operationalized a definition of frailty, and investigated its prevalence and incidence in a population-based study of older adults. Additionally, they explored its cross-sectional correlations and assessed its validity in predicting the adverse outcomes commonly linked with frail older adults by geriatricians (Fried et al., 2001). The Fried phenotype stands out as potentially the most frequently employed concept (\geq 200 citations) (Buta et al., 2016), thereby establishing the Fried frailty instrument as the premier method for evaluating physical frailty, often considered the "gold standard" (Fried et al., 2001). This mixed assessment concept includes five criteria: unintentional weight loss, low walking speed, low physical activity, self-reported exhaustion, and low grip strength. To be categorized as frail, a minimum of three criteria must be met. Conversely, having one of two indicators is labeled as pre-frail, while the absence of any indicator is referred to as robust (Fried et al., 2001).

The occurrence and onset of phenotypic frailty relates to modified energy metabolism across various metabolic pathways (Fried et al., 2021). This includes disruptions in glucose-insulin dynamics, glucose intolerance, insulin resistance, and alterations in energy-regulating hormones like leptin, ghrelin, and adiponectin. Furthermore, changes affect musculoskeletal function, energy efficiency, mitochondrial energy production, and mitochondrial copy number. Notably, individuals classified as frail exhibit impaired energy production and utilization across these systems. This implies that age-related irregularities in energy regulation contribute to overall physiological imbalance and the emergence of frailty. This theory stems from the idea that the physiological and biological pathways essential for health and resilience are seen as interconnected elements within a complex, dynamic system where substantial dysregulation of this system leads to physical frailty (Fried et al., 2021) (depicted in Figure 4).



Figure 4. The concept of physical frailty phenotype and its underlying processes, adapted from (Fried et al., 2021).

Introduction

The crucial understanding of this concept is that an individual's physiological condition results from various interacting elements at different temporal and spatial scales (such as genes, cells, organs) that collectively form a unified entity (Fried et al., 2021). At the level of observable traits as stated above, five criteria play a role in the emergence of frailty (see Figure 4, highlighted in green).

Fried et al. defined the phenotype and verified its validity by demonstrating its correlation with the incidence of mobility and ADL disability over 3 and 7 years. This association held true independently of comorbidity in men and women aged 65 years and older (Fried et al., 2001). In Europe, the Survey of Health, Aging and Retirement in Europe (SHARE) furnishes data for assessing frailty (Macklai et al., 2013). The study of Macklai and colleagues (2013) intended to assess the validity of the SHARE operationalized frailty phenotype, using a similar construct with modifications in the metrics by examining its prospective correlation with adverse health outcomes. Following a 2-year observation, individuals initially identified as frail faced an elevated risk for developing disability in mobility (OR 3.07, 95 % CI, 1.02-9.36), instrumental ADL (OR 5.52, 95 % CI, 3.76-8.10), which are essential for independent living, and basic ADL (OR 5.13, 95 % CI, 3.53-7.44) along with worsening morbidity (OR 1.77, 95 % CI, 1.35-2.32). Even among the pre-frail older adults, these associations remained significant, albeit with a reduced magnitude of effect (Macklai et al., 2013). Additional validation studies, including the extensive cohort conducted by Woods at al. (Woods et al., 2005) and Bandeen-Roche et al. (Bandeen-Roche et al., 2006), used a similar construct to define each frailty criterion. Despite these variances, the frailty criteria consistently demonstrate robust independent associations to adverse health outcomes. These findings greatly support the generalizability of the frailty phenotype across diverse populations (Macklai et al., 2013). This underscores that both the risk associated with physical frailty and frailty itself pose a threat to the independence of daily living, especially in mobility and ADL disability, in older individuals.

Although the current frailty phenotype instruments are beneficial to identify frailty, they are criticized to be clinically cumbersome and time consuming for busy clinical settings (Cesari et al., 2014). Additionally, they are not suitable for mobility-impaired patients, like patients in bedridden conditions (Juma et al., 2016; Toosizadeh et al., 2015), are costly, need trained staff to administer the tests, require age and gender adjustments, and could be easily biased by methods of administration of gait tests such as type of footwear (Fried et al., 2001; Lee et al., 2018) or incorporating static start or stop (Krumpoch et al., 2021). Furthermore, the frailty phenotype faces criticism for its lack of sensitivity to small physiological changes (Gill et al., 2006). Frailty is perceived as a multidimensional construct, and its operational components may undergo distinct alterations, posing a challenge for comprehensive capture through categorical measures (Buchman et al., 2009). Moreover, the approach, dependent on questionnaires for evaluating weight loss, fatigue, and energy expenditure, is susceptible to participant bias (da Câmara et al., 2012; Khezrian et al., 2017; Melzer et al., 2004; Tudor-Locke & Myers, 2001).

1.5 Instrumented assessment of daily life performance in physical frailty

Impairments in mobility and ADL are of great importance for individuals with physical frailty, threatening independent living in a complex manner. Understanding aspects of independence in daily living may hinge, inter alia, on the interplay between the task capacity of activities of daily living, behavior (engagement), and the self-reporting (self-perception). Especially instrumented assessment methods can add important information for assessing a person's ability to maintain their autonomy and effectively manage their daily activities.

1.5.1 Task performance, behavior, and self-report

As mentioned, limitations in mobility and both basic and instrumental ADL are critical factors that significantly jeopardize the independence of frail older adults (Macklai et al., 2013), carrying an unfavorable prognosis in this regard (Fried et al., 2001; Nourhashémi et al., 2001). As the majority of elderly individuals desire to age in their own homes, one of the primary objectives is to uphold "the ability to perform functions related to daily living – i.e., the capacity of living independently in the community with no and/or little help from others" (World Health Organization, 2002). Hence, these functional activities are deemed more reflective of the inherent functional status of older individuals (Panhwar et al., 2019), compared to movements with less relevance to everyday life.

Activities of daily living usually involve a spectrum of self-care tasks that vary in complexity. In general, basic ADL (b-ADL) include essential abilities typically required to address basic physical needs (Mlinac & Feng, 2016), such as feeding. They can be defined as "activities essential for an independent life or necessary survival, representing everyday tasks required for self-care" (Van Der Vorst et al., 2016). In contrast, instrumental ADL (i-ADL) encompass a more complex set of behaviors (Lawton & Brody, 1963) related to independent living in the community (e.g., using public transportation) and are particularly sensitive to early cognitive decline (Mlinac & Feng, 2016). Therefore, ADL refer to the regular tasks and actions that are crucial for maintaining an individual's independence (Covinsky, 2006; Khusainov et al., 2013). Consequently, daily life activities such as b-ADL and i-ADL together cover categories, like food preparation, feeding, transportation, housekeeping, leisure time, and ambulation (Khusainov et al., 2013). Information on ADL is typically assessed through subjective questionnaires such as those designed by Katz et al. (Katz et al., 1970) or Lawton & Brody (Lawton & Brody, 1963). These ratings provide insights into the level of independency in various activities, along with information on additional assistance needed, as reported by participants, their relatives, or caregivers. Nevertheless, these assessments frequently rely on low level ratings (e.g., yes / no or Likert-scales easy / with difficulties / not possible) to track changes in activity and perceived difficulty (e.g., climbing stairs, walking one block, food preparation capacity), which generally lack validation from real-time studies of these activities (Dobkin, 2013). Reported levels of independency and activity might differ from what clinicians find in tests. Furthermore, questionnaires are not only limited by, for example, recall biases (e.g., (Dobkin, 2013)) but might also be biased by the Hawthorne effect and general difficulties in comprehension and in interpretation (Dobkin, 2013; Godfrey et al., 2008).

In general, performing any type of ADL requires the expenditure of energy (energy expenditure - EE) (Khusainov et al., 2013). The concept of EE comprises three distinct elements: Basal metabolic rate (BMR), which is the minimal energy needed for bodily functions during rest, diet induced thermogenesis (DIT), and physical activity (PA). In comparison to ADL, the term PA is therefore more generally defined as "any bodily movement produced by skeletal muscles that result in energy expenditure" (Caspersen et al., 1985), and within the context of this dissertation often termed as behavior or engagement. Everyday physical activity encompasses all forms of activity such as occupational tasks, sports, conditioning, household chores, leisure activity, and other pursuits (Caspersen et al., 1985). This constitutes the most fluctuating element of an individual's daily EE. The considerable variability in daily activity related EE observed both within and between individuals in real-life conditions presents a challenge for interpretability (Montove & Taylor, 1984). Over time, energy exchange and utilization become less efficient, which is influenced by factors such as aging, stress, and history of sedentarism (i.e., disuse). As activity level drop and energy flow reduces within the system, the mismatch between structure and function becomes increasingly evident. Due to an energetic imbalance, the system contracts and becomes frail, significantly reducing its capacity to handle stressors. This imbalance further weakens the system, highlighting PA as a crucial factor in determining physical frailty and the risk of developing disabilities (Fried et al., 2021; Peterson et al., 2009). However, most studies examining PA in older adults, often rely on self-report measures, which are susceptible to limitations including recall bias, socially desirable responses, and the influence of factors such as mood or cognition. Many individuals tend to overestimate their PA level (Jansen et al., 2015). For instance, Watkinson et al. (2010) discovered that nearly half of objectively categorized inactive individuals overestimated their PA and reported themselves as active (Watkinson et al., 2010). Overestimating one's level of PA may hinder efforts to change behavior, as individuals may be unaware that they are not engaging in sufficient levels of PA (Jansen et al., 2015).

The relationship between motor capacity assessed in laboratory setting and performance in daily activities among older adults continues to be a subject of discussion. Understanding this connection is crucial as it may contribute to the development of more reliable assessment methods (Jansen et al., 2019). So far, clinical assessments have predominantly focused on evaluating physical capacities leaving open the questions on the execution of less strenuous (submaximal) daily activities and their realization in daily life. Only few attempts have been made to extend beyond PA assessment and estimate the wearer's (health-related) sensorimotor capacity in the real-world setting (David et al., 2021; Gulde et al., 2023, 2024). In this regard, it is essential not only to determine one's capacity to perform an activity but also whether one is engaging in the activity in daily life (Gulde et al., 2023). As frailty may develop due to a discrepancy between energy metabolism and demands, this implies that maintaining robust capability requires regular practice (Sciacchitano et al., 2024). At the same time, understanding how older individuals perceive and express these challenges is crucial, as they seek medical advice when they identify a health-related problem or experience feelings of loneliness. Particularly since the self-assessment of frailty is often used as an initial screening tool (Barreto et al., 2012; Nunes et al., 2015). Importantly, this perspective may differ, for instance, from that of clinicians, as older adults and their family members tend to prioritize complex social and emotional aspects more than clinicians may do (Studenski et al., 2004). Additionally, individuals with frailty may feel older than their chronological age (Sciacchitano et al., 2024). As such, subjective age can predict an individual's health condition better than simple chronological age (e.g., Stephan, Sutin, and Terracciano 2015). Thus, understanding the interconnection between task capacity ("can do"), behavior ("does do"), and self-reporting ("thinks can do") is essential for effectively guiding the care pathway (Figure 5).



Figure 5. Self-reporting, task complexity, and behavior as important aspects of the general care pathway, own illustration.

In summary, it can be concluded that both quantitative and qualitive aspects need to be considered when carrying out activities with the general ambition to identify objective measures, as human movement is multifaceted phenomenon influenced by various factors such as physiology, mechanics, psychology, and more. The capacity to evaluate the quality and/or quantity of movement can serve as a valuable resource for clinicians to diagnose and treat a wide range of conditions with precision (Godfrey et al., 2008). For instance, the risk of falling in a home environment plays a significant role in frailty (Ensrud et al., 2007, 2009) and therefore solely relying on ordinal scales to measure independency may not adequately capture the quality and safety of independent living. Furthermore, possessing the ability to perform a certain activity, might not necessarily imply that the individual will engage in it (Gulde et al., 2023; Rand & Eng, 2012; Suominen, 2011). It is crucial to pinpoint the skills required for performing daily tasks and understand how individuals approach these activities. With this knowledge in hand, it becomes feasible to explore methods for identifying impending factors, enhancing task efficiency, or facilitating greater independence for

individuals with disabilities (Godfrey et al., 2008). As a result, assessing complex instrumental activities of daily living becomes essential for elderly individuals with frailty, as it signifies their capacity to live independently at home (Nourhashémi et al., 2001). A promising approach involves evaluating these ADL abilities within a controlled laboratory setting to verify their capacity of execution, followed by observing their practical application in the uncontrolled everyday life. To quantify frailty more precisely, a deeper understanding of motor capacity and daily behavior is crucial. For that, particularly wireless motion sensor devices such as inertial measurement units (IMUs), combining accelerometers, gyroscopes, and sometimes magnetometers, can provide raw data to reveal daily activities (Dobkin, 2013).

1.5.2 Wearable-based approaches for assessing physical frailty in everyday life

In general, various methods are employed to evaluate human movement, encompassing observation, technologies rooted in the natural sciences (foot switches, gait mats, force plates, optical motion analysis), diaries, and questionnaires. Several of these methods present distinct drawbacks for continuous analyses, particularly the natural science technologies, which are primarily used in laboratory settings (Culhane et al., 2005). So far, to evaluate frailty, several approaches exist to utilize a single modality to measure frailty as a quantifiable physical parameter or to utilize instrumented methods assessing a person's ability to manage their daily activities, including force platforms, bathroom scales, cameras, and wearable sensors (Panhwar et al., 2019). Recent developments in portable technologies (wearables) and data processing systems have revealed new opportunities for creating practical and automated tools (Mohler et al., 2015) that enable the conduction of clinical investigations in natural settings outside of a laboratory (Deutsch & Burgsteiner, 2016; Lee et al., 2018; Razjouyan et al., 2018; Toosizadeh et al., 2015; Wile et al., 2014). In general, wearable sensors integrate multiple technologies enabling physiological and motion sensing (e.g., heart rate or steps). They can be integrated into footwear and clothing, worn as pendants, affixed to the wrist, ankles or trunk, or conveniently carried in a pocket (Zampogna et al., 2020). Through components like accelerometers, gyroscopes, pedometers (based on acceleration data), or heart rate monitors, wearable sensors possess the capability to capture activity frequency, duration, and intensity (Vavasour et al., 2021).

In 2021, a review from Vavasour et al. was published, which provides valuable insights into the use of wearable sensors to assess frailty in older adults. This includes information regarding sensor types, their placement on the body, and key parameters of PA and mobility that are most effective in discriminating between frailty states. Most of the studies used tri-axial accelerometers, gyroscopes, or a combination of both, with the inclusion of a magnetometer in some of the studies. The lumbar spine was the most common sensor placement. The most frequently used parameters were postural transitions, number of steps, percentages allocated to PA, and intensity of PA. Gait speed was the next most frequently studied metric, consistently demonstrating a correlation with frailty levels across all studies. While a total of 29 studies were included in the review, only three (approximately 10 %) focused on the investigation of upper limb kinematics (Vavasour et al., 2021). However, it is worth noting that mobility limitations, although a criterion of physical frailty, are not exclusively linked to frailty. For instance, a 60-year-old paraplegic individual

using a wheelchair does not necessarily manifest frailty. Therefore, reducing frailty to just mobility aspects seems overly simplistic. A comprehensive understanding of frailty requires considerations of additional aspects, such as upper extremity functionality (e.g., Toosizadeh et al. 2015). Given the importance of managing daily activities for older individuals' quality of life, with upper limb performance being key for ADL, assessing activities that represent their overall functional status is crucial (Panhwar et al., 2019).

Kinematic approaches have been employed to study upper limb performance during ADL across different neurological conditions. In these investigations, motion capture techniques were used to record hand movement trajectories during a variety of ADL tasks, involving patients with conditions such as aging, spinal cord injury, stroke, and dementia (Alt Murphy et al., 2011, 2012, 2013; De Los Reyes-Guzmán et al., 2016; Gulde et al., 2017, 2018, 2019; Gulde & Hermsdörfer, 2015; K. Kim et al., 2014; Thrane et al., 2018). These investigations indicated prolonged task durations accompanied by reduced speed, increased periods of in-activity, and more segmented velocity profiles with multiple peaks in stroke patients and elderly compared to younger participants. Consequently, young participants typically exhibited faster task performance than older individuals, while the elderly participants moved more quickly than stroke survivors. Moreover, the movements of young individuals covered shorter distances compared to the other groups. This suggests that factors such as distance and duration are influenced not only by stroke but by the aging process. Therefore, kinematic analyses of ADL offer insights into distinct performance patterns (Schmidle et al., 2022).

So far, only few studies have investigated the kinematics of the upper limb in relation to frailty (Vavasour et al., 2021). For instance, some studies have approved the effectiveness of variables derived from a task involving elbow flexion/extension at maximum speed in distinguishing between levels of frailty (Lee et al., 2018; Toosizadeh et al., 2015, 2016, 2017), even with the use of a single wrist-wearable sensor (Lee et al., 2018). Others have focused on measuring rapid focal arm-raising movements with a Vicon[®] system (i.e., pointing at a stimulus while standing), while balance aspects were measured using a force plate (Kubicki et al., 2012). Despite the importance of ADL performance in understanding the impact of frailty, there is still a lack of movement analysis on kinematic markers during for more complex upper extremity-based ADL tasks in individuals with frailty (Schmidle et al., 2020, 2022). Furthermore, as previously mentioned, not only task capacity might be of importance but also patterns of daily and routine physical activity (i.e., activity volume), encompassing both exercise and non-exercise behaviors in identifying frailty (Blodgett et al., 2015; Huisingh-Scheetz et al., 2018). As an example, Wanigatunga and colleagues (2022) showed that unfavorable patterns of objectively measured daily physical activity using a wrist-worn device correlates with frailty and certain frailty components (Wanigatunga et al., 2022). Such wearable-based approaches assessing daily activity have the advantage of capturing also less intense activities (e.g., preparing breakfast, picking up the mail), as these activities can constitute over 80 % of daily activity in older adults (Buman et al., 2010).

Upon reviewing the existing literature on upper limb activity in the context of the physical frailty syndrome, a notable research gap is evident, particularly regarding the motor performance for instrumental activities of daily living. These activities, which heavily rely on upper limb function, are crucial for maintaining independence and hold substantial aspects of functionality relevant to everyday life. Given their complexity, impairments in i-ADL typically manifest before impairments in b-ADL (primarily covering lower limb functions) and the loss of autonomy (Nourhashémi et al., 2001). Additionally, when assessing physical frailty, subjective methods like self-reports are often used as initial screening method (Barreto et al., 2012; Nunes et al., 2015) providing valuable insights into self-perception, but encompass inherent limitations. As such, it is crucial to validate these self-reports against actual activity behavior. This validation is particularly important because the ability to perform a specific activity does not necessarily mean the individual will engage in it (Gulde et al., 2023; Rand & Eng, 2012; Suominen, 2011). Nonetheless, self-reports have been found to be validly associated with everyday behavior; though with limited reliability (Gulde & Rieckmann, 2022).

Introduction

1.6 Objective of the thesis

The overall aim of this cumulative dissertation was to shed light on everyday life performances of older adults with frailty. In particular, the thesis investigated how the frailty syndrome influences specific i-ADL and further explored the relationship between everyday life behavior, as a measure of activity volume, and individuals' self-reported and perceived frailty status.

Based on the gaps in the existing literature, this thesis focuses on the following research aims:

Publication I:

The objective of the initial (proof-of-concept) study was to investigate the feasibility of utilizing a commercially available activity tracking sensor (IMU) to assess activities of daily living and distinguish between different levels of frailty among elderly individuals. The use of an IMU sensor instead of an optical motion tracking system enables the conduction of investigations with minimal distractions of the participants, allows for measurements in familiar settings, and offers feasibility for real-world measurements (e.g., by activity recognition).

Publication II:

This publication is considered the extension of the first study. The primary aim of this experimental study was to assess the performance of manual i-ADL tasks, utilizing unilateral activity measurements derived from an acceleration sensor integrated into a smartwatch, across two different tasks.

Publication III:

The objective of this study was to investigate the relationship between different components of sensorbased daily activity metrics, including those primarily related to gait activity (ambulation) and those primarily related to upper limb activity, and self-perceived frailty. Chapter 2

Methods

2. Methods

The first proceeding was designed as a pilot project (proof-of-concept) testing the feasibility of the ADL measurement mainly focusing on the technical aspects of the data collection with a smartwatch (acceleration-based data). In the second study, we extended the data set and analysis to further explore the difference between the ADL tasks aiming to better understand the interaction between frailty and the executed tasks (group x task interaction). The third study presented aimed for investigating the relationship between self-estimated frailty and the overall activity behavior of elderly individuals, with an additional aspect of the differentiation between the volume of upper and lower limb activity. In particular, we elaborated possible discrepancies between self-reported and objectively measured PA and investigated the relevance of upper limb performance. In all three studies, participants or their legal representatives gave informed consent. Ethical approval was given by the ethics committee of the Medical Faculty of Technical University of Munich (reference number 101/19 s) and conforms to the Declaration of Helsinki.

Initially, this chapter provides a concise overview to facilitate comprehension of the FRAIL project, which laid the groundwork for subsequent research findings. Subsequently, a summary is provided outlining the primary research questions along with the central methods and materials used in the studies.

Study	Population	Frailty Assessment	Performance measure	Measurement duration
Ι	Older adults $n = 17$	Physical frailty in ac- cordance with Fried	Kinematic ADL (tea and gar- dening task) performance of the upper limb	One time
II	Older adults $n = 27$	Physical frailty in ac- cordance with Fried	Kinematic ADL (tea and gar- dening task) performance of the upper limb	One time
III	Older adults $n = 88$	Self-reported physi- cal frailty in accord- ance with Fried	Physical activity measure in- cluding lower- and upper-ex- tremity activity	Up to 21 days

Table 1. Overview of the performed experiments, including study population, type of frailty assessment, performance measure, and measurement duration.

The Frail Project

FRAIL project – "Frailty Assessment in Daily Living" (https://eithealth.eu/product-service/frail/), funded by EIT Health (https://eithealth.eu/), was led by the TUM Chair of Human Movement Science. It involved partners from the Belgium-Netherlands region (IMEC, https://www.imec-int.com/en), France (Cap Digital, https://www.capdigital.com/en/ & MADoPA, http://www.madopa.fr/) and Munich (Qolware GmbH, https://lola-health.com/). The main goal was to develop a smartwatch app to support elderly people in various aspects of their daily living. Specifically, the app was designed to measure core features of frailty syndrome such as falls, low levels of physical activity, and interruptions in routine activities, to detect the onset of frailty and prevent its negative consequences. This project aimed to enhance an existing health-monitoring app, LOLA (developed by Qolware), by incorporating new monitoring features at a low cost, covering three essential aspects (https://eithealth.eu/product-service/frail/):

- Fall detection and prevention: This feature records fall data to improve the LOLA algorithm for automatic fall detection.
- Physical activity indicators for frailty: It generates physical activity indicators from a wrist-worn device.
- Frailty detection in activities of daily living: This provides specific parameters to assess differences in frailty levels.



Figure 6. Photo of the smartwatch as measuring device. Copyright: Stephanie Schmidle / TUM

Kinematic approach

A kinematic approach provides an objective, specific, and sensitive analysis of movements covering a range from simple reaching up to complex activities of daily living (De Los Reyes-Guzmán et al., 2014; Gulde et al., 2024; Gulde & Hermsdörfer, 2018). Until now, the prevailing approach for analyzing end effector movements has been through motion capturing, often utilizing technologies like optoelectronic motion capture (Alt Murphy & Häger, 2015; Zhou & Hu, 2008). The method quantifies movements by considering various aspects derived from the spatio-temporal positioning of body parts, such as the end effectors of the

upper limbs (i.e., hands). However, it does not directly evaluate qualitative parameters like errors. Given that cognitive impairments can manifest as motor symptoms (Hermsdörfer et al., 1996), employing the kinematic approach on activities of daily living allows for the assessment of not just motor capabilities but also the linked cognitive functions (Gulde et al., 2019; Gulde & Hermsdörfer, 2017).

There is a growing interest in wearables due to their small size and inconspicuous nature, offering significant potential for various applications (Mohler et al., 2015). Instead of relying on velocity data obtained by mathematically integrating the acceleration signal from the smartwatch used, we chose to utilize the raw acceleration signal. Although it is possible to calculate velocity and position through twofold integration, the resulting discrepancy poses challenges for accurate interpretation (Kowalczuk & Merta, 2015).

In the FRAIL project, an innovative method using a smartwatch was employed to evaluate various aspects of daily life discreetly and with minimal intrusion. The novelty of this method was particularly evident in its focus on using a wrist-worn device to gather information on upper-extremity activities as well.

2.1 Study I & II: Kinematic analysis of daily living activities

The subsequent section covers the methodologies employed in both the HCII proceedings paper (Publication I) and the BMC paper (Publication II) on the analysis of ADL performance. The HCII proceedings served as a proof-of-concept and laid the groundwork for the more sophisticated BMC publication. A more detailed description of the methodological approach of the proof-of-concept can be found in the respective publication from Schmidle et al. (2020). The BMC Geriatrics study expanded upon this research through more advanced analyses involving a larger number of participants (Schmidle et al. 2022). Therefore, in the following, the precise methodology of study II will be elucidated. The primary objective of the initial two studies was to examine whether the performance of ADL tasks among elderly individuals with frailty could be evaluated using an activity measurement derived from an acceleration sensor integrated into a smartwatch. Additionally, the studies aimed to assess the extent to which kinematic parameters remained consistent regardless of the specific task being performed (Schmidle et al., 2020, 2022).

2.1.1 Study population and setting

In total, twenty-seven older adults were recruited to participate in the experimental study. The main recruitment process was done in care institutions and the community. To be eligible for inclusion, individuals needed to be at least 60 years old and achieve a minimum score of 24 points on the Mini Mental State Examination (MMSE) (Folstein et al., 1975). Those with cognitive impairments or severe neurological conditions were not considered for participation, due to the primary focus on physical frailty. Overall, each participant was measured for approximately 30 minutes. A posthoc power analysis (using G*Power 2) conducted for "MANOVA: Repeated measures, within-between interaction" revealed a power exceeding 0.99 (Lakens, 2013), indicating that our approach had sufficient sample size.
2.1.2 Frailty assessment

To evaluate the frailty status of each participant, we assessed physical frailty by an adapted Fried phenotype as described by Kunadian et al. (Kunadian et al., 2016). Hence, we measured five different criteria, with detailed description provided in the Appendix (Appendix 1): "weight loss" (BMI < 18.5kg/m²), "exhaustion" (two questions from the geriatric depression scale), "low physical activity" (rarely or never engaging in moderate or vigorous activities), "low grip strength" (measured using a dynamometer), and "slow walking speed" (Timed up & go (TUG) \geq 19 seconds). A score of 0 is classified as robust, while scores of 1 or 2 are considered pre-frail, and scores of 3 or higher are indicative of frailty. The "weight loss" criterion was assessed by computing the BMI and applying a threshold of < 18.5 kg/m². Additionally, gait speed was evaluated using the TUG with a threshold of \geq 19 seconds. Depression was measured by asking participants two questions: a) "do you feel full of energy?" and b) "during the last 4 weeks how often did you rest in bed during the day?". As a result, each participant was assigned a score between 0 and 5, reflecting their degree of frailty.

2.1.3 Analysis of daily life performance

To initiate the first step of moving the measurement process from the conventional laboratory setting to the participants' natural surroundings, we created a measurement environment integrated into the daily living context. The subsequent picture illustrates the setup within the common room of a senior residence.



Figure 7. Photography of a participant performing the TEA task. Copyright: Stephanie Schmidle / TUM

Task and procedure

The selection of the tasks was based on the "Assessment of Motor and Process Skills" (AMPS) (Gary, 2011) and a study of Gulde and colleagues (Gulde et al., 2017). All participants executed two different tasks, replanting a plant (GARDENING task) and preparing a cup of tea (TEA task), see Figure 7 and Figure 8. Participants performed each task once in a pseudorandomized order. Individuals unable to stand

were allowed to sit. To create comparable conditions for each participant, the included items and the test setup were standardized (Table 2).

	TEA Task	GARDENING Task
	Water container (approximately 250 ml water	Water can (approximately 500 ml
	at room temperature)	of water)
Items	Electric kettle	Container of soil
	Box filled with tea bags	Plant
	Bowl of sugar	Flowerpot
	Plate for discarding the used tea bags	Planting container
	Teacup	Pair of gloves
	Teaspoon	Hand trowel

Table 2. Overview of all items used in the performed tasks.

To avoid any common misunderstanding in task performance and to ensure comparability among participants, we provided clear and standardized instructions aimed at achieving typical everyday behavior including a natural speed of execution.

In TEA, the following instructions were given:

"Can you prepare a cup of tea with one spoon of sugar, standing behind the table? Please execute the task in a natural way, as you would do it at home and in a speed and a way which is appropriate for you."

In GARDEN, the following instructions were given:

"Can you replant this plant into the pot and water it, standing behind the table? Please execute the task in a natural way, as you would do it at home in a speed and a way which is appropriate for you."



Figure 8. Setup of the standardized gardening task and tea task, published in (Schmidle et al., 2020, 2022). Throughout the execution of the two ADL, the movement of the dominant hand was recorded using a smartwatch attached with a size-adjustable Velcro strap.

Kinematic analysis

The analysis in this paper stems from previous experience with kinematic analysis of position and velocity data across different populations (e.g., stroke (Gulde et al., 2017), dementia (Gulde et al., 2018), and older adults (Gulde et al., 2019; Gulde & Hermsdörfer, 2017)).

In our study, the hand movement of the dominant hand was captured with a Huawei 2 (4G) smartwatch (Huawei Technologies Co., Ltd., Shenzhen, China). Although the bimanual measurement of hand usage has provided valuable information on, for example, frequency of hand use in daily life (Bailey et al., 2015; Bailey & Lang, 2013; Kalisch et al., 2006), we decided for a unilateral use of the smartwatch as it reflects the normal purpose of a watch. Three-dimensional acceleration signal was recorded with a sampling frequency of 100 Hz. The absolute acceleration vector was determined through the Euclidean mean calculation of the measured orthogonal acceleration and gravity was compensated by subtracting a fixed offset from the Euclidean mean of the three raw acceleration signals (Euclidean Norm Minus One - ENMO). Hence, this can be seen as the adjusted acceleration signal independent of the static gravitational element, representing the dynamic acceleration component (Bakrania et al., 2016). Following this, a local regression algorithm with a window size of 420 ms was employed to smooth the signal. All data processing was performed using MatLab R2020a (The MathWorks Inc., Natick, MA, USA).

Kinematic parameters (Schmidle et al., 2020, 2022)

Activity

- Trial duration (TD): The duration of the task execution in seconds was measured. The investigator initiated the start and end of the recording by activating and deactivating the sensor. The trial duration is widely utilized across various populations, including stroke, dementia, and aging (Gulde et al., 2017, 2018; Gulde & Hermsdörfer, 2017), indicating prolonged trial durations across different tasks. The duration offers a broad estimate of performance.
- Relative Activity (RA): The timeframe during which the absolute acceleration signal exceeded 0.2 m/s² in relation to TD. The scale for this duration ranges from > 0.0 to 1.0, with a value of 1.0 denoting the absence of any periods of inactivity. The inactive intervals can be interpreted as cumulative reaction times. Hence, like reaction times, alterations in this relative activity metric can serve as an indicator of processing speed, with lower values presenting decreased processing speed.

Agility

• Peak Standard Deviation (STD): The standard deviation of all acceleration peaks (local maxima) is measured in m/s². This parameter aims to capture the intensity of actions, with higher values indicating more agile movement execution. Low values, on the other hand, suggest a relatively monotonous behavior.

Smoothness

• Peaks Per Second (PPS): The quantity of acceleration peaks per second serving as an indicator of movement smoothness, with higher number indicating less smooth movement.

- Peak Ratio (RATIO): This measure quantifies the smoothness of movement by comparing the number of acceleration peaks with a minimum prominence of 0.2 m/s² to the total number of acceleration peaks. It provides an indication of the number of distinct movements relative to all movements, encompassing both meaningful movements and noise. Higher values are related to a higher ratio of distinct movements.
- Signal to Noise Ratio (S2N)¹: The ratio between the sum of the frequency spectrum obtained through fast Fourier transformation, ranging from 0.01 to 3 Hz and from 0.01 to 50 Hz, serves as an indicator of movement smoothness (Gulde & Rieckmann, 2019).

Energy

- Weighted Sum of Acceleration per Second (SUM): Temporal mean of squared acceleration. This parameter serves as an estimate for (non-linear) energy expenditure. By squaring the acceleration, the intention is to assign less weight to noise and small movements. Higher values of the SUM parameter indicate increased energy expenditure.
- Acceleration per Second (APS): This parameter reflects the absolute acceleration per second, measured in m/s³ as a measure of energy expenditure. Higher values of the APS parameter typically indicate increased energy expenditure.

Intensity

- Mean Peak Acceleration (MPA): The mean of acceleration peaks is utilized as a metric to quantify the intensity of action, adapted from a similar measure of velocity, for evaluating overall movement speed or intensity (Gulde & Hermsdörfer, 2017). Higher values indicate more intense of faster activity.
- 95th Percentile of Acceleration Peaks (MAX95): The 95th percentile of acceleration peaks is considered an outlier-resistant metric for measuring movement speed or intensity. Higher values of the MAX95 parameter generally indicate faster movements speeds or greater intensity, while lower values suggest slower movement speeds or reduced intensity.

2.1.4 Statistical analysis

To examine interaction effects between task (GARDEN and TEA) and frailty level (robust = R, prefrail = P, and frail = F), we initially conducted a two-way mixed MANCOVA with age as a covariate to account for significant age discrepancies among the groups. Subsequently, we performed one-way ANO-VAs with Tukey post hoc tests to compare kinematic parameters across groups (R, P, and F) and tasks (GARDEN, TEA, and the average of both tasks). To assess the task specificity of the measures, kinematic parameters were correlated between both activities. This approach aimed to identify specific kinematic parameters that were less influenced by the task variation, potentially serving as individuality markers suitable for tracking in real-world scenarios. In the final step, we explored the predictability of the 5-point

¹ This parameter (S2N) was solely employed in paper I and was subsequently omitted from paper II due to insufficient findings.

frailty score using only upper limb performance data. This involved conducting multiple linear regressions on kinematic parameters from both tasks and their average. For the MANOVA analyses, we utilized the R package "MANOVA.RM", which incorporates MATS statistics designed for multivariate data. This package was chosen due to its robustness against data distribution variations and varying dispersion of covariates across groups (Friedrich et al., 2018). Given the limited sample size (n = 27), we employed a bootstrap resampling approach (100 k) as suggested by either Konietschke (Konietschke et al., 2015) or Friedrich (Friedrich et al., 2017).

Effect sizes were presented using partial eta squared η_p^2 and Cohen's d. The critical variance inflation was set at 5.0, and the significance level α was established at 0.05. All statistical computations were conducted using SPSS version 26 software (IMB, NY, United States) and R Studio (version 3.5.1, RStudio Inc., Vienna, Austria).

2.2 Study III: Self-reported physical frailty and sensor-based physical activity measures

The main goal of study III was to explore how sensor-based daily activity measures, such as walking and upper limb activity, relates to self-reported frailty in a group of elderly individuals. To gain deeper insights into this relationship, we further examined behavioral patterns and verified the self-reports through clustering (Schmidle et al., 2023).

2.2.1 Study population and setting

In total, 114 participants were recruited through a convenience sampling method. As outlined in the initial section of the methods chapter, recruitment was conducted as part of the FRAIL project, involving the engagement of partners in France. Therefore, recruitment occurred in both Germany and France from May to November 2019. As part of the project, older adults residing in nursing homes, assisted living facilities, and private residences were invited to take part in the study. Two key persons, one in France and one in Germany, were mainly in charge for regulating the recruitment process. The recruitment within nursing homes and assisted living environments was delegated by respective care managers. In France, four nursing homes were recruited, while in Germany, two nursing homes participated, resulting in a total of six care managers across the institutions (n = 6). Contact with older individuals residing in private residences was facilitated through dissemination efforts in public forums. The study was showcased during senior citizen events, offering older adults the chance to register on a contact list. Subsequently, these individuals were contacted by the respective recruitment organizers. The admission requirements included a minimum age of 60 years and a basic understanding of the processes relevant to the smartwatch measurement. The criteria for exclusion comprised pronounced parchment skin with an increased risk of injury posed by the smartwatch, conditions involving cognitive impairment or dementia that hindered comprehension of the informed consent and the utilization of the smartwatch. The measurement procedure occurred within the participants' respective living environments. A post hoc analysis, utilizing the lowest derived odds ratio (2.93), yielded a power of 0.96. This suggested an adequate sample size.

2.2.2 (Frailty) assessment

The measurements consisted of two components: the subjective frailty questionnaire, which included sociodemographic information and overall physical status (see Appendix 2), and the ongoing activity monitoring conducted with the smartwatch. Initially, the examiner provided an explanation of the technical smartwatch, and participants signed the informed consent form. Subsequently, participants were guided by the trained examiner (i.e., the respective recruitment organizer) to complete the questionnaire.

The self-reported frailty status was evaluated using a questionnaire (Sirven & Rochereau, 2014) following the methodology outlined by Santos-Eggimann et al. (Santos-Eggimann et al., 2009). This questionnaire was designed based on the five criteria derived from Fried's frailty phenotype (Fried et al., 2001). The questions were formulated based on the SHARE cohort survey (2004) incorporating the following operationalized criteria: a) "exhaustion" was identified positive if participants reported insufficient energy to carry out daily tasks, b) the aspect of "weight loss" was assessed by asking about appetite reduction, c) the criterion for "weakness" was considered affirmative if individuals reported an inability to lift objects weighing more than 5 kilograms, d) "low gait speed" was evaluated by inquiring about the ability to climb one or several flights of stairs, c) "low physical activity" was captured with a question about the frequency of engaging in moderate activities. Depending on the number of positive criteria, people were assigned to the respective frailty level (0 = robust, 1-2 = pre-frailty, 3-5 = frailty).

Data concerning sociodemographic status and physical condition were collected through the following aspects: (i) sex (male/female), (ii) age (in years), (iii) BMI (kg/m²), (iv) multimorbidity (number of chronic diseases), such as stroke, hypertension, asthma, and multiple sclerosis, (v) health status (self-rated state of health) rated on a scale of 1 to 5: 1) excellent, 2) very good, 3) good, 4) fair, 5) poor, (vi) course of health status over the past year rated on a scale of 1 to 5: 1) much better now, 2) somewhat better now, 3) about the same, 4) somewhat worse now, 5) much worse now, (vii) feeling of safety at home rated on a scale of 1 to 5: 1) fully, 2) quite a bit, 3) moderately, 4) slightly, 5) not at all, (viii) feeling of safety outside the home rated on a scale of 1 to 5: 1) fully, 2) quite a bit, 3) moderately, 4) slightly, 5) not at all, (ix) living condition: living alone (yes/no), if no, with whom, and (x) use of walking aids (yes/no).

2.2.3 Analysis of daily life performance

As a constitution of studies I and II, with the aim of establishing a naturalistic setting for kinematic data collection, study III integrated the measurement and thus the assessment of everyday performance into the direct daily environment of the participants.

Procedure

For the acquisition of objective physical activity data, we employed (cf. on study I & II) a Huawei 2 (4G) smartwatch (Huawei Technologies Co., Ltd. Shenzhen, China) worn on the participants' preferred wrist. To enhance compliance, participants were provided with the option of selecting their preferred wrist (left wrist = 73; right wrist = 15), as there is no significant difference in counts between dominant and non-

dominant wrist (r = 0.88), and both locations are strongly correlated with counts from a waist-worn sensor (r = 0.88) (Dieu et al., 2017). The onset of the measurement varied among subjects concerning both the day of the week and the time of the day.

Data was periodically transmitted via mobile network to a central server using custom software. Step detection relied on the device's integrated acceleration-based pedometer. Acceleration data was sampled at a frequency of 100 Hz. To document different activities, a 5-second time frame was utilized (Matthews et al., 2012; Vähä-Ypyä et al., 2015) (equivalent to 500 samples per 5-second period). Consequently, the vector magnitude (r) was computed at each time point (i), followed by determining the mean vector magnitude for the 5-second interval (r). This process enabled the calculation of the mean amplitude deviation (MAD) metric – serving as a measure of the intensity of acceleration changes, or in other words, the level of physical activity, for every 5-second dataset (Bakrania et al., 2016):

Mean Amplitude Deviation (MAD) =
$$\frac{1}{n}x\sum_{i=1}^{n}|r_i-\bar{r}|$$

where;

 $r_i = \sqrt{x^2 + y^2 + z^2} = i^{th}$ vector magnitude at each time point \bar{r} = mean vector magnitude within the time period of interest n = length of time period

The MAD represents the average of the dynamic acceleration component. It is derived from the resultant vector of the measured orthogonal acceleration, encompassing a dynamic component caused by velocity variations and a static element due to gravity. The static element is eliminated from the analyzed period, and the remaining dynamic component is reassessed. Consequently, the MAD value can be seen as the mean of the revised acceleration signal, independent of the static element within the timeframe (Bakrania et al., 2016). The MAD metric has been validated across various studies. For instance, Bazuelo-Ruiz and colleagues (2022) reported robust associations between MAD and indirect calorimetry (r = 0.94) (Bazuelo-Ruiz et al., 2022).

Sensor-based parameters

The following figure provides a graphical overview of the MAD-based activity parameters used.



Figure 9. Visualization of the MAD parameters, published in (Schmidle et al., 2023).

- Mean MAD (MADmean): the average of all MAD values in milli-g. Higher values denote greater physical activity. This encompasses more vigorous physical activity.
- Standard deviation of MAD (MADstd): The fluctuation in physical activity measured in millig. Elevated values signify greater variability in physical activity, such as periods of intense activity.
- Relative MAD (MADrel): The proportionate duration spent in MAD levels exceeding 100 milli-g. Increased values suggest greater (health-relevant) physical activity.
- Median MAD (MADmedian): The median of all MAD values in milli-g calculated. Higher values indicate increased physical activity, regardless of the peak MAD levels achieved. It does not specifically account for more intense physical activity.
- 95th percentile of MAD (MAD95): The 95th percentile of all MAD values measured in milli-g. Higher values indicate spikes of intense physical activity. However, it does not consider the overall level of physical activity.
- Fragmentation rate of MAD (MADfrag): The standard deviation of the first derivative of the MAD time-series, measured in milli-g/s. Higher values indicate increased fragmentation of physical activity. While commonly used to characterize the relationship between long and short bouts in ratio, this parameter focuses the adjustment of energy expenditure. Higher values suggest task-specific changes in intensities and are strongly correlated with the total volume of physical activity.
- 95th percentile of cadence (STEP95): The 95th percentile of cadence, measured in steps per minute. Increased values suggest better gait function. However, this measure does not consider overall physical activity related to gait.

• Average number of steps per 5 s (STEPmean): The mean number of steps taken every 5 seconds. Elevated values suggest increased gait-related physical activity.

Data analysis

Participants were considered for analysis only if data were available for a minimum of six days of wear time within a 21-day period, with at least eight hours of measurement between 8:00 am and 8:00 pm. These criteria aimed to ensure reliability (Aadland & Ylvisåker, 2015) and maximize participant inclusion. This approach was based on Aadland & Ylvisåker (2015) that a one-week measurement period already demonstrates acceptable-to-good reliability (Aadland & Ylvisåker, 2015).

2.2.4 Statistical analysis

Initially, we examined the association between the subjective questionnaire score and the accelerationbased parameters "STEP95" and "MADmedian" through Spearman correlation analysis. Despite the high intercorrelation among the sensor-based parameters (as depicted in the publication III, page 72, Figure 4), these two parameters were utilized as proxies. Correlations were computed for both frailty scores: the complete score (ranging from 0 to 5) and the reduced score (ranging from 0 to 3). The distinction between the two frailty scores lay in the exclusion of the criteria "muscle strength" and "weight loss" in the reduced version. This was done to investigate whether the explained variance would rise upon omitting these parameters, which might not be directly measurable using a wrist-worn sensor. Subsequently, a two-component confirmatory principal component analysis (PCA) was performed on the sensor data, employing a varimax rotation. This analysis aimed to differentiate participants' component scores, where one component reflected gait/ambulation and the other reflected upper limb activity. Thresholds for the Kaiser-Meyer-Olkin sample adequacy were set at ≥ 0.50 , and the minimum communalities were defined as ≥ 0.50 .

Utilizing the component scores of individuals, a cluster analysis employing k-medoid clustering was conducted. The determination of the cluster count was obtained from a scree plot. Moreover, we conducted a correlation matrix encompassing all objective activity parameters (smartwatch-based), subjective frailty scores, and the gait and activity dimensions (PCA-based). The difference between clusters in terms of behavioral and person-related attributes were examined using analyses of variance (one-way ANOVAs with Tukey post hoc tests), and for variables such as feeling of security and health status, Kruskal-Wallis tests were employed (Dunn's pairwise comparison post hoc test). The Pearson's Chi-squared test (Fisher's exact post hoc test with Bonferroni correction) was applied for variables such as sex, use of walking aids, and frailty status. Odds ratios and their 95 % confidence intervals were calculated for sex and frailty distribution, as well as for each criterion individually (weight loss, muscle strength, exhaustion, weakness, and low physical activity). Additionally, one-way ANOVAs were conducted to compare each subjective criterion with the objective activity data separately. Effect sizes were indicated as eta squared (η^2), Cramer's V, Cliff's Delta d, Cohen's f², and Cohen's d. The threshold for critical variance inflation was set to 5.0, and the significance level (α) was set to 0.05. All analyses were performed using R Studio (version 2021.09.2, RStudio Inc., Vienna, Austria). Chapter 3

Publication Record

3. Publication record

This section presents the three publications defining this dissertation, including a summary of the abstract of each study, a statement of the authors' contributions, and the original publications.

Study	Title	Authors	Journal	Date of Publi- cation
Ι	Frailty Assessment in Daily Liv- ing (FRAIL) – Assessment of ADL Performance of Frail El- derly with IMUs	Schmidle, S.	Communications in Computer and In- formation Science	08 November 2020
II	Kinematic analysis of activities of daily living performance in frail elderly	Schmidle, S.	BMC Geriatrics	23 March 2022
III	The relationship between self-re- ported physical frailty and sen- sor-based physical activity measures in older adults – a mul- ticentric cross-sectional study	Schmidle, S.	BMC Geriatrics	24 January 2023

3.1 Publication I:

- Authors: Stephanie Schmidle, Philipp Gulde, Bart Jansen, Sophie Herdegen & Joachim Hermsdörfer
- Title: Frailty Assessment in Daily Living (FRAIL) Assessment of ADL Performance in Frail Elderly with IMUs
- o Journal: Communications in Computer and Information Science
- o DOI: <u>https://doi.org/10.1007/978-3-030-60703-6_12</u>
- Citation: Schmidle, S., Gulde, P., Jansen, B., Herdegen, S., & Hermsdörfer, J. (2020). Frailty Assessment in Daily Living (FRAIL) Assessment of ADL Performance of Frail Elderly with IMUs. Communications in Computer and Information Science, 1294, 92–101.

3.1.1 Summary

Frailty is accompanied by limitations in activities of daily living (ADL). These are associated with reduced quality of life, institutionalization and higher health care costs. Long-term monitoring ADL could allow creating effective interventions and thus reduce the occurrence of adverse health outcomes. The main objective of this study was to evaluate if ADL task performance can be assessed by activity measurements based on IMUs, and whether these measures can differentiate individual's frailty. ADL data was obtained from seventeen elderly who performed two ADL tasks - tea making task (TEA) and gardening task (GAR-DEN). Acceleration data of the dominant hand was collected using an activity sensor. Participants were split up in two groups, FRAIL (n = 6; Fried score ≥ 2) and CONTROL (n = 11; Fried score ≤ 1)

retrospectively. Collected data were used to determine trial duration (TD), relative activity (RA), peak standard deviation (STD), peaks per second (PPS), peaks ratio (RATIO), weighted sum of acceleration per second (SUM), signal to noise ratio (S2N) and mean peak acceleration (MPA). STD, RATIO, SUM and MPA showed good reliability over both tasks. Four of the calculated parameters (RA, PPS, RATIO, SUM) revealed significant results differentiating between FRAIL and CONTROL (effect sizes 1.30–1.77). Multiple linear regression showed that only STD correlated with the Fried score. In summary, the results demonstrate that ADL task performance can be assessed by IMU-based activity measures and further allows drawing conclusions on the frailty status of elderly, although the predictability of the exact Fried score was limited.

3.1.2 Author's contributions

Stephanie Schmidle is the first author and corresponding author of this manuscript. Each author contributed to the final version of the manuscript, reviewed it, and gave approval for its publication.

Stephanie Schmidle:	Conceptualization, methodology, validation, formal analysis, in- vestigation, writing – original draft preparation, visualization
Philipp Gulde:	Software, validation, formal analysis, writing – review and edit- ing
Bart Jansen:	Software
Sophie Herdegen:	Methodology, investigation, visualization
Joachim Hermsdörfer:	Resources, writing – review and editing, supervision, project ad- ministration, funding acquisition

3.1.3 Original publication I



Frailty Assessment in Daily Living (FRAIL) -Assessment of ADL Performance of Frail Elderly with IMUs

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Abstract. Frailty is accompanied by limitations in activities of daily living (ADL). These are associated with reduced quality of life, institutionalization and higher health care costs. Long-term monitoring ADL could allow creating effective interventions and thus reduce the occurrence of adverse health outcomes. The main objective of this study was to evaluate if ADL task performance can be assessed by activity measurements based on IMUs, and whether these measures can differentiate individual's frailty. ADL data was obtained from seventeen elderly who performed two ADL tasks - tea making task (TEA) and gardening task (GARDEN). Acceleration data of the dominant hand was collected using an activity sensor. Participants were split up in two groups, FRAIL (n = 6; Fried score \geq 2) and CONTROL (n = 11; Fried score \leq 1) retrospectively. Collected data were used to determine trial duration (TD), relative activity (RA), peak standard deviation (STD), peaks per second (PPS), peaks ratio (RATIO), weighted sum of acceleration per second (SUM), signal to noise ratio (S2N) and mean peak acceleration (MPA). STD, RATIO, SUM and MPA showed good reliability over both tasks. Four of the calculated parameters (RA, PPS, RATIO, SUM) revealed significant results differentiating between FRAIL and CONTROL (effect sizes 1.30-1.77). Multiple linear regression showed that only STD correlated with the Fried score. In summary, the results demonstrate that ADL task performance can be assessed by IMU-based activity measures and further allows drawing conclusions on the frailty status of elderly. although the predictability of the exact Fried score was limited.

Keywords: Activities of daily living · Frailty · Kinematic analysis · Wearables

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1 Introduction

In Western societies, the prevalence of frailty and its adverse health outcomes including falls, delirium, institutionalization, hospitalization and mortality increases [1, 2]. Frailty is understood as a complex concept consisting of various cognitive, psychological, nutritional and social factors [3], representing a high burden for affected individuals, care professionals as well as health care systems [4]. According to the well-known standardized phenotype of frailty by Fried et al. [2], the following five criteria are assessed to determine frailty status: unintentional weight loss, exhaustion, slow walking speed, low grip strength and low physical activity. To be classified as *frail*, at least three criteria have to be present. In contrast, the presence of one or two indicators is categorized as *pre-frail*, whereas the absence of any indicator is termed *robust*.

Elderly people categorized as frail, show an elevated risk of disability [5, 6]. Moreover, compared to non-frail elderly frail individuals demonstrate higher rates of disability in activities of daily living (ADL), often termed as basic ADLs, which are relatively more preserved in light of declined cognitive function. In general, those activities are defined as 'activities essential for an independent life or necessary for survival, representing everyday tasks required for self-care' [7] (e.g., bathing, dressing, eating, toileting and transferring) [4]. Those activities can be separated form instrumental ADLs (IADLs), which include more complex tasks and are more sensitive to early cognitive decline [8]. Changes in ADL performance and especially altered daily activity levels are associated with poor quality of life, increased health care costs, higher mortality and institutionalization [8]. Furthermore, they can provide important information regarding functional and cognitive abilities, loss of autonomy and deterioration in health status [9].

In recent years, the interest in automated methods of real-time, unobtrusive monitoring of ambulation, activity and wellness with technologies typically basing on inertial measurement units (IMUs) has steadily increased [10]. Thus, the analysis of such data has been subject to a plethora of intense research projects including the development of feasible algorithms that are required to translate such measurements into clinically relevant markers [10]. Research focuses on automated monitoring of mobility, ADL and physiological (vital) signs of elderly adults living independently in their homes [10]. Until now, the analysis of ADL performance was limited to subjective scoring and timed actions. Regardless of their validity, these approaches are time-consuming, they often lack objectivity and they are typically bound to a standardized lab setting [11]. Decreased costs of activity tracking systems and devices that are small, mobile and reliable, offer the possibility of a stronger embedding in the clinical routine [12]. Thus, the aim of this cohort study was to assess if ADL task performance can be assessed through a commercially available activity tracking sensor, and whether these measures can differentiate individual's frailty. 94 S. Schmidle et al.

2 Methods

2.1 Subjects

Seventeen older adults (≥ 60 years) participated (for detailed information, see Table 1). Subjects were recruited form care institutions and communities. Inclusion criteria for participation were defined as a minimum age of 60 years and a score of at least 24 points in the Mini Mental State Examination (MMSE) [13]. Elderly people with cognitive impairments (<24 MMSE) or severe neurological conditions were excluded. Ethical approval was given by the ethics committee of the Medical Faculty of Technical University of Munich. All participants gave written informed consent.

2.2 Tasks and Procedure

The measurements were conducted in the participants' homes or in the respective institutions. Each subject received verbal explanation of the procedure in advance. After completion of the demographics form, MMSE and frailty screening were assessed. To ensure a constant setting, the ADL performance was measured in standing position (if possible) behind a table with all equipment placed similarly in front of every participant (see Fig. 1).

Frailty Status. Adopted Fried criteria were applied according to Kunadian et al. [15].

ADL. Participants were instructed to perform two different ADLs. The ADL tasks were to either prepare a cup of tea (tea making - TEA) or to replant a plant (gardening - GARDEN).

In TEA, the following items were given: water container with approximately 250 ml of room-temperatured water, a kettle, a paper box filled with tea bags, a bowl of sugar, a plate to remove the used tea bag, a cup and a teaspoon. Standardized instruction was given to each participant as follows: '*Can you prepare a cup of tea with one spoon of sugar, standing behind the table? Please execute the task in a natural way, as you would do it at home and in a speed, which is appropriate for you'.*

In GARDEN, the following items were given: a box of soil, a watering can filled with approximately 0.5 l of water, a plant, a pot, a planter, gloves and a hand shovel.

Standardized instruction was given to each participant as follows: '*Can you replant this plant into the pot and water it, standing behind the table? Please execute the task in a natural way, as you would do it at home in a speed and a way which is appropriate for you'.*



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Fig. 1. Experimental set-up for the ADL TEA (left) and GARDEN (right).

During the ADL performance, the hand movements of the dominant hand were captured using a Huawei 2 (4G) smartwatch. The 3-dimensional accelerations were recorded with a sampling frequency of 100 Hz. The absolute acceleration vector was calculated, and the signal was smoothed using a 420 ms local regression algorithm [14]. An additional video recording was made to identify the individual action step of boiling time in TEA.

Kinematic Parameters. The analysis was based on previous experience with kinematic analyses of position and velocity data in different populations such as in stroke and dementia patients [16–18]. Instead of velocity, information contained in the acceleration signal was exploited. In this case of mixed, complex ADLs, commonly implemented parameters for movement smoothness, like SPARCL, could not be used [12]. All data processing was performed using MatLab R2020a (Mathworks, Natick, MA, USA). One participant (FRAIL) had to be excluded due to missing watch data. However, information about trial duration was available.

Trial Duration (TD). Time to execute the task in seconds. Time for boiling the water (if passive during this interval) in TEA was removed.

Relative Activity (RA). Period of time in which the absolute acceleration signal exceeded 0.2 m/s^2 related to TD. It ranges from 0.0 to 1.0, with 1.0 indicating the absence of any pauses.

Peak Standard Deviation (STD). Standard deviation of all acceleration peaks (maxima) in m/s². This parameter intends to reflect agility and the capability to adapt one's behavior to varying task demands. Low values represent a rather peculiar monotone behavior.

Peaks Per Second (PPS). Number of acceleration peaks per second.

Peak Ratio (RATIO). Ratio between the number of acceleration peaks with a minimum prominence of 0.2 m/s^2 and the total number of acceleration peaks. A measure of movement smoothness reflecting the amount of distinct movements relative to all movements including noise.

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Weighted Sum of Acceleration per Second (SUM). Temporal mean of squared acceleration. A parameter to estimate energy expenditure.

Signal to Noise Ratio (S2N). Ratio of the sum of the frequency spectrum by a fast Fourier transformation from 0.01 to 3 Hz and from 0.01 to 50 Hz. A measure of movement smoothness [19].

Mean Peak Acceleration (MPA). Mean of acceleration peaks, a measure of the intensity of actions adapted from a similar measure of velocities [17].

Statistical Approach. In a first step, parameters were correlated between the two ADLs (e.g., RA for TEA with RA for GARDEN) in order to estimate the task specificity of the measures. In a second step, kinematic parameters as well as the MMSE were used to model the Fried score by a model of multiple linear regression. Third, ANOVAs (with post-hoc tests) were run in order to compare the above mentioned kinematic parameters for both tasks between groups. Due to the low sample size, we decided to differentiate between subjects with a Fried score below or equal to 1 (CONTROL) and subjects with scores above 1 (FRAIL) (resulting in a sample size of 11 and 6). Effect-sizes are given in Cohen's *d*, the critical variance inflation was 5.0, and α was set to 0.05. All tests were run in SPSS version 26 software (IMB, NY, United States).

3 Results

The cohort consisted of 8 males and 9 females. There was a significant difference in BMI and MMSE between the groups, whereby the frail participants represented the group with the highest BMI and the lowest MMSE values (see Table 1). From the eleven participants of the CONTROL group, 6 scored '0' on the Fried score and 5 scored '1'. From the six participants of the FRAIL group, 3 scored '2', 1 scored '3' and 2 scored '4' on the Fried score.

Not all parameters were significantly correlated between the tasks, but STD, RATIO, SUM and MPA showed significant coefficients of correlation between 0.52 and 0.67 (Table 2). Except STD, which only revealed a trend, all those measures were

Parameter	Age [years]	BMI [kg/m ²]	MMSE
CONTROL $(n = 11)$	77.9	25.9	28.5
	(5.4)	(4.6)	(2.0)
FRAIL $(n = 6)$	82.3	32.3	26.2
	(9.2)	(5.8)	(1.9)
Total $(n = 17)$	79.5	28.2	27.6
	(7.1)	(5.8)	(2.2)
p-value	0.23	0.03*	0.04*

Table 1. Demographics of CONTROL (Fried score ≤ 1) and FRAIL (Fried score ≥ 2).

Mean values, standard deviations and p-values (*p < .05). BMI, Body mass index; MMSE, Mini Mental State Examination. FRAIL - Assessment of ADL Performance of Frail Elderly with IMUs 97

able to significantly differentiate between subjects with a Fried score below or equal to 1 (CONTROL) and subjects with higher Fried scores (FRAIL), when averaging over both tasks. The calculated effect-sizes were very strong, ranging from 1.30 to 1.77 (Table 4). Modelling by multiple linear regressions revealed a significant model with an $R_{adjusted}^2$ of 0.21 (p < 0.05), with only one factor (STD, β-weight = -0.51) (Table 3).

Table 2. Inter-task correlations of the kinematic parameters.

Parameter	TD	RA	STD	PPS	RATIO	SUM	S2N	MPA
r	-0.22	0.49	0.61	-0.04	0.52	0.63	-0.30	0.67
p	0.42	0.06	0.01	0.89	0.04	< 0.01	0.26	< 0.01
D	1							

Pearson's *r*, p-values.

Table 3. Model of multiple linear regression for the Fried score.

Parameter	\mathbb{R}^2	p-value	ß-weight		
Model	(adjusted) 0.21	0.04			
STD		0.04	-0.51		
STD mask standard deviation					

STD, peak standard deviation.

Table 4. Kinematic assessment of TEA and GARDEN in C (CONTROL: Fried score ≤ 1) and F (FRAIL: Fried score ≥ 2).

Parameter		TD	RA	STD	PPS	RATIO	SUM	S2N	MPA
TEA	С	76	0.61	0.66	2.4	0.55	36.2	0.85	0.60
		(14)	(0.10)	(0.16)	(0.5)	(0.09)	(14.1)	(0.06)	(0.15)
	F	88	0.50	0.51	3.4	0.45	26.7	0.75	0.45
		(30)	(0.06)	(0.13)	(1.2)	(0.07)	(8.0)	(0.19)	(0.12)
	<i>p</i> -value	0.25	0.05	0.10	0.03	0.05	0.19	0.10	0.08
	d				1.34				
GARDEN	С	102	0.74	0.84	3.3	0.74	85.8	0.70	0.89
		(43)	(0.02)	(0.18)	(1.6)	(0.05)	(32.7)	(0.21)	(0.16)
	F	75	0.63	0.69	2.7	0.59	42.1	0.82	0.64
		(25)	(0.14)	(0.25)	(0.8)	(0.15)	(31.3)	(0.12)	(0.20)
	<i>p</i> -value	0.23	0.02	0.21	0.42	< 0.01	0.03	0.25	0.02
	d		1.38			1.72	1.35		1.46
Mean of	С	89	0.67	0.76	2.9	0.65	61.0	0.77	0.74
TEA &		(22)	(0.05)	(0.15)	(0.9)	(0.06)	(20.6)	(0.09)	(0.14)
GARDEN	F	80	0.57	0.60	3.0	0.52	34.4	0.78	0.54
		(21)	(0.10)	(0.18)	(0.8)	(0.09)	(18.2)	(0.11)	(0.15)
	<i>p</i> -value	0.44	0.01	0.11	0.68	< 0.01	0.03	0.91	0.02
	d		1.56			1.77	1.30		1.44

Mean values, standard deviations, p-values and Cohen's d. N = 16 except for TD: N = 17.

TD, trail duration [s]; RA, relative activity [-]; STD, peak standard deviation $[m/s^2]$; PPS, peaks per second [1/s]; RATIO, peak ratio [-]; SUM, weighted sum of acceleration per seconds $[m^2/s^5]$; S2N, signal to noise ratio [-]; MPA, mean peak acceleration $[m/s^2]$.

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4 Discussion

The aim of this cohort study was to investigate the feasibility of assessing ADL performance in elderly by accelerometry using an IMU (smartwatch) positioned at the wrist of the dominant upper limb. We adopted and developed a series of parameters, of which four (STD, RATIO, SUM and MPA) showed good reliability over two different tasks (coefficient of correlation > 0.51 between two complex ADLs). Frailty of subjects was defined by the adopted Fried score [15], which was only correlated with the standard deviation of acceleration peaks (STD). When differentiating between subjects with lower and higher Fried scores, four of the used kinematic parameters revealed significant results with effect-sizes between 1.30 and 1.77 (Cohen's d). Interestingly, trial duration (TD) in both ADL were a) not correlated and b) not different between subjects with higher and lower Fried scores. In TEA, the FRAIL group needed on average 155 s to complete the task, whereby the CONTROL group needed 146 s. For GARDEN, the average duration time for FRAIL was 88 s and for CONTROL 75 s. Considering our experience with the increase of TD related to aging [17, 18] and neurological diseases [16] in similar tasks, we hypothesized that these prolongations are due to cognitive aspects of the tasks. However, this is the first time that TD is not a good estimate of general task performance, which should be inferior in persons with higher Fried scores, as actually illustrated by the other kinematic parameters. Since subjects of the FRAIL group did not show this prolongation in the current study, it seems that cognitive factors did not limit performance in these patients. This seems to contradict the reduced MMSE score in the FRAIL group (p = 0.04, d = 1.17). However, the MMSE score is a screening tool for dementia symptoms and probably inadequate to predict impairments of motor function. When averaging kinematic outcomes over both ADLs, subjects with higher Fried scores tended to show less continuous activity throughout the execution of the tasks (RA), less smooth or smaller movements (RATIO), less energy expenditure (SUM), and less intense changes of action (MPA). Subjects with higher Fried scores, thus, revealed a kinematic performance that appeared to be driven by energy saving strategies, which do not necessarily have to lead to different TD. Although the investigated study population and tasks differ, our study is in line with recent research showing that differences in upper limb kinematics in acquired brain injury patients can be detected via IMU sensors and, therefore, offers the opportunity for valuable addition to standardized clinical measures [20].

In summary, subjects' higher Fried scores were associated with slower, more monotonous movements and an overall reduction activity when performing the two ADLs. A smartwatch, attached to the dominant upper limb, was able to detect such kinematic differences and further, parameters showed acceptable inter-task reliability. Such approaches could, in future, help to detect changes of frailty in elderly, not only in nursing homes, but also in hospitals and clinics or in private settings. It remains unclear, if the adopted Fried score in its current form is optimal for categorizing frailty in the elderly. For instance, in our sample, subjects with higher Fried scores were rather obese (BMI: 32.9 ± 5.8 , lower Fried scores BMI: 25.9 ± 4.6 , p = 0.03, d = 1.20), indicating that sarcopenia and loss of appetite does not prevent strong gains in body fat

mass and reflecting the huge variability of the measure. In addition, the amount of predicted variability of the exact adopted Fried score ($R^2 = 0.21$, thus 21%) by the assessment was quite limited. Given the relatively low number of participants in the present study, this analysis should however not be considered conclusive.

Despite many positive findings, this study includes several limitations that need to be addressed. First, data was collected unilateral (dominant upper limb) in two highly complex bimanual ADL tasks. Consequently, detailed evaluation of the upper limb performance including bilateral interaction was not possible. This would be of particular interest, as older adults seem to generate strategies to compensate for their decreased motor capacity probably resulting, among others, in less motor asymmetry and a more equal performance of both hands [e.g., 21], raising the question of how frailty might influence those bimanual interactions. Second, taking the verbal feedback of the participants into account, especially the GARDEN task might have been influenced by motivational factors and highly dependent on the thoroughness of each individual. Further work should consider more standardization strategies for the task set-up and instructions in domestic environment. Lastly, the study successfully proved the value of using acceleration information from an IMU in a commercially available smartwatch for assessing ADLs, while the parameters derived from more classical motion capture systems are calculated from position information and would still be considered the gold standard. Further research should implement a proof of concept by comparing the measurement accuracy and reliability of the used devices.

Even though more data on a larger number of participants is warranted, the results show, that ADL task performance can be assessed by IMU-based activity measures and further allows drawing conclusions on the frailty status of elderly people, although the predictability of the exact Fried score was limited.

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3.2 Publication II:

- Authors: Stephanie Schmidle, Philipp Gulde, Sophie Herdegen, Georg-Eike Böhme & Joachim Hermsdörfer
- o Title: Kinematic analysis of activities of daily living performance in frail elderly
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3.2.1 Summary

Frailty is accompanied by limitations of activities of daily living (ADL) and frequently associated with reduced quality of life, institutionalization, and higher health care costs. Despite the importance of ADL performance for the consequence of frailty, movement analyses based on kinematic markers during the performance of complex upper extremity-based manual ADL tasks in frail elderly is still pending. The main objective of this study was to evaluate if ADL task performance of two different tasks in frail elderlies can be assessed by an activity measurement based on an acceleration sensor integrated into a smartwatch, and further to what degree kinematic parameters would be task independent. ADL data was obtained from twenty-seven elderly participants (mean age 81.6 ± 7.0 years) who performed two ADL tasks. Acceleration data of the dominant hand was collected using a smartwatch. Participants were split up in three groups, F (frail, n = 6), P (pre-frail, n = 13) and R (robust, n = 8) according to a frailty screening. A variety of kinematic measures were calculated from the vector product reflecting activity, agility, smoothness, energy, and intensity. Measures of agility, smoothness, and intensity revealed significant differences between the groups (effect sizes combined over tasks $\eta_p^2 = 0.18 - 0.26$). Smoothness was particularly affected by frailty in the tea making task, while activity, agility, a different smoothness parameter and two intensity measures were related to frailty in the gardening task. Four of nine parameters revealed good reliability over both tasks (r = 0.44 - 0.69). Multiple linear regression for the data combined across tasks showed that only the variability of the magnitude of acceleration peaks (agility) contributed to the prediction of the frailty score $(R^2 = 0.25)$. The results demonstrate that ADL task performance can be assessed by smartwatch-based measures and further shows task-independent differences between the three levels of frailty. From the pattern of impaired and preserved performance parameters across the tested tasks, we concluded that in persons with frailty ADL performance was more impaired by physiological deficiencies, i.e., physical power and endurance, than by cognitive functioning or sensorimotor control.

3.2.2 Author's contributions

Stephanie Schmidle is the first author and corresponding author of this manuscript. The study was led by the TUM. Each author contributed to the final version of the manuscript, reviewed it, and gave approval for its publication.

Stephanie Schmidle:	Conceptualization, methodology, validation, formal analysis, in-
	vestigation, writing – original draft preparation, visualization
Philipp Gulde:	Software, validation, formal analysis, writing – review and edit- ing
Sophie Herdegen:	Methodology, investigation, visualization
Georg-Eike Böhme:	Project administration
Joachim Hermsdörfer:	Resources, writing – review and editing, supervision, project ad- ministration, funding acquisition

3.2.3 Original publication II

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RESEARCH

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Kinematic analysis of activities of daily living performance in frail elderly

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Abstract

Background: Frailty is accompanied by limitations of activities of daily living (ADL) and frequently associated with reduced quality of life, institutionalization, and higher health care costs. Despite the importance of ADL performance for the consequence of frailty, movement analyses based on kinematic markers during the performance of complex upper extremity-based manual ADL tasks in frail elderly is still pending.

The main objective of this study was to evaluate if ADL task performance of two different tasks in frail elderlies can be assessed by an activity measurement based on an acceleration sensor integrated into a smartwatch, and further to what degree kinematic parameters would be task independent.

Methods: ADL data was obtained from twenty-seven elderly participants (mean age 81.6 ± 7.0 years) who performed two ADL tasks. Acceleration data of the dominant hand was collected using a smartwatch. Participants were split up in three groups, F (frail, n = 6), P (pre-frail, n = 13) and R (robust, n = 8) according to a frailty screening. A variety of kinematic measures were calculated from the vector product reflecting activity, agility, smoothness, energy, and intensity.

Results: Measures of agility, smoothness, and intensity revealed significant differences between the groups (effect sizes combined over tasks $\eta^2_p = 0.18 - 0.26$). Smoothness was particularly affected by frailty in the tea making task, while activity, agility, a different smoothness parameter and two intensity measures were related to frailty in the gardening task. Four of nine parameters revealed good reliability over both tasks (r = 0.44 - 0.69). Multiple linear regression for the data combined across tasks showed that only the variability of the magnitude of acceleration peaks (agility) contributed to the prediction of the frailty score ($R^2 = 0.25$).

Conclusion: The results demonstrate that ADL task performance can be assessed by smartwatch-based measures and further shows task-independent differences between the three levels of frailty. From the pattern of impaired and preserved performance parameters across the tested tasks, we concluded that in persons with frailty ADL performance was more impaired by physiological deficiencies, i.e., physical power and endurance, than by cognitive functioning or sensorimotor control.

Keywords: Activities of Daily Living, Frailty, Kinematic Analysis, Wearables, Accelerometry

Introduction

Life expectancy rapidly increases in virtually all developed countries [1], which consequently leads to a

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larger number of older people as well as an altered ratio between young and old. Old age and its complex processes is known to be accompanied by many geriatric phenomena, like multimorbidity [2] disability [3], and frailty [4], which are, as they are quite unspecific concepts, highly interrelated. The phenomenon of frailty has increasingly received attention during the past decades,

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as it has been shown to be linked to adverse health outcomes including falls, delirium, institutionalization, and mortality [4-6]. In a broader sense, frailty is understood as a complex concept consisting of various physical, cognitive, nutritional, and social factors [7, 8], representing a high burden for affected individuals, formal and informal caregivers as well as health care systems [9]. According to the well-known standardized phenotype of frailty by Fried et al. [4], the following five criteria are assessed to determine frailty status: unintentional weight loss, exhaustion, slow walking speed, low grip strength, and low physical activity. To be classified as *frail*, at least three criteria must be present. In contrast, the presence of one or two indicators is categorized as pre-frail, whereas the absence of any indicator is termed robust. It is assumed that frailty among older persons is a dynamic process which is characterized by frequent transitions between frailty states over time. Within this context, transitions to states of advanced frailty are more common than vice versa (hysteresis) [6].

Therefore, early detection of risks associated with the aging process is important to minimize and/or slow down its negative consequences [10]. In case of frailty, this becomes particularly clear when we take a closer look at the disease-related risks that threaten independency of daily living in older people. Elderly people, categorized as frail, show an elevated risk of disability [5, 11, 12]. Thus, frail individuals demonstrate higher rates of developing or worsening disabilities in mobility as well as in basic (b-ADL) and instrumental (i-ADL) activities of daily living over time. These associations can equally be observed among pre-frail elderly, though with a lower magnitude of effect (e.g., [5, 13-16]). ADL typically involve various self-care activities with different degrees of complexity. In general, b-ADL are defined as 'activities essential for an independent life or necessary for survival, representing everyday tasks required for self-care' [10]. Whereby i-ADL cover somewhat a more complex set of behaviors [17] and are more sensitive to early cognitive decline [18]. Limitations of b-ADL are frequently measured using the Katz ADL scale [19] or the Barthel Index [20]. I-ADL, on the other hand, are commonly assessed by the Lawton & Brody scale [17]. Changes in ADL performance and especially altered daily activity levels are associated with poor quality of life, increased health care costs, higher mortality, and institutionalization [18]. Furthermore, they can provide important information regarding functional and cognitive abilities, loss of autonomy, and deterioration in health status [21]. Macklai and colleagues [13], as an example, illustrated in their study involving 11,015 community-dwelling men and women, that at 2-year follow up, frail individuals had odds ratios of developing disability in mobility OR 3.07 (95% CI 1.02-9.36),

i-ADL OR 5.52 (95% CI 3.76–8.10), and b-ADL OR 5.13 (95% CI 3.52–7.44). Thus, deficits of all types of ADL are associated with frailty and these deficits are of highest relevance.

Sensitive and objective assessment of ADL meets several methodological challenges. This is partly due to the fact that the performance of ADL and especially i-ADL often involves complex sequences of actions and a large amount of degrees of freedom in the strategies and ways to execute those [22]. In manual ADL, such as preparing meal, action sub steps like transporting, grasping, rotating, circling, or balancing, repeatedly alternate with each other and with phases of inactivity [23]. The analysis of ADL performance is in general often limited to subjective scoring of health professionals or the individuum itself, with scores as indicated above. In addition, performance is quantified by measuring the duration of activities, such as walking a certain distance or executing a task. Questionnaire-based methods are subjective, and the time-based assessment does not necessarily represent the characteristics of the movements and the underlying causes for such alterations. It has therefore been concluded that the quantification of movement characteristics employing kinematic analyses may be critical for measuring the extent of frailty [24]. So far, the evaluation of ADL in frail elderly is primarily covered by subjective questionnaires (see above) and approaches involving kinematic analyses of ADL have been mainly focused on lower extremity measures [24], such as various gait parameters and posture, or analyzed kinematics of the upper extremity as secondary outcome. Kubicki and colleagues [25], for example, investigated postural control during self-generated perturbations (rapid focal armraising movement towards a target) in frail older adults. Hand kinematics were measured via a Vicon motion capturing system. According to their results, compared to healthy controls, frail participants showed slower hand movements accompanied with delayed postural control, with the latter deficit being the main finding of this study.

Both video analyses and kinematic approaches have been used in studies of upper limb ADL characteristics in various neurological conditions. Investigations of disturbances of ADL in the context of apraxia in stroke or dementia have evaluated videos of execution with respect to defined criteria [26–31]. These studies revealed characteristic error profiles for the different diseases depending on the ADL under examination. However, they are also time-consuming and request expertise to achieve sufficient test reliability. Also, they lack information about speed and fluency of motor execution. In studies utilizing the kinematic approach, trajectories of hand movements were recorded using motion capture methods during execution of a variety of ADL in the context of aging, spinal cord injury as well as in stroke and dementia patients [22, 32–40]. These studies revealed increases in task duration combined with decreases of speed and increased ratios of inactivity as well as more segmented velocity profiles with multiple peaks in stroke patients and elderly compared to young participants. Thus, young participants tended to be faster in task performance than elderly participants and the elderly participants tended to be faster than stroke survivors. Additionally, the movements of young subjects covered less distance compared to the other groups. This suggests that e.g., distance and duration are not only influenced by stroke but also by the aging process. Therefore, kinematic analyses of ADL revealed detailed characteristic performance patterns with high precision and sensitivity.

Recent advances in wearable technologies and data processing technologies have opened new opportunities for the development of practical and automated tools [41] to perform clinical screening in the natural environment outside the laboratory (e.g., [42-45]). Activity tracking systems based on inertial measurement units (IMUs) are small and mobile and enable kinematic analyses independent of a special lab environment. Recently, an approach to assess the dimensions of frailty, as it was characterized by Fried [4], in hand movements in the geriatric population using IMU-based wrist sensors has been introduced [43]. By performing repetitive elbow flexion movements, IMU signals were processed to represent information on the frailty criteria slowness, weakness, and exhaustion. The results showed that there was clear difference in speed of flexion (slowness), power of movement (weakness), and speed variation (exhaustion) between elderly participants associated to the three frailty stages according to the Fried criteria.

Despite the importance of ADL performance for the consequence of frailty (see above), to date and to the best of our knowledge, a movement analysis based on kinematic markers during the performance of complex upper extremity-based manual ADL tasks in frail elderly is still pending. Thus, the main objective of this experimental study was to analyze manual ADL task performance for two different tasks assessed by unilateral activity measurements based on an acceleration sensor integrated into a wrist-worn smartwatch. In a second step, we analyzed whether these measures differ between individual stages of frailty. Additionally, to better understand hand kinematics in the context of frailty, we evaluated possible interaction effects and the effect of task to gain a more comprehensive understanding of the interplay between frailty and task and task-related differences between parameters. Using accelerometry assessment we envisioned a proof-of-concept for this wearable-based approach, which avoids the need for direct observation, Page 3 of 15

video recording, laborious and expensive equipment, and is not bound to laboratory testing. Further, with the outlook of assessments in daily life without standardized tasks, we were interested to examine to what degree kinematic parameters would be task independent. Accordingly, we tested two different ADL in a group of seniors without or with different degrees of frailty. A report which mainly assessed the technical aspects of the approach in a sub-group of the participant has recently been published elsewhere [46].

Materials and Methods

Participants

Twenty-seven older adults aged 60 years and older (min – max: 68 – 96 years) participated in this study. Subjects were recruited from care institutions and the community. Inclusion criteria for participation were defined as a minimum age of 60 years and a score of at least 24 points on the Mini Mental State Examination (MMSE) [47]. Elderly people with cognitive impairments (<24 MMSE) or severe neurological conditions were excluded (see Fig. 1). Ethical approval was given by the ethics committee of the Medical Faculty of Technical University of Munich. All participants gave written informed consent.

A posthoc power analysis (G*Power 2) for 'MANOVA: Repeated measures, within-between interaction resulted in a power of > 0.99 [48], indicating a sufficient sample size for our approach.

To assess the frailty status of each participant, an adapted version of the Fried frailty score was applied according to Kunadian et al. [49]. Similar to the original Fried score (see Introduction), the performance on five criteria 'weight loss', 'exhaustion', 'low physical activity', 'low grip strength', and 'slow walking speed' was assessed. With failures in one or two criteria, a person was categorized as 'pre-frail' (P), above as 'frail' (F), and with no failure as 'robust' (R). Table 1 shows the resulting number of participants in each frailty category as well as the participants' age, anthropometrics, MMSE, grip strength, timed up & go test (TUG), and sex. Eight participants had no positive criterion and were thus in the group of robust. From the 13 participants of the pre-frail group, six scored '1' and seven scored '2'. From the six participants of the frail group, three scored '3' and three scored '4' Fried points. Statistical analysis for differences between the subgroups revealed no difference for sex, height, weight, BMI, and MMSE but a statistical difference for age, grip strength, and the TUG (one-way ANOVA: age, height, weight, BMI, MMSE, grip strength, and TUG; and Pearson Chi-Squared test: sex). Pairwise post hoc tests (Tukey tests) confirmed age differences between the frail group and the two other groups (R-F p = 0.003, P-F p = 0.004), but no significant difference between the age of the

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Table 1 Descriptive statistics of the subsamples

Characteristics	Robust R	Pre-frail P	Frail F	Total	P-value	Effect Size
	n=8	n=13	n=6	n=27		
Female, n (%)	6 (75)	7 (54)	5 (83)	18 (67)	0.304	V 0.291
Age (years)	78.4 (6.5)	79.8 (5.6)	89.8 (4.2)	81.6 (7.0)	0.002*	n ² _p 0.413
Height (cm)	165.0 (6.6)	167.4 (9.1)	164.3 (12.3)	166.0 (9.0)	0.750	n ² 0.024
Weight (kg)	76.1 (23.6)	80.8 (15.9)	83.8 (16.3)	80.1 (18.0)	0.728	n ² _p 0.026
BMI (kg/m ²)	27.9 (8.4)	28.6 (4.0)	31.3 (7.8)	29.0 (6.3)	0.586	n ² _p 0.044
MMSE	28.1 (1.9)	27.5 (2.0)	25.8 (1.9)	27.3 (2.1)	0.111	n ² _p 0.167
Grip strength (kg)	24.4 (7.2)	19.4 (8.3)	10.8 (7.2)	19.0 (9.0)	0.012*	n ² 0.308
TUG (sec)	11.9 (4.4)	20.7 (11.5)	30.3 (9.5)	18.9 (10.9)	0.023*	n ² p 0.302

Mean values, standard deviations, and p-values of sample comparison (an asterisk indicates a statistically significant group effect). Effect Sizes: η_p^2 partial eta squared and Cramer's V. BMI Body mass index, BMSE Mini Mental State Examination, TUG timed up & go test

robust and the pre-frail group. For grip strength, there was a significant difference between the robust and the frail group (R-F p = 0.009) and a tendency between pre-frail and frail participants (P-F p = 0.081). Furthermore, the TUG differed between the robust and the frail group (R-F p = 0.025). Three of the six individuals classified as frail were unable to perform the TUG test at all.

Task and procedure

The measurements were conducted in the participants' homes or in the respective institutions. Each subject received verbal explanation of the procedure in advance. After completion of the demographics form, MMSE and frailty status were assessed. ADL performance was measured in standing position (if possible) behind a table with all items placed in front of every participant in a standardized way (Fig. 2). Participants who were not able to stand were allowed to sit on a chair. Post hoc inspection of their results did not reveal any obvious discrepancy with the standing participants.

Activities of daily living

Participants were instructed to perform two different ADL. Each ADL was performed once in a pseudorandomized order. The ADL tasks were to prepare a cup of tea (tea making – TEA) or to replant a plant (gardening – GARDEN), see Fig. 2.

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In TEA, the following items were given: water container with approximately 250 ml of room-temperatured water, a kettle, a paper box filled with tea bags, a bowl of sugar, a plate to remove and place used tea bags, a cup, and a teaspoon. Standardized instruction was given to each participant as follows:

'Can you prepare a cup of tea with one spoon of sugar, standing behind the table? Please execute the task in a natural way, as you would do it at home and in a speed and a way which is appropriate for you.'

In GARDEN, the following items were given: a box of soil, a water can filled with approximately 500 ml of water, a plant, a pot, a planter, gloves, and a hand shovel. Standardized instruction was given to each participant as follows:

'Can you replant this plant into the pot and water it, standing behind the table? Please execute the task in a natural way, as you would do it at home in a speed and a way which is appropriate for you.'

During the ADL performance, the hand movement of the dominant hand was captured using a Huawei 2 (4G) smartwatch attached with a size-adjustable velcro strap.

Sensor-based kinematic parameters

Sampling frequency of the 3-dimensional acceleration signals was 100 Hz. The absolute acceleration vector was calculated by the Euclidean mean. The gravitation was subtracted as a constant (see Discussion), and the signal was smoothed using a 420 ms local regression algorithm [50]. The analysis was based on kinematic parameters using acceleration data identified in our previous study [46]. Two additional parameters (*Acceleration per Second* (APS) and 95th Percentile of Acceleration Peaks (MAX95)) were included to have supplementary parameters for energy expenditure and an outlier-robust measure of speed/intensity. Additionally, parameters were grouped according to their intention of measure (activity, agility, smoothness, energy, and intensity). All data processing was performed using MatLab R2020a (The MathWorks Inc., Natick, MA, USA).

Activity

- Trial Duration (TD): Time to execute the task in seconds. The start and end was triggered by the investigator by starting and stopping the sensor recording.
- *Relative Activity (RA):* Period of time in which the absolute acceleration signal exceeded 0.2 m/s² related to TD. It ranges from > 0.0 to 1.0, with 1.0 indicating the absence of any phases of inactivity.

Agility

• *Peak Standard Deviation (STD):* Standard deviation of all acceleration peaks (local maxima) in m/s². This parameter intends to reflect the intensity of actions with high values reflecting more agile movement execution. Low values represent a rather peculiar monotone behavior.

Smoothness

 Peaks Per Second (PPS): Number of acceleration peaks per second as a measure of movement smoothness.

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 Peak Ratio (RATIO): Ratio between the number of acceleration peaks with a minimum prominence of 0.2 m/s² and the total number of acceleration peaks. A measure of movement smoothness reflecting the amount of distinct movements relative to all movements including noise.

Energy

- Weighted Sum of Acceleration per Second (SUM): Temporal mean of squared acceleration. A parameter to (non-linearly) estimate energy expenditure. Noise and small movements were intended to be weighted less by using the square of acceleration.
- Acceleration per Second (APS): Absolute acceleration per second in m/s³ as a measure of energy expenditure.

Intensity

- Mean Peak Acceleration (MPA): Mean of acceleration peaks as a measure of the intensity of actions adapted from a similar measure of velocity to assess general movement speed/intensity.
- 95th Percentile of Acceleration Peaks (MAX95): The 95th percentile of all acceleration peaks thought as an outlier-robust measure of movement speed/intensity.

Statistical Approach

In a first step, a two-way mixed MANCOVA was run to test for an interaction effect between task and frailty status with age as covariate. One-way ANOVAs (Tukey post hoc) were run to compare the above-mentioned kinematic parameters for group (R, P, and F) and task (task average, TEA, GARDEN). In a second step, kinematic parameters were correlated between the two ADL (e.g., RA for TEA and RA for GARDEN) to estimate the task specificity of the measures. Third, it was investigated whether the 5-point-frailty score can be predicted from the performance data. To that aim, kinematic parameters (TEA, GARDEN, and average) were used to model the adapted Fried score by models of multiple linear regression (MLR). For MANCOVA analyses, the R package "MANOVA.RM" including MATS statistics for multivariate data was used as it proved to be independent of distribution of the data and unequal dispersion of covariates between groups [51]. Furthermore, a bootstrap resampling approach (100 k) was used as proposed by Konietschke et al. [52] or Friedrich et al. [53] in case of small sample sizes. Effect-sizes were given in partial eta squared η_p^2 and Cohen's *d*, the critical variance inflation was 5.0, and α was set to 0.05. All tests were run in SPSS version 26 software (IMB, NY, United States) and R Studio (version 3.5.1, RStudio Inc., Vienna, Austria).

Results

The following plots illustrate the rectified and smoothed (2 s 'loess' filtered absolute accelerations for illustration purposes) acceleration profiles of a frail and non-frail participant for the GARDEN and the TEA task. Profile a) (Fig. 3) shows the movement graph with the majority absolute accelerations between 0.5-1.0 m/s² and maximal peaks of about 4 to 4.5 m/s². The profile illustrates a pause between second 40 and 70 most probably indicating a segment of the boiling phase of the water (expected standardized boiling time of 60 s for each participant). The activity graph of the frail participant (Fig. 3b) shows total accelerations primarily between 0.2 and 0.6 m/s². The acceleration peaks achieved values of up to 1.2 m/ s^2 . It is noticeable, that there seems to be no clear movement pause during the boiling period of the water. The total duration between the frail and non-frail person in this case was quite equal. Profiles c) and d) illustrate the GARDEN task. Again, there are obvious differences in the magnitude of acceleration between the non-frail and frail participant, with values as high as 6 m/s² compared to approximately 2 m/s². Additionally, the frail person executed the task in less time (45 s vs. 114 s).

Many (but not all) of these findings turned out to be representative for the groups of participants, as shown below.

Group differences and Inter-task correlations

Our initial MANCOVA revealed no significant impact of age. Therefore, we reanalyzed the data using a MANOVA. The analysis showed significant main effects of frailty status (group) and task and no significant interaction effect of frailty status and task (see Table 2). Table 3 shows the main effect of group and task for each kinematic parameter. Table 4 illustrates the results of the post hoc ANOVAs for the group effect for the two tasks separately. Figure 4 provides graphical representations of the results for four selected parameters.

The main effect of task revealed significant differences for the kinematic parameters, F (9.000, 16.000) = 320.446, p = < 0.001. All parameters, except the 'energy' measure SUM, showed significant differences between the tasks with effect sizes ranging from 0.15 to 0.72 (η_p^2 partial eta squared), see Table 3. Additionally, there was a significant main effect of group, F (18.000, 34.000) = 55.856, p = 0.03. Further comparisons showed that the 'agility' measure STD, the 'smoothness' measure PPS, and the 'intensity'

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Table 2 Results of MANO	AVC	
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Effect	F (18.000, 34.000)	p-Value	
Group	55.856	0.03*	
Task	320.446	< 0.01*	
Group x Task	36.078	0.12	

* Significant effect is reached

measure MPA statistically differed between subjects with frailty scores of '0' (R), of '1–2' (P), and \geq '3' (F) (see Table 3). Post hoc tests revealed significant differences between robust subjects and subjects who were pre-frail or frail. No significant post hoc test was found comparing

the group of pre-frail and frail. The calculated effect sizes for the post hoc comparison tests ranged between -1.73 – 1.40 (Cohen's d). Smoothness RATIO and intensity MAX95 revealed trends for statistically significant differences between groups (p=0.08 and 0.06), Table 3.

For the TEA task, the parameter PPS, characterizing movement smoothness, significantly differed between the groups, F (2,24) = 3.694, p = 0.04, see Table 4 and Fig. 4. A Tukey post hoc test confirmed PPS differences between the frail group and the robust group (F-R p_{tukey} = 0.04), but no significant differences between the PPS values of the robust and the pre-frail group as well as the pre-frail group and frail group. ANOVAs for the STD

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Parameter		Activity		Agility	Smoothness		Energy		Intensity	
		TD (s)	RA (-)	STD (m/s ²)	PPS (1/s)	RATIO (-)	SUM (m ² /s ⁵)	APS (m/s ³)	MPA (m/s ²)	MAX95 (m/s ²)
Group	R	116 (21)	0.57 (0.04)	0.73 (0.14)	3.3 (0.1)	0.55 (0.05)	23.87 (6.33)	21.05 (3.12)	0.67 (0.11)	1.39 (0.26)
	Р	134 (46)	0.55 (0.10)	0.61 (0.12)	3.5 (0.3)	0.49 (0.08)	25.20 (13.90)	19.94 (5.20)	0.54 (0.12)	1.18 (0.24)
	F	118 (38)	0.56 (0.08)	0.51 (0.20)	3.7 (0.3)	0.47 (0.09)	26.39 (11.17)	21.74 (4.00)	0.50 (0.14)	1.01 (0.37)
	р	0.56	0.92	0.03*	0.04*	0.08	0.92	0.69	0.03*	0.06
	η^2_p			0.26	0.18				0.26	
Task	Теа	145 (35)	0.44 (0.13)	0.52 (0.14)	3.6 (0.3)	0.34 (0.10)	25.23 (10.44)	17.88 (6.17)	0.38 (0.11)	0.93 (0.24)
	Garden	105 (61)	0.67 (0.11)	0.74 (0.22)	3.4 (0.3)	0.67 (0.12)	24.91 (15.63)	23.46 (5.44)	0.75 (0.24)	1.47 (0.46)
	р	0.005*	< 0.001*	< 0.001*	0.003*	< 0.001*	0.93	<0.001*	< 0.001*	< 0.001*
	η^2_p	0.15	0.47	0.28	0.15	0.72		0.19	0.51	0.37

Table 3 Main effects of group (robust, pre-frail, frail) and task (TEA, GARDEN) for the kinematic parameters

Mean values, standard deviation, *R* robust: '0', P pre-frail: '1–2', F frail: '3–5', p-value, η_p^2 partial eta squared. *TD* Trial Duration, *RA* Relative Activity, *STD* Peak Standard Deviation, *PPS* Peaks Per Second, *RATIO* Peak Ratio, *SUM* Weighted Sum of Acceleration per Second, *APS* Acceleration per Second, *MPA* Mean Peak Acceleration, *MAX95* 95th Percentile of Acceleration Peaks

Table 4 Kinematic assessment of the tea and gardening task in R (robust: '0'), P (pre-frail: '1-2') and F (frail: '3-5')

Parameter		Activity		Agility	Smoothness		Energy		Intensity	
		TD (s)	RA (-)	STD (m/s ²)	PPS (1/s)	RATIO (-)	SUM (m ² /s ⁵)	APS (m/s ³)	MPA (m/s ²)	MAX95 (m/s ²)
TEA	R	137 (28)	0.40 (0.08)	0.60 (0.11)	3.4 (0.2)	0.36 (0.10)	22.81 (7.76)	16.30 (3.06)	0.39 (0.09)	0.99 (0.19)
	Ρ	150 (42)	0.44 (0.16)	0.51 (0.11)	3.7 (0.4)	0.32 (0.09)	24.15 (11.90)	17.61 (8.27)	0.38 (0.14)	0.95 (0.27)
	F	147 (30)	0.51 (0.12)	0.42 (0.16)	3.9 (0.2)	0.34 (0.05)	30.79 (9.67)	20.57 (2.82)	0.38 (0.05)	0.83 (0.24)
	р	0.74	0.28	0.06	0.04*	0.72	0.33	0.06	0.97	0.47
	η^2_p				0.24					
GARDEN	R	96 (32)	0.74 (0.03)	0.88 (0.18)	3.3 (0.2)	0.75 (0.05)	24.93 (9.24)	25.80 (4.43)	0.94 (0.18)	1.78 (0.39)
	Р	117 (76)	0.66 (0.11)	0.71 (0.20)	3.3 (0.4)	0.64 (0.12)	26.24 (18.77)	22.26 (5.14)	0.69 (0.20)	1.42 (0.39)
	F	90 (59)	0.61 (0.15)	0.61 (0.24)	3.6 (0.4)	0.60 (0.15)	21.99 (17.05)	22.92 (7.09)	0.61 (0.25)	1.19 (0.50)
	р	0.64	0.03*	0.05*	0.28	0.02*	0.87	0.35	0.01*	0.04*
	η^2_p		0.20	0.22		0.23			0.31	0.24
Inter-task correlation	r	0.19	-0.15	0.61	0.69	0.16	0.45	0.11	0.11	0.44
	p	0.34	0.46	<.001	<.001	0.54	0.02	0.59	0.60	0.02

Mean values, standard deviation, p-value, r inter-task correlation, n²_p partial eta squared. *TD* Trial Duration, *RA* Relative Activity, *STD* Peak Standard Deviation, *PPS* Peaks Per Second, *RATIO* Peak Ratio, *SUM* Weighted Sum of Acceleration per Second, *APS* Acceleration per Second, *MPA* Mean Peak Acceleration, *MAX95* 95th Percentile of Acceleration Peaks

('agility') and APS ('movement energy') revealed trends for differences between groups (p = 0.06, see Table 4).

For the GARDEN task, RA ('activity'), STD ('agility'), the RATIO ('smoothness'), and the two measures for movement 'intensity' MPA and MAX95 significantly differed between the groups with effect sizes ranging from $\eta^2_{\ p}$ =0.20 – 0.31 (see Table 4). The RA values for the GARDEN task showed a decreasing tendency between the robust group towards the frailer participants. Post hoc comparison revealed that RA and RATIO only showed differences between the robust group and the pre-frail group (R-P $p_{tukey}=0.05$ and 0.03, d=0.91 and 1.07). MPA, on the other hand, showed differences between the robust and the pre-frail group as well as between the robust and the frail group (R-P, R-F Cohen's d=1.30 and 1.58). STD and MAX95 differed between robust and frail (R-F Cohen's d=1.30

(See figure on next page.)

Fig. 4 Boxplots of four kinematic parameters for TEA, GARDEN, and task average for the frailty status robust (R), pre-frail (P), and frail (F). *TD* Trial Duration as a measure of activity, *STD* Peak Standard Deviation ('agility'), *PPS* Peaks Per Second ('smoothness'), *MPA* Weighted Sum of Acceleration per Second ('intensity'), * statistically significant group effect (< 0.05), *x* group means, *error bars* standard error. For all measures besides TD, significant group effects were found

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and 1.33), but not between the pre-frail and the frail group.

Compared to the TEA task, task average trial duration (TD) of the GARDEN task was shorter and the ratio of inactivity (1.0 - RA) was also lower (see Table 4) indicating fewer and shorter breaks compared to the TEA task where the boiling of water frequently resulted in movement breaks (see Figure 4). The measures for 'energy' and 'intensity' were all clearly higher than in the TEA task (see Table 4). Of the 'smoothness' measures, PPS was about equal in both tasks, while RATIO was higher in the GARDEN task.

As could be expected from the significant group effects for the averaged measures, the parameters STD, PPS, SUM, and MAX95 showed significant coefficients of correlation between the TEA and GARDEN task ranging from r = 0.44 - 0.69, being particularly high for agility (STD) and smoothness (PPS), see Table 4. In the following figure (Figure 4), TD, STD, PPS and MPA are plotted for each task divided by the three frailty groups.

Models of multiple linear regression

Multiple linear regressions were performed to predict the frailty score with its maximum 5 levels from the kinematic measures obtained from the execution of the two daily living tasks. The kinematic parameters were added to the regression. The prediction model of the frailty status by the task average explained 25% of variance by the parameter STD, F (2, 24)=9.593, p=0.005 (see Table 5). The beta weight was -0.527.

For the TEA task, the smoothness measure PPS and the activity measure RA statistically added to the prediciton of the frailty model, F (2, 24) = 7.116, p 0.004, explaining 32% (R^2_{adj}) of variance (see Table 6). The beta weights were between 0.332 and 0.512.

For the GARDEN task, STD statistically added to the prediction of the frailty status, F (2, 24) = 6.855, p = 0.015, R^2 = 0.184. This variable added statistically to the prediction with a beta weight of -0.464 (see Table 7).

Discussion

The aim of this experimental study was to investigate complex manual ADL task performance employing kinematic analyses based on unilateral acceleration sensor data from a wrist-worn smartwatch. Furthermore, we

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Table 6 Model of frailty score by parameters of the tea task

R ² (adjusted)	p-value	ß-weight	VIF
0.320	0.004		
	0.004	0.512	1.000
	0.051	0.332	1.000
	R ² (adjusted)	R ² (adjusted) p-value 0.320 0.004 0.004 0.004 0.004 0.004	R ² (adjusted) p-value ß-weight 0.320 0.004

PPS Peaks Per Second (1/s), RA Relative Activity (-), frailty score (0-5)

wanted to analyze whether these measures differ between individual stages of frailty and to examine to what degree kinematic parameters would be task independent. The findings of the present analysis indicate that task performance can be assessed via acceleration sensors and do show differences in kinematic parameters for the separate levels of frailty.

Our analyses revealed that there was no significant impact of age and no interaction between the ADL tasks (GARDEN and TEA) and the level of frailty of the participants, which was defined by an adopted version of the Fried score [49]. However, there were significant effects of task and group. All parameters except the 'energy' measure SUM differed significantly between the tasks with large effect sizes between 0.20 - 0.31 (partial eta squared). The main effect of group revealed differences for 'agility' (STD), 'smoothness' (PPS), and 'intensity' (MPA) measures with lower 'agility' (lower STD), less smoothness (higher PPS), and lower 'intensity' (MPA) for participants categorized as pre-frail or frail compared to robust participants. Furthermore, four out of nine parameters (STD, PPS, SUM, and MAX95) showed good reliability over both tasks (coefficient of correlation > 0.43). Models of multiple linear regression were able to predict between 0.18 and 0.32 of the variances in the frailty scores of the elderly, depending on the used task kinematics (TEA, GARDEN, combined tasks). For GARDEN and the combined task, STD significantly contributed to the prediction (beta = -0.46 and -0.53). While in TEA, PPS and RA contributed the most to the model (beta = 0.51 and 0.33, p values = 0.004 and 0.051).

There was a clear difference between the tasks. Except for the energy measure SUM (weighted sum of acceleration per second), all parameters showed significant differences between TEA and GARDEN. This might be

Table 5 Model of frailty score by parameters of the task average

Parameter	R ²	p-value	ß-weight	VIF
Model – Frailty Score	0.248	0.005		
STD		0.005	-0.527	1.000

STD Peak Standard Deviation (m/s²), frailty score (0-5)

 Table 7
 Model of frailty score by parameters of the gardening task

Parameter	R ²	p-value	ß-weight	VIF	
Model – Frailty Score	0.184	0.015			
STD		0.015	-0.464	1.000	

STD Peak Standard Deviation (m/s²), frailty score (0-5)

due to differences in task complexity and requirements [54]. While TEA can be seen as a task requesting precise movements, for example to put the tea bag into the mug, the garden task might demand more energetic and powerful movements with manipulation of heavier objects like the hand shovel or the box with soil. Further group analyses split up for each task separately demonstrated, that for TEA, the smoothness parameter PPS increased with increasing frailty level. MLR revealed that RA and PPS contributed to the prediction. Since smoothness is typically related to movement coordination [23, 55], this finding underpins the assumption, that this task is more dependent on fine motor control. For the GARDEN task, on the other hand, the activity measure RA, the agility measure STD, the smoothness measure PPS, and both intensity measures MPA and MAX95 differed between the groups. Consequently, people with higher level of frailty had more movement pauses during the task execution of GARDEN and less intense and agile movements than the robust ones. This might be related to prolonged planning phases or resting/energy saving under equal duration. MLR showed that only STD ($R^2 = 18\%$) was a significant factor in the model. Additional analysis for the aspect of strength in GARDEN showed that there was a significant correlation between grip strength and STD (r=0.625, p<0.001). Therefore, GARDEN might be more depending on gross motor control.

Interestingly, trial durations (TD) in both complex ADL were not correlated and showed no differences between subjects with higher (frail, F), intermediate (pre-frail, P), and lower frailty scores (robust, R). In TEA, the frail group needed on average 147 s to complete the tasks, whereas the pre-frail group took 150 and the robust group 137 s to complete. For GARDEN, the average duration for the frail participants was 90 s and for the pre-frail and robust individuals 117 and 96 s. This is particularly striking in relation to previous literature that reported clear increases of the duration of similar ADL tasks in the context of neurological conditions, such as spinal cord injury, stroke, and dementia, but also in regards to aging [22, 32-40]. With reference to this rational, we would have expected to find increased TDs in this cohort as well. However, TD seems to be not a good estimate of general task performance (at a natural pace) for people with different levels of frailty. This might be the case in particular if the accuracy is not controlled [56]. Furthermore, given our experience with increases in TD associated with aging [35, 57] and neurological diseases [22] in similar tasks, we hypothesized that these prolongations are due to cognitive aspects of the tasks. In a previous study of our work group [57], young and healthy older adults had to execute a quite similar tea task. The elderly participants committed a higher number of errors

per trial while showing an increase of trial duration (by almost 50%) and path length. The prolongations were particularly dependent on the inactivity phase, while their movement speed and smoothness were comparable to those of the young participants. It was suggested that this pattern might be due to a motor planning and/or a sequencing deficit of the task ([58-60]). Subjects of the frail group did not show this prolongation or increased phases of inactivity (1.0 - RA) in the current experiment, although RA appeared to be a significant predictor in the model of MLR in TEA (frailty score 0-5). Still, cognitive factors may not be the primarily limitation of performance in pre-frail or frail participants if compared to the robust participants. This seems to be in line with equal MMSE scores between the groups (p = 0.11, $\eta_p^2 = 0.167$). Additionally, we excluded participants with lower MMSE scores than 24 to avoid comprehension problems of the tasks. However, it is questionable whether recording the MMSE alone is sufficient for the assessment of the wide range of different cognitive abilities, as other cognitive functions, such as executive functions, might also play an important role (e.g., Trail Making Task (TMT) [35]). Our findings support the assertion of Panhwar and colleagues [24] that, for example, time-based assessments do not necessarily represent the characteristics of the movements and the underlying causes for changes and that, therefore, quantifying movement characteristics using kinematic analyses can be crucial for measuring the extent of frailty.

From the perspective of motor control, movement arises from a close interaction between the individual, the task, and the environment [61]. Consequently, the kinematic variables may reflect individual manifestations of frailty since the task in our experiment was standardized with stable constraints of task and environment. The between-group difference in motor performance (at natural speed) detected by accelerometer-derived measures showed a rather noticeable monotonous behavior in frail participants. This is notable, as the tasks were performed at a natural pace and did not aim to challenge the individual's performance limits. Nevertheless, the analysis revealed clear differences between the groups without a concomitant difference in task duration. This might be comparable to previous findings of our work group where we investigated natural vs. maximal execution speed of ADL between young, old, and retirees. The results showed that the retirees were not able to decrease their trial duration or improve any other kinematic parameter in the fast condition in comparison with the natural condition. This might be based on the assumption that they were already executing the task at their maximum kinematic capacities [35]. This may also have been the case for the frail elderly in our current study. Furthermore, differences in motor performance between frailty levels are in line with literature [25, 43], however, these research groups aimed to predict the Fried score by performing tasks at a fast pace and did find differences in velocities and durations. For example, Toosizadeh and colleagues [43] introduced a quick, simple upper extremity task to categorize frailty levels. Their analyses demonstrated that the speed of elbow flexion showed the largest effect size to distinguish between robust and pre-frail older adults. Power of movement, on the other hand, had the largest effect size for the differentiation between the level of pre-frail and frail. Likewise, Kubicki and colleagues [25] involved arm motion for identifying frailty. The participants were asked to perform a rapid focal arm-raising movement, pointing to a stimulus in standing posture, while their balance was measured using a force platform. Compared to non-frail elderly, the velocity profiles of the hands were flattened. Hand movements were slowed down with longer hand movement times and lower hand peak velocities. Additionally, time peak velocities were longer for the frail group compared to the control group. However, the prefrail category was excluded. In comparison, our results showed that for TEA, PPS and for GAR-DEN STD, MPA and MAX95 differed between robust and frail. The parameters RA, RATIO and MPA (only for GARDEN) showed additional differences between robust und pre-frail. None of the parameters revealed differences between pre-frail and frail, though. The present study shows that without instructing maximum speed but rather emphasizing natural behavior, frail condition can be differentiated from robust and conditions with adequate kinematic measures. The parameter trial duration, however, might not be a good estimate of natural-paced upper-limb task performance with regards to frailty.

As mentioned in the sections above, frail elderly showed more monotonous behavior compared to less frail, with no differences in trial duration and MMSE scores. Compared to problems in motor control, decreased force and power as well as attempts to save energy may be the main reason behind impaired ADL performance in frail and pre-fail participants. Furthermore, this raises questions about additional influential factors contributing to the performance. Considering the verbal feedback from the participants, the gardening task might have been influenced by motivational factors and depended strongly on the thoroughness and interests of each individuum. Furthermore, participants were classified according to an adopted version of the Fried score, which mainly covers the physiological aspect of the construct of frailty. Levers and colleagues [8] stated in their review that, although many different definitions of frailty exist, physical factors, aging,

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and disease are the three main contributing factors in theoretical and research literature. However, there are other opinions suggesting to include physical, cognitive/psychological, socio-economic, nutritional, and social factors as well as disease and aging as a reflection of bio-psycho-social-spiritual view of health [62]. We do not know whether our measures would also differentiate levels of frailty if classified with different or additional factors. However, since ADL performance requests many other performance aspects than physical power and endurance, we speculate this would be the case. In fact, the amount of variance of the adapted Fried score that could be explained by our data was not very high ($\mathbb{R}^2 = 25\%$) leaving room for many other contributing factors.

In our cohort, 46% of the participants were robust, 41% pre-frail, and 13% were classified as frail. While BMI, MMSE and gender showed no differences between the groups, there was a significant age difference between the robust (min - max: 71-90, mean: 78.4 years) or prefrail (min - max: 68-89, mean: 79.8 years) group compared to the frail participants (min - max: 86 - 96, mean: 89.8 years). However, the repeated MANCOVA with age added as covariate revealed no significant impact of age. In addition, participants up to 90 years of age are also represented in the robust group, and the pre-frail and frail group did not differ in most measures despite the difference in age. Therefore, the age difference was probably not critical for our results. The age differences between groups is, however, in line with literature stating that this is a status closely associated with ageing and is consistent with Fried's statement that, on average, those who were frail were older than those who were not frail or were in the intermediate group. Additionally, Mitnitski et al. [63] illustrated that the accumulation of deficits was shown to increase monotonically with chronological age, and proposed measuring the frailty index FI (different frailty measure) as a proxy of aging. Levers and colleagues [8] stated in their review, that study populations chosen suggest a belief in the existence of a relationship between frailty and aging as all participants were over the age of 60. This of course implies a relation between frailty and aging. However, the relationship between frailty and aging and how this relates to daily life performance must be clarified in further studies.

Despite many positive findings, this study includes several limitations that need to be addressed. First, in this experimental cohort study, we did not use the original Fried frailty score. Nevertheless, the five characteristics were observed and their construct and predictive validity demonstrated elsewhere [49]. Second, as stated above, the number of errors being made during the execution of a task increases with age [e.g., 30].
We did not control for errors during both ADL tasks. However, as the number of errors increases, the execution time would be expected to increase too if errors were corrected by the subjects. Third, as stated in our methods section, the absolute acceleration vector was calculated by the Euclidean mean and the gravitation was subtracted as a constant. This can lead to errors, particularly during low horizontal accelerations. Our results were, however, not substantially impacted by these errors and appeared to be valid but are still in the need for simulations. Additionally worth mentioning is the problem that known and standardly collected kinematic parameters, such as path length and velocities [22, 57], cannot be calculated precisely based on acceleration measures. In future studies, the addition of gyroscope data could be promising [64]. Fourthly, the smartwatch was attached to the dominant wrist of the participants. Hand dominance, however, was only assessed by verbal information without using standardized questionnaires like the Edinburgh Handedness Inventory (EHI) [65]. Lastly, as mentioned elsewhere [46], data were collected unilaterally in two highly complex bimanual ADL tasks. Therefore, an assessment of upper limb bimanual performance was not possible. This should have added interesting information as older adults seem to develop strategies to compensate for their reduced motor capacity, resulting in, among other things, less motor asymmetry and more equal performance of both hands ([e.g., 66]). This raises the question of how frailty might affect these bimanual interactions. However, unilateral measurement of the dominant upper limb seems to be an important first step in real-world application. In our experiment only two exemplary ADL tasks were tested. Therefore, the measured parameters should be tested in different ADL tasks and/or over a longer period of time, as frailty is a syndrome constantly present, but assumes a dynamic process which is characterized by frequent transitions between frailty states over time [6].

Conclusion

In summary, this experimental cohort study showed that pure time-based measures, like trial duration, may not be a proper parameter to assess ADL motor performance in older adults with and without frailty. However, some of the calculated parameters (e.g., STD, PPS and MPA) seem to be good measures showing differences between frailty levels even in natural-paced ADL tasks. Therefore, kinematic parameter gathered during upper-extremity ADL tasks might have the potential to give further information on the motoric status of older adults with different stages of frailty or in other aspects of aging or in Page 13 of 15

neurological diseases. Furthermore, assessments based on accelerometry avoid the need for direct observation or video recording and thereby save time. Further research should analyze the reliability of the measured parameters over a longer period (several consecutive days) as kinematics have the potential to give additional information about the temporal dynamics of an individual's upper extremity status.

Abbreviations

ADL: Activities of daily living; F: Frail; P: Pre-frail; R: Robust; i-ADL: Instrumental activities of daily living; b-ADL: Basic activities of daily living; OR: Odds ratio; CI: Confidence interval; IMUs: Inertial measurement units; e.g.: For example; MMSE: Mini Mental State Examination; BMI: Body mass index; TUG: Timed up & go test; TD: Trial duration; RA: Relative activity; STD: Peak standard deviation; PPS: Peaks per second; RATIO: Peak ratio; SUM: Weighted sum of acceleration per second; APS: Acceleration per second; MPA: Mean peak acceleration; MAX95: 95Th percentile of acceleration peaks; EHI: Edinburgh Handedness Inventory; MLR: Multiple linear regression; VIF: Variance inflation factor; TMT: Trail making task; FI: Frailty index.

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Authors' contributions

Conceptualization, S.S. and J.H.; methodology, S.S. and S.H.; software, P.G.; validation, P.G., S.S.; formal analysis, S.S. and P.G.; investigation, S.S. and S.H.; resources, J.H.; writing—original draft preparation, S.S.; writing—review and editing, J.H. and P.G.; visualization, S.S. and S.H.; supervision, J.H.; project administration, J.H. and E.B.; funding acquisition, J.H. All authors have read and agreed to the published version of the manuscript.

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Availability of data and material

All datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Medical Faculty of Technical University of Munich (reference number 101/19 s). Written informed consent was obtained from all subjects. The study was conducted according to local regulatory requirements and laws and the ethical principles for medical research involving human subjects detailed in the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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3.3 Publication III:

- Authors: Stephanie Schmidle, Philipp Gulde, Raphael Koster, Cristina Soaz & Joachim Hermsdörfer
- Title: The relationship between self-reported physical frailty and sensor-based physical activity measures in older adults a multicentric cross-sectional study
- o Journal: BMC Geriatrics
- o DOI: <u>https://doi.org/10.1186/s12877-022-03711-2</u>
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3.3.1 Summary

The decline in everyday life physical activity reflects and contributes to the frailty syndrome. While especially self-reported frailty assessments have the advantage of reaching large groups at low costs, little is known about the relationship between the self-report and objective measured daily physical activity behavior. The main objective was to evaluate whether and to what extent a self-reported assessment of frailty is associated with daily physical activity patterns. Daily activity data were obtained from 88 elderly participants (mean 80.6 ± 9.1 years) over up to 21 days. Acceleration data were collected via smartwatch. According to the results of a self-report frailty questionnaire, participants were retrospectively split up into three groups, F (frail, n = 43), P (pre-frail, n = 33), and R (robust, n = 12). Gait and activity-related measures were derived from the built-in step detector and acceleration sensor and comprised, i.a., standard deviation of 5-s-mean amplitude deviation (MADstd), median MAD (MADmedian), and the 95th percentile of cadence (STEP95). Parameters were fed into a PCA and component scores were used to derive behavioral clusters. The PCA suggested two components, one describing gait and one upper limb activity. Mainly gait related parameters showed meaningful associations with the self-reported frailty score (STEP95: $R^2 = 0.25$), while measures of upper limb activity had lower coefficients (MADmedian: $R^2 = 0.07$). Cluster analysis revealed two clusters with low and relatively high activity in both dimensions (cluster 2 and 3). Interestingly, a third cluster (cluster 1) was characterized by high activity and low extent of ambulation. Comparisons between the clusters showed significant differences between activity, gait, age, sex, number of chronic diseases, health status, and walking aid. Particularly, cluster 1 contained a higher number of female participants, whose self-reports tended towards a low health status, the frequent use of a walking aid, and a higher score related to frailty questions. The results demonstrate that subjective frailty assessments may be a simple first screening approach. However, especially older women using walking aids may classify themselves as frail despite still being active. Therefore, the results of self-reports may be particularly biased in older women.

3.3.2 Author's contributions

Stephanie Schmidle is the first author and corresponding author of this manuscript. The study was led by the TUM in collaboration with the project partner Qolware (Munich) and MADoPA (France). Each author contributed to the final version of the manuscript, reviewed it, and gave approval for its publication.

Stephanie Schmidle:	Conceptualization, methodology, validation, formal analysis, in-
	vestigation, data curation, writing - original draft preparation,
	writing – review and editing, visualization
Philipp Gulde:	Methodology, software, validation, formal analysis, writing - re-
	view and editing, visualization
Raphael Koster:	Conceptualization, investigation, data curation
Cristina Soaz:	Software, data curation, project administration
Joachim Hermsdörfer:	Conceptualization, resources, writing - review and editing, super-
	vision, project administration, funding acquisition

3.3.3 Original publication III

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RESEARCH

BMC Geriatrics

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The relationship between self-reported physical frailty and sensor-based physical activity measures in older adults - a multicentric cross-sectional study

Stephanie Schmidle^{1*}, Philipp Gulde¹, Raphael Koster², Cristina Soaz³ and Joachim Hermsdörfer¹

Abstract

Background The decline in everyday life physical activity reflects and contributes to the frailty syndrome. While especially self-reported frailty assessments have the advantage of reaching large groups at low costs, little is known about the relationship between the self-report and objective measured daily physical activity behavior. The main objective was to evaluate whether and to what extent a self-reported assessment of frailty is associated with daily physical activity patterns.

Methods Daily activity data were obtained from 88 elderly participants (mean 80.6 ± 9.1 years) over up to 21 days. Acceleration data were collected via smartwatch. According to the results of a self-report frailty guestionnaire, participants were retrospectively split up into three groups, F (frail, n=43), P (pre-frail, n=33), and R (robust, n=12). Gaitand activity-related measures were derived from the built-in step detector and acceleration sensor and comprised, i.a., standard deviation of 5-s-mean amplitude deviation (MADstd), median MAD (MADmedian), and the 95th percentile of cadence (STEP95). Parameters were fed into a PCA and component scores were used to derive behavioral clusters.

Results The PCA suggested two components, one describing gait and one upper limb activity. Mainly gait related parameters showed meaningful associations with the self-reported frailty score (STEP95: $R^2 = 0.25$), while measures of upper limb activity had lower coefficients (MAD median: $R^2 = 0.07$). Cluster analysis revealed two clusters with low and relatively high activity in both dimensions (cluster 2 and 3). Interestingly, a third cluster (cluster 1) was characterized by high activity and low extent of ambulation. Comparisons between the clusters showed significant differences between activity, gait, age, sex, number of chronic diseases, health status, and walking aid. Particularly, cluster 1 contained a higher number of female participants, whose self-reports tended towards a low health status, the frequent use of a walking aid, and a higher score related to frailty questions.

Conclusions The results demonstrate that subjective frailty assessments may be a simple first screening approach. However, especially older women using walking aids may classify themselves as frail despite still being active. Therefore, the results of self-reports may be particularly biased in older women.

Keywords Frailty, Ageing, Assessment, Self-report, Accelerometry, Actigraphy, Physical activity

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Introduction

Frailty is commonly described as a condition, which increases the risk for adverse health outcomes (such as sarcopenia, fractures, and death) even after exposure to minor stressors [1, 2]. Within this context, frailty is seen as a transitional state in the dynamic progression of functional decline [3]. Until now, the causes of frailty are not fully understood [4]. While frailty is considered to be age-associated, it is not necessarily age-dependent and often, but not exclusively, occurs as a comorbidity of specific diseases. However, frailty can also be present in the absence of disease and not all affected elderlies experience the same symptoms [4, 5]. The vulnerability of the population and its multifaceted burden is high. Therefore, regular screenings are recommended [1]. However, limited resources (e.g., lack of time) constitute barriers to a frequent and comprehensive frailty-screening in primary care settings [6, 7]. In addition, frailty is an entity that clinicians derive from a variety of symptoms, which impedes diagnosis [3]. As a result, a definitive and consent operational definition remains still unspecified [6].

There is a plethora of frailty assessments [8], which can be divided into two main subcategories: a) the frailty phenotype instruments, which focus primarily on measuring motor function as well as activity and result in a categorical score from robust to frail (e.g., frailty phenotype [9]), or b) frailty index instruments that add a variety of factors (up to 70), resulting in a continuous scale with higher frailty scores for a greater number of 'conditions' [8, 10] (e.g., deficit accumulation approach – Frailty Index [11]). Further, these assessments can be categorized as subjective (only self-reported items), objective, and mixed [12]. While objective performance-based instruments offer several advantages, such as more precise and valid results and an increased sensitivity to changes over time, scoring methods based on observation and subjective assessments are typically quick and easy to administer. They can assess complex behavior but lack objectivity. A special case of self-report (subjective) assessments are questionnaires, which can be an effective way to reach larger groups at low costs [12, 13]. These questionnaires are well accepted, impose a relatively low burden on the individual, and do not interfere much with usual habits [13]. However, those self-reports are generally prone to a diversity of biases, e.g., perceptual errors and memory biases [14]. Nevertheless, self-reports might be especially useful for initial screening purposes [15]. In general, assessments should be brief and simple in order to increase the chance of implementation into clinical practice and, thus, should be chosen by indication: screening for the presence or level of frailty, tracking the dynamic changes in frailty, or with the goal of monitoring therapeutic interventions [1].

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An older individual's level of physical activity (PA) constitutes an important criterion of frailty [16]. While a decline in everyday life PA may both reflect and contribute to frailty, regular PA is thought to play an important role as a preventive factor and, thus, could positively influence the continuum [17]. Besides self-reports and simple clinical tests (e.g., strength or gait speed), a variety of tools already exists to assess PA at different levels of frailty, including accelerometers, heart rate monitors (HR), portable electromyography devices (EMG), and global positioning systems (GPS) [18]. In particular, portable sensors, also called wearables, offer the possibility to measure activity in everyday life in a simple, inexpensive, unobtrusive, and reliable way [19]. There is a wide range of evidence showing that activity levels detected by sensors (e.g., sedentary behavior, light and moderate-to-vigorous physical activity levels) are strongly associated with the frailty status [20] and can discriminate between different levels of frailty (e.g., [18, 19, 21–23]). In particular, the wearable-derived number of steps and duration of activity measured with accelerometers seem to be more strongly correlated with the level of frailty than other measures (e.g., number of bursts in EMG and gait speed assessed via GPS) [18]. In 2021, Wanigatunga and colleagues [24] investigated the associations between accelerometer-derived patterns of routine daily physical activity and phenotypic frailty. They showed that unfavorable activity patterns (fewer active minutes, more sedentary minutes, lower activity counts, and higher activity fragmentation) predicted an increased likelihood of frailty [24]. In fact, there has been a marked increase in the amount of information on the association between daily activity and physical frailty as measured by mostly mixed assessments. Different from these approaches, self-reported frailty assessments have the advantage of reaching larger groups and achieving high response rates, and thus can be used as a simple first step screening tool [15, 25]. Nunes and colleagues [15], for instance, compared the phenotype frailty score with a self-reported instrument and concluded that the latter can be used as simple, rapid, and low-cost screening tool offering a satisfactory level of reliability and sensitivity [15]. To date, little is known about the relationship between an individual's exclusively self-reported frailty status and objective measures of daily physical activity behavior. Since most of the questionnaire items are including PA aspects, one might use PA to investigate the accordance with the actual movement behavior. Therefore, we aimed towards investigating the relationship between different aspects of sensor-based daily activity measures, such as those mainly expressing gait activity (ambulation) and those mainly expressing upper limb activity, with the self-estimation of frailty in a cohort of elderly individuals potentially vulnerable to frailty. To better understand how objective measures of daily activity relates to self-reported frailty, we further analyzed behavioral patterns by deriving clusters to validate the self-reports. We decided to examine this relationship by using smartwatches, as wrist-worn assessments have the advantage to capture more commonly performed tasks of daily living (e.g., cooking and housework) in addition to ambulation and might therefore provide a more comprehensive picture of total daily activity [26]. Based on previous reports, we hypothesized that objective gait function would be a stronger predictor of self-assessed frailty status than other sensor-based measures. Additionally, we hypothesized that the cluster analyses would reveal clusters of participants with meaningful differences concerning their behavioral patterns and health states.

Materials and methods

Sample and procedure

We recruited a convenience sample of 114 older adults within the EIT Health project 'FRAIL - Frailty Assessment in Daily Living. The FRAIL project aimed towards improving the supervision of frail elderly (e.g., health state and falls). The recruitment took place in Germany and France between May and November 2019. Within the project, older adults living in nursing homes, assistive living environments, and private homes were approached to participate. Within this project, two key persons were in charge for the recruitment process; one in Germany and one in France. In both countries, the recruitment of the older adults within the nursing homes and assistive living environments was done by the respective care manager after being contacted and informed about the inclusion and exclusion criteria by the recruitment organizers. In France, a total of four nursing homes were recruited, whilst in Germany two nursing homes were involved (with one care manager per institution, n=6). The contact to older people living in private homes was done by dissemination actions in public forums. For this purpose, the study was presented during senior citizen days and older adults had the opportunity to sign up in a contact list. Later, those individuals were contacted by their respective recruiting organizers. The inclusion criteria were a minimum age of 60 years and the basic understanding of the operations relevant to the measures of the watch. Exclusion criteria were pronounced parchment skin with increased risk of injury due to the smartwatch, diseases with cognitive impairment, or dementia which prevented understanding of the informed consent and usage of the smartwatch. An important issue was the ability to handle the smartwatch with two major challenges: continuous data collection and regular recharging. Unfortunately, not all buttons of the smartwatch Page 3 of 17

could be deactivated which increased the risk of an unintentional termination of the recording. Furthermore, the smartwatch had to be charged once to twice a day. We collected a questionnaire covering the categories 'health status,' 'personal environment' (e.g., sociodemographic and physical condition), and 'frailty status' and equipped all participants with a smartwatch for up to 21 days. The measurement procedure took place in the respective living environment of the participants:

In a first step, the examiner explained the technical device (smartwatch) and participants signed the informed consent. In the next step, the participants were asked to complete the questionnaire together with the trained examiner (i.e., the respective recruitment organizer). To increase compliance, participants were given the choice of wrist. This was based on the findings of Dieu and colleagues [27], who showed that counts do not profoundly differ between the dominant and the nondominant wrist and both locations are well associated with counts derived from a sensor worn around the waist (both rs=0.88) [27]. Therefore, 73 chose the left and 15 persons the right wrist. We asked participants to wear the smartwatch for up to 21 days. The start of the measurement was variable between subjects in terms of both day of the week and time of the day.

Participants were only included in the analysis if data was available for at least 6 measurement days of wear time within the 21 days period with a minimum of eight measurement hours between 08:00 am and 08:00 pm. With this inclusion criteria, we aimed to preserve reliability [28] and include as many patients as possible. This is based on the statement of Aadland & Ylvisåker [28] that a one-week measurement already shows acceptable-to-good reliability. Ethical approval was given by the ethics committee of the Medical Faculty of Technical University of Munich. All participants provided written informed consent. A post hoc power analysis, using the weakest derived OR (2.93), resulted in a power of 0.96. This indicates a sufficient sample size.

Measures

The measurements consisted of two components: the subjective frailty questionnaire, which included sociodemographic information and physical condition, and the continuous activity measurement with the smartwatch.

Sociodemographic and physical condition

Information on sociodemographic status and the physical condition was obtained from the following questions: (i) sex (male/female); (ii) age (in years); (iii) BMI (kg/m²); (iv) multimorbidity (number of chronic diseases), e.g., stroke, hypertonia, asthma, and multiple sclerosis; (v) health status (self-classified state of health): 1: excellent; 2: very good; 3: good; 4: fair; 5: poor; (vi) course of health status (self-rated health compared to one year ago): 1: much better now; 2: somewhat better now; 3: about the same; 4: somewhat worse now; 5: much worse now; (vii) feeling of safety at home: 1: fully; 2: quite a bit; 3: moderately; 4: slightly; 5: not at all; (viii) feeling of safety outside the home: 1: fully; 2: quite a bit; 3: moderately; 4: slightly; 5: not at all; (ix) living condition: living alone yes/no (if no, with whom); (x) use of walking aids: yes/no.

Subjective frailty assessment

The self-reported frailty status was assessed by a questionnaire [29] in accordance with Santos-Eggimann et al. [30]. The questionnaire was based on the five constructs from Fried's frailty phenotype [9]: (1) unintentional weight loss: a) self-reported loss of appetite and b) decreased amount of food intake; (2) exhaustion: binary (yes/no) self-report response on whether the subject has too little energy to execute daily tasks; (3) low muscle strength: binary (yes/no) self-reported ability to lift or carry objects heavier than 5kg; (4) low physical activity: self-reported frequency of engagement in moderate PA (e.g., gardening, cleaning the car or going for a walk); (5) weakness: self-reported flights of stairs that can be climbed without rest (a) one flight of stairs or b) several flights of stairs. The dimension coding for each criterion was rated as follows: (1) if the individual reported a loss of appetite or if the response was having eaten less than usual; (2) if the individual reported having lacked energy; (3) if the individual reported having difficulty carrying out the activity mentioned; (4) if the individual reported less than once a week; (5) if the individual reported limitations in one of the two activities proposed.

Sensor-based physical activity tracking

To collect objective physical activity data, we used a Huawei 2 (4G) smartwatch (Huawei watch 2 (4G), Huawei Technologies Co., Ltd., Shenzhen, China) at the participants' wrist of choice. Data was sent regularly via mobile net to a main server using custom software. For step detection, the device's built-in acceleration-based pedometer of the device was used. The accelerometer data was captured at a frequency of 100 Hz. For reporting different activities, a 5 second time period was used [31, 32] (i.e., 500 samples per 5s period). Therefore, the vector magnitude (r) was calculated at each time point (i), followed by the mean vector magnitude for the 5 second time period (\overline{r}). This allowed the computation of the mean amplitude deviation (MAD) metric - which provides a measure of the intensity of acceleration changes, i.e., the intensity of PA, for every 5 seconds of data [33]:

Mean Amplitude Deviation (MAD) =
$$\frac{1}{n} \sum_{i=1}^{n} |r_i - \overline{r}|$$

(where;) $r_i = \sqrt{x^2 + y^2 + z^2} = i^{th}$ vector magnitude at each time point \overline{r} = mean vector magnitude within the time period of interestn = number of data points of the time period.

The metric of MAD has been validated in multiple studies, e.g., Bazuelo-Ruiz [34] found strong associations of MAD with indirect calorimetry (r=0.94). Additionally, the Huawei smartwatch has a reliable and sensitive acceleration sensor, which we were able to show in our previous study about kinematic analyses of ADL [35].

Data analysis

The parameters derived from the smartwatch data comprised the mean MAD (MADmean), the standard deviation of MAD (MADstd), the relative MAD (MADrel), the median MAD (MADmedian), the 95% percentile of MAD (MAD95), the fragmentation rate of MAD (MADfrag), the 95% percentile of cadence (STEP95), and the average number of steps per 5s (STEPmean). While we used the MAD-related parameters to assess the kinematic physical activity (see Fig. 1), the step-related parameters aimed to assess gait (ambulation). We used two frailty scores for analysis: the classical range from 0 to 5 including all 5 criteria of physical frailty ('weight loss', 'exhaustion', 'muscle strength', 'PA', and 'weakness') and a reduced version omitting the two parameters ('muscle strength' and 'weight loss') that cannot be assessed by a wrist worn sensor.

Mean MAD (MADmean): The mean of all MAD values in milli-g. Higher values indicate more physical acitivity. More intense physical activity is accounted for.

Standard deviation of MAD (MADstd): The variability of physical activity in milli-g. Higher values indicate a more variable physical activity (e.g., by phases of intense activity).

Relative MAD (MADrel): Relative amount time spent in MAD levels >100 m-g. Higher values indicate more (health relevant) physical activity.

Median MAD (MADmedian): The median of all MAD values in milli-g. Higher values indicate more physical activity, independent from the height of the achieved maximum MAD levels. More intense physical activity is not accounted for.

95th percentile of MAD (MAD95): The 95. percentile of all MAD values in milli-g. Higher values indicate peaks of intense higher physical activity. Overall physical activity level is not accounted for.

Fragmentation rate of MAD (MADfrag): Standard deviation of the first derivative of the MAD time-series in

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Fig. 1 Graphical representation of the MAD-based activity parameters

milli-g/s. Higher values indicate higher fragmentation of physical activity. While this is commonly used to describe the relation of long and short bouts in ratio, this parameter targets the adaptation of energy expenditure, where higher values indicate task specific changes in intensities and are strongly associated with the total amount of physical activity.

95th percentile of cadence (STEP95): The 95. percentile of cadence in steps per minute. Higher values indicate a higher gait function. Overall gait related physical activity is not accounted for.

Average number of steps per 5s (STEPmean): Average number of steps taken per 5s. Higher values indicate more gait related physical acitvity.

Statistical approach

In a first step, we assessed the relationship between the subjective questionnaire score and the acceleration-based parameters 'STEP95' and 'MADmedian' by means of Spearman correlation analyses. While the sensor-based parameters were highly intercorrelated (Fig. 4), the two parameters were used as a surrogate. Correlations were calculated for both frailty scores, the full score (0:5) and the reduced score (0:3). In a second step, we conducted a two-component confirmatory principal component analysis with a varimax rotation for the sensor-data (one component as gait/ambulation and one as upper limb activity) to calculate the participants' component scores. Thresholds for the Kaiser-Meyer-Olkin sample adequacy was set to >0.50 and minimum communalities to >0.50. Based on the individuals' component scores, a cluster analysis using k-medoid clustering was performed. The number of clusters was derived from a scree plot. Additionally, we generated a correlation matrix including all objective activity parameters, the subjective frailty scores, and the dimensions gait and activity. Third, cluster differences in terms of behavioral and person-related properties were tested using analyses of variance (oneway ANOVAs with Tukey post hoc tests) and, in case of feeling of security and health status, by means of Kruskal Wallis tests (Dunn's pairwise comparison post hoc test). In case of sex, walking aid, and frailty status, we used the Pearson's Chi-squared test (Fisher's exact post hoc test with Bonferroni correction). Odds ratios and the 95% CI were calculated for sex and frailty distribution, as well as for each criterion separately. Furthermore, we calculated one-way ANOVAs comparing each subjective criterion with the objective activity data separately. Effect-sizes were expressed as eta squared η^2 Cramer's V, Cliff's Delta d, Cohen's f², and Cohen's d. The threshold for critical variance inflation was set to 5.0, α was set to 0.05. All tests were run in R Studio (version 2021.09.2, RStudio Inc., Vienna, Austria).

Results

In sum, a total of n = 88 participants (France: n = 37; Germany: n = 51) were included in the final analysis with a mean age of 80.6 years (range: 62 - 99 years) (Fig. 2). After an initial invitation of 147 older adults, 33 had to be excluded due to comprehension issues or motoric problems. 15 participants from Germany and 11 participants from France had to be excluded due to not meeting wear time-related inclusion criteria.

Of the total sample (n=88), 13% people were robust, 38% were pre-frail, and 49% were frail. Weakness was the most prevalent frailty criterion (68%), whereas the weight loss criterion was the least prevalent (32%) one. In the French cohort, 18% of the participants were robust, 32% were pre-frail, and 50% were frail. In the German cohort, we observed a similar distribution, with 10% of

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Fig. 2 Flowchart of the recruitment procedure

participants being robust, 40% pre-frail participants, and 50% frail. A Pearson's Chi-squared test comparing the distribution of frail, pre-frail, and robust participants between France and Germany did not show significant differences (p = 0.42) (Table 1).

On average, the measurement duration was 17.5 (\pm 5.1) days with \geq 8 hours per day, see Table 1. Figure 3 shows the percentage of participants and the related measurement period. Hence, the majority (90%) of participants wore the smartwatch for at least 10 days.

 Table 1
 Demographics of the sample

Characteristic	Robust R, $n = 12$	Pre-frail P, n = 33	Frail F, <i>n</i> = 43	Total, <i>n</i> = 88
Female, n (%)	4 (33)	15 (45)	29 (67)	48 (55)
Age (years)	72.5 (5.8)	80.9 (9.3)	82.7 (8.6)	80.6 (9.1)
BMI (kg/m ²)	25.6 (4.0)	25.8 (3.4)	27.4 (5.3)	26.5 (4.6)
Multimorbidity	0.9 (0.7)	1.2 (0.8)	1.5 (1.0)	1.3 (0.9)
Health status	2.6 (0.8)	3.1 (0.7)	3.9 (0.8)	3.4 (0.9)
Course health status	3.1 (0.8)	3.2 (0.7)	3.7 (1.1)	3.4 (0.9)
Feeling of safety (home)	1.3 (0.5)	1.5 (0.7)	1.7 (0.9)	1.6 (0.8)
Feeling of safety (outside)	1.6 (0.5)	2.0 (1.0)	2.3 (1.3)	2.4 (1.2)
Days of measurement	16.4 (5.2)	17.9 (4.8)	17.5 (5.4)	17.5 (5.1)
Living condition, n (%)				
Alone	2 (17)	7 (21)	12 (28)	21 (24)
Partner/relatives	7 (58)	13 (39)	16 (37)	36 (41)
Nursing home	3 (25)	13 (39)	15 (35)	31 (35)
Walking aid, n (%)	0 (0)	14 (42)	31 (72)	45 (51)
Frailty criteria, n (%)				
Unintentional weight loss	0 (0)	5 (15)	23 (53)	28 (32)
Exhaustion	0 (0)	6 (18)	32 (74)	38 (43)
Low muscle strength	0 (0)	13 (39)	35 (81)	48 (55)
Low physical activity	0 (0)	6 (18)	28 (65)	34 (39)
Weakness	0 (0)	20 (61)	40 (93)	60 (68)

Mean values, standard deviations. *Multimorbidity* mean number of comorbidities (0 - 9), *Health status* self-rated (best: 1; worst: 5), *Course health status* self-rated comparison to health 1 year ago (improvement: 1; deterioration: 5), *Feeling of safety* 1: fully; 5 not at all, *Unintentional weight loss* loss of appetite or decreased food intake, *Exhaustion* too little energy to execute daily tasks, *Low muscle strength* not able to carry objects of more than 5 kg, *Low physical activity* being engaged in at least moderate PA on less than once per week, *Weakness* not being able to take more than one flight of stairs without rest

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Fig. 3 Kaplan Meier curve for measurement days per participants

\mathbb{R}^2	Frailty	Frailty red.	Activity	MADmean	MADstd	MADrel	MADmedian	MAD95	MADfrag	STEP95	STEPmean	Gait
Frailty	1.00	0.78	0.02	0.07	0.07	0.05	0.07	0.06	0.05	0.24	0.24	0.14
Frailty red.	0.78	1.00	0.03	0.12	0.10	0.09	0.14	0.10	0.09	0.24	0.27	0.17
Activity	0.02	0.03	1.00	0.31	0.27	0.33	0.25	0.27	0.28	0.00	0.00	0.01
MADmean	0.07	0.12	0.31	1.00	0.86	0.97	0.86	0.89	0.89	0.11	0.17	0.15
MADstd	0.07	0.10	0.27	0.86	1.00	0.81	0.53	0.99	0.93	0.13	0.13	0.14
MADrel	0.05	0.09	0.33	0.97	0.81	1.00	0.84	0.85	0.84	0.08	0.14	0.13
MADmedian	0.07	0.14	0.25	0.86	0.53	0.84	1.00	0.59	0.62	0.09	0.20	0.13
MAD95	0.06	0.10	0.27	0.89	0.99	0.85	0.59	1.00	0.94	0.12	0.14	0.14
MADfrag	0.05	0.09	0.28	0.89	0.93	0.84	0.62	0.94	1.00	0.09	0.11	0.13
STEP95	0.24	0.24	0.00	0.11	0.13	0.08	0.09	0.12	0.09	1.00	0.66	0.43
STEPmean	0.24	0.27	0.00	0.17	0.13	0.14	0.20	0.14	0.11	0.66	1.00	0.32
Gait	0.14	0.17	0.01	0.15	0.14	0.13	0.13	0.14	0.13	0.43	0.32	1.00

Fig. 4 Correlation matrix (reporting the coefficient of determination R²) including all objective activity parameters, the subjective frailty scores, and the dimensions gait and activity derived from the confirmatory principal component analysis. *Frailty 0:5, Frailty red.* reduced frailty score 0:3, *MADmean* mean of all MAD values, *MADstd* standard deviation of all MAD values, *MADrel* relative amount time spend in MAD levels > 100 m-g, *MADmedian* median of all MAD values, *MAD95* 95th percentile of all MAD values, *MADfrag* standard deviation of the first derivate of the MAD time-series in milli-g, *STEP95* 95th percentile of cadence in steps per minute, *STEPmean* average number of steps taken per 5 s

Chi-squared test revealed no differences in the occurrence of the different days of the week (p = 0.59). Furthermore, 2nd degree polynomial regressions revealed no meaningful association between month of the year and neither of the component scores (gait: $\mathbb{R}^2 < 0.05$, p = 0.87; activity: $\mathbb{R}^2 = 0.05$, p = 0.23).

Both, gait parameters and activity parameters, were highly correlated (Fig. 4). Therefore, only one parameter from each category was representatively correlated with the frailty scores (full score 0:5; reduced score 0:3). Correlation analyses revealed moderate negative correlations between the gait parameter 'STEP95' and both frailty scores (R^2 =0.25 & 0.26). Furthermore, weak to moderate negative correlations between the activity parameter (MADmedian) and both scores were found (R^2 =0.07 & 0.14). Figure 5 presents the scatterplots including the corresponding regression lines of the correlations. In addition, Fig. 4 shows the comparisons between the two surrogates (MADmedian & STEP95) and the other measures.

Table 2 illustrates the analyses of variance between objective activity parameters and the subjective frailty score criteria. The analyses showed significant differences with medium effects between the parameter 'STEP95' and the frailty criteria 'weakness' and 'physical activity' (both *p*-values ≤ 0.01 , $\eta^2 = 0.10 - 0.12$). This was also true for the dimension 'gait' (both *p*-values ≤ 0.01 , $\eta^2 = 0.10 - 0.12$). This was also true for the dimension 'gait' (both *p*-values ≤ 0.01 , $\eta^2 = 0.10 - 0.15$). For MADmedian, the frailty criterion 'physical activity' revealed a significant difference with a medium effect ($p \leq 0.01$, $\eta^2 = 0.10$). The dimension 'activity' showed a significant difference for the frailty criterion 'physical activity' ($p \leq 0.01$, $\eta^2 = 0.10$).

The overall measure of sampling adequacy was 0.79. The Kaiser-Meyer-Olkin factor adequacy of the parameters was within the range of 0.61 - 0.92. The principal component analyses including the two components (activity and gait/ambulation) revealed 0.92 explained variance, and communalities of 0.99 for MADmean, 0.92 for MADstd, 0.96 for MADrel, 0.95 for MAD95, 0.79 for MADmedian, 0.94 for MADfrag, 0.91 for STEP95, and



Fig. 5 Both frailty scores (full 0:5, reduced 0:3) for the parameters STEP95 and MADmedian. STEP95 95th percentile of cadence, MADmedian median of all MAD values

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Objective parameters	Subjective frailty components	F value	p - value	Effect size, η ²
STEP95 (steps)	Weight loss	3.277	0.074	0.04
	Muscle strength	5.926	0.017*	0.07
	Exhaustion	4.858	0.030*	0.06
	Weakness	8.983	0.004**	0.10
	Physical activity	11.402	0.001**	0.12
MADmedian (milli-g)	Weight loss	0.713	0.401	< 0.01
-	Muscle strength	2.453	0.121	0.03
	Exhaustion	0.012	0.915	< 0.01
	Weakness	1.618	0.207	0.02
	Physical activity	9.238	0.003**	0.10
Activity	Weight loss	2.920	0.102	0.03
	Muscle strength	0.896	0.338	0.01
	Exhaustion	0.017	0.899	< 0.01
	Weakness	0.886	0.364	0.01
	Physical activity	9.136	0.003**	0.10
Gait	Weight loss	4.296	0.041*	0.04
	Muscle strength	4.253	0.042*	0.05
	Exhaustion	6.334	0.014*	0.07
	Weakness	14.627	< 0.001***	0.15
	Physical activity	8.728	0.004**	0.10

 Table 2
 Comparisons between the objective parameters and the subjective frailty components

* ≤ 0.05 , *** ≤ 0.01 , *** ≤ 0.001 . Effect size: eta-squared η^2 . STEP95 95th percentile of cadence, *MADmedian* median of all MAD values, *Unintentional weight loss* loss of appetite or decreased food intake, *Exhaustion* too little energy to execute daily tasks, *Low muscle strength* not able to carry objects of more than 5 kg, *Low physical activity* being engaged in at least moderate PA on less than once per week, *Weakness* not being able to take more than one flight of stairs without rest

0.91 for STEPmean. The subsequent cluster analysis of the participants' component scores resulted in three clusters (number of clusters based on scree plot). The acceleration-based and person-related outcomes are reported in Table 3 including statistical comparisons of the three clusters. The statistical differences between the resulting clusters with regards to the frailty score and reduced frailty score are presented in Fig. 7. Regarding the application side of the watch (right or left wrist), 24 participants (69%) in cluster 1, 32 participants (97%) in cluster 2, and 3 participants (85%) in cluster 3, wore the watch on the left wrist (Chi-squared test: p=0.008; V=0.33). Post hoc comparisons (Fisher's exact test) revealed a significant difference between cluster 1 and cluster 2 (p=0.02).

Cluster 1 included 35 older adults, cluster 2 included 33, and cluster 3 had 20 persons included. By sorting and weighting (PCA) the activity data, two dimensions could be confirmed (cumulative variance of 0.92); activity and gait (ambulation). As a result, there were three different types of behavior - cluster: (1 - red) participants with high activity and low extent of ambulation, (2 - green) participants showing high activity and high extent of ambulation, and (3 - blue) participants with low activity and low extent of ambulation (see Fig. 6, left scatterplot). Analyses between the clusters showed statistically significant differences for the variables activity, gait, age, sex, number of chronic diseases, current state of health, and the use of a walking aid. Gait and activity showed high effect sizes between f^2 1.07 - 1.40. All clusters were comperable concerning their BMI, the comparison to the health status one year ago (course of health), and feeling of security inside and outside the house (Table 3). Figure 6 shows the three different clusters (indicated by different colors) in relation to acceleration-based activity and gait component scores (Fig. 6, left side) and in relation to age and self-reported frailty status (Fig. 6, right side).

When comparing activity and gait between the clusters, cluster 2 (green) appeared to contain the most active group in both categories; activity as well as gait (ambulation). The distribution in relation to age and frailty status shows a location primarily in younger age and lower levels of subjectivly reported frailty status (see Fig. 6, right). This is supported by statistical comparison showing age differences between cluster 1 and 2 (Table 3). Cluster 3 (blue) represented the most inactive group indicated by low extent of ambulation and low activity. In relation to age and frailty status, cluster 3 showed a more intermediate distribution across all ages and frailty levels (see Fig. 6, right side) with no significant difference in comparison to the other clusters (cluster 1 and cluster 2). In comparison, cluster 1 was primarily represented by older



Fig. 6 Individuals' component scores in relation to 'gait' and 'activity' (left side) and in relation to age and self-reported frailty status (right)

Variables	Cluster 1	Cluster 2	Cluster 3	Comparison	Post hoc
	n=35	n=33	n = 20		p value, effect size
Activity	0.39 (0.64)	0.40 (0.80)	-1.34 (0.55)	<i>p</i> < 0.001, f ² 1.07	2-3: <i>p</i> < 0.001, d 2.43 1-3: <i>p</i> < 0.001, d 2.84
Gait	-0.79 (0.51)	1.02 (0.55)	-0.30 (0.76)	<i>p</i> < 0.001, f ² 1.40	1-2: p < 0.001, d - 3.42 2-3: p < 0.001, d 2.07 1-3: p = 0.012, d - 0.80
Age (years)	85.0 (8.0)	76.3 (7.5)	80.1 (10.1)	p < 0.001, f ² 0.47	1-2: <i>p</i> < 0.001, d 1.12
Female, n (%)*	25 (71)	15 (45)	8 (40)	<i>p</i> = 0.033 ∨ 0.28	1-2 p = 0.03, OR 2.93 95% CI 1.08-8.35 1-3 p = 0.03, OR 3.63 95% CI (1.15-12.22)
BMI (kg/m ²)	27.3 (5.5)	25.8 (3.2)	26.1 (4.5)	p = 0.374, f ² 0.15	-
Multimorbidity	1.6 (0.7)	1.0 (0.8)	1.5 (1.3)	p = 0.013, f ² 0.33	1-2: p = 0.014, d 0.80
Health Status**	3.6 (0.9)	3.0 (0.8)	3.8 (0.9)	$p = 0.006, \eta^2 0.10$	2-3: p = 0.022, d - 0.90 1-2: p = 0.019, d - 0.71
Course health status**	3.5 (0.9)	3.2 (1.0)	3.6 (0.9)	$p = 0.294, \eta^2 0.01$	-
Feeling of safety (home)**	1.5 (0.7)	1.6 (0.7)	1.7 (1.0)	$p = 0.637, \eta^2 - 0.01$	-
Feeling of safety (outside)**	2.5 (1.2)	2.0 (0.8)	2.8 (1.6)	$p = 0.145, \eta^2 0.02$	-
Walking aid, n (%)*	28 (80)	4 (12)	13 (65)	p<0.001, V 0.62	2-3: <i>p</i> <0.001, OR 12.34 95% CI 3.27-57.69 1-2: <i>p</i> <0.001, OR 26.25 95% CI 7.55-116.66
Frailty Status, n (%)*				p = 0.21, V 0.18	-
Robust	3 (9)	7 (21)	2 (10)		-
Pre-frail	11 (31)	15 (45)	7 (35)		-
Frail	21 (60)	11 (33)	11 (55)		-

Mean values, standard deviations. Effect sizes: Cramer's V, Cohen's d, Cohen's f² eta-squared η², Cliff's Delta d, * tested by Chi test and OR comparison, ** tested by Kruskal-Wallis test. *BMI* body mass index, *Multimorbidity* number of comorbidities (0 - 9), *Health status* self-rated (best: 1; worst: 5), *Course health status* self-rated comparison to health 1 year ago (improvement: 1; deterioration: 5), *Feeling of security* 1: fully; 5 not at all

paricipants with higher frailty status, but low ambulation and high activity. A post hoc analysis showed significant differences in the extent of ambulation (gait) between all 3 clusters (effect sizes from d - 3.42 - 2.07), with cluster 1 being the group with the lowest extent of ambulation followed by cluster 3 and cluster 2. Whereas for activity, differences appeared to be present only between cluster 1 and 3 and cluster 2 and 3. Cluster 1 and 2 showed comperable levels of activity. In general, the post hoc analysis confirmed the distribution into the different clusters. Additionally, the number of chronic diseases and selfreported health status differed between cluster 1 and 2.

Self-reported health status differed between cluster 2 and cluster 3, see Table 3. The odds of being female in cluster 1 was significanly increased with an OR of 3.63 (95% CI 1.15-12.22, p=0.03). Consequently, the odds of being male in and allocated in cluster 2 or 3 was significanly increased but did not differ from each other (p=0.71). The odds ratio of being frail was increased for participants in cluster 1 (OR 2.93, 95% CI 1.10 - 8.22, p=0.03) and cluster 3 (OR 2.39, 95% CI 0.76 - 7.82, p=0.14), while only cluster 1 reached the level of significance. Overall, 38% of men used a walking aid in daily life, compared with 62% of women. Therefore, the odds of having a walking aid as women compared to men was significanlty increased with an OR of 2.73 (95% CI 1.16 - 6.68; p = 0.02). All smartwatch derived parameters are listed in Table 4.

The analysis of separate odds ratios for the reported frequency of frailty components, showed that especially cluster 1 (primarily older women) had an increased risk for low PA (OR 6.67, 95% CI 1.86 - 20.28, p < 0.01) and for weakness (OR 3.65, 95% CI 1.27 - 11.43, p < 0.01). Additionally, there was a trend towards increased exhaustion for this cluster (OR 2.33, 95% CI 0.88 - 6.46, p = 0.09), see Table 5. The most frail group (cluster 3) had an increased risk for low PA (OR 6.46, 95% CI 1.82 - 26.29, p < 0.01) and showed tendencies towards

Table 5 The odds ratios for each self-reported frailty criteria across the three clusters

Frailty Criteria	Frequency, n (%)	OR	95% CI	p - value
Unintentional we	eight loss			
Cluster 1	13 (37)	1.56	0.56 - 4.53	0.38
Cluster 3	6 (30)	1.15	0.32 - 3.96	0.83
Exhaustion				
Cluster 1	19 (54)	2.33	0.88 - 6.46	0.09
Cluster 3	8 (40)	1.33	0.41 - 4.29	0.64
Low muscle strer	ngth			
Cluster 1	19 (35)	1.42	0.54 - 3.76	0.47
Cluster 3	14 (54)	2.72	0.85 - 9.54	0.08
Low physical acti	vity			
Cluster 1	18 (51)	6.67	1.86 - 20.28	< 0.01**
Cluster 3	11 (55)	6.46	1.82 - 26.29	< 0.01**
Weakness				
Cluster 1	28 (80)	3.65	1.27 - 11.43	0.01*
Cluster 3	15 (75)	2.73	0.83 - 10.29	0.09

Cluster 2 was used as reference (Chi² test). OR Odds ratio, Frequency frequency of frailty components, *<0.05, **<0.01, ***<0.001. Unintentional weight loss loss of appetite or decreased food intake, Exhaustion too little energy to execute daily tasks, Low muscle strength not able to carry objects of time than 5 kg, Low physical activity being engaged in at least moderate PA on less than once per week, Weakness not being able to take more than one flight of stairs without rest

Parameters	Cluster 1 n = 35	Cluster 2 n=33	Cluster 3 n=20	Comparison	Post hoc p - value, effect size
MADmean (milli-g)	74.3±18.8	86.3±22.6	32.7±12.3	<i>p</i> < 0.001, f ² 1.09	1 - 3: < 0.001, d 2.48 2 - 3: < 0.001, d 2.76 1 - 2: 0.03, d -0.58
MADstd (milli-g)	89.3±12.2	96.2±13.7	52.8±12.1	p < 0.001, f ² 1.35	1 - 3: < 0.001, d 3.00 2 - 3: < 0.001, d 3.31 1 - 2: 0.08, d -0.53
MADrel (milli-g)	30.1±8.0	33.6±9.0	11.9±5.6	<i>p</i> < 0.001, f ² 1.10	1 - 3: < 0.001, d 2.52 2 - 3: < 0.001, d 2.75 1 - 2: 0.20, d -0.41
MADmedian (milli-g)	36.8±22.9	52.8±25.5	11.4±8.6	p < 0.001, f ² 0.73	1 - 3: < 0.001, d 1.33 2 - 3: < 0.001, d 1.98 1 - 2: < 0.01, d -0.66
MAD95 (milli-g)	252.4±39.2	276.3±44.9	131.9±42.2	<i>p</i> < 0.001, f ² 1.36	1 - 3: < 0.001, d 2.99 2 - 3: < 0.001, d 3.29 1 - 2: 0.06, d -0.57
MADfrag (milli-g)	84.5±12.2	89.8±15.4	50.3±12.9	p < 0.001, f ² 1.16	1 - 3: < 0.001, d 2.75 2 - 3: < 0.001, d 2.72 1 - 2: 0.25, d -0.38
STEP95 (steps)	58.3±14.7	97.4±9.0	63.5±19.9	p < 0.001, f ² 1.28	1 - 3: 0.41, d-0.31 2 - 3: < 0.001, d 2.41 1 - 2: < 0.001, d-3.19
STEPmean (steps)	0.2±0.1	0.9±0.3	0.2±0.2	<i>p</i> < 0.001, f ² 1.36	1 - 3: 0.93, d 0.00 2 - 3: < 0.001, d 2.62 1 - 2: < 0.001, d-3.17

 Table 4
 Smartwatch derived parameters across the three clusters

Mean values, standard deviations. Effect sizes: Cohen's d, Cohen's f² MADmean mean of all MAD values, MADstd standard deviation of all MAD values, MADrel relative amount time spend in MAD levels > 100 m-g, MADmedian median of all MAD values, MAD95 95th percentile of all MAD values, MAD values, MADrel relative derivate of the MAD time-series in milli-g, STEP95 95th percentile of cadence in steps per minute, STEPmean average number of steps taken per 5 s

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Fig. 7 Mean scores of both self-reported frailty scores (full 0:5, reduced 0:3) between the three clusters

increased weakness (OR 2.73, 95% CI 0.83 - 10.29, p = 0.09) as well as for low muscle strength (OR 2.72, 95% CI 0.85 - 9.54, p = 0.08).

Analysis of variance revealed a significant difference with a large effect between the full frailty status (0:5) and the clusters (p = 0.007, $f^2 = 0.35$), see Fig. 7. Post hoc analyses showed a significantly higher level of frailty in cluster 1 as compared to cluster 2 (1 - 2: p = 0.02). The comparison of cluster 1 and cluster 3 did not reach significance, but showed a trend towards higher frailty scores in cluster 1 (1 - 3: p = 0.06). When running the same analysis with the reduced version of the frailty score (0:3), again, significant differences with a large effect between the clusters were found (p = 0.002, $f^2 = 0.40$), see Fig. 7. Post hoc analyses revealed that participants in cluster 1, on average, had significantly higher frailty scores when compared to participants allocated to cluster 2 (1 - 2: p = 0.005). And again, we observed a tendency towards higher frailty scores in cluster 1 compared to cluster 3 (1 -3: p = 0.05).

Discussion

In this study, we examined smartwatch-derived characteristics of everyday behavior (physical activity) and subjective frailty status in older adults. The main objective was to investigate and better understand the relation between sensor-based measures of daily physical activity, separated into upper limb activity and gait (ambulation), and the self-estimation of frailty levels. The correlation of the derived components gait and activity with the selfreported frailty scores were weak to moderate. Cluster analysis resulted in two clusters with either low (cluster 3) or high activity (cluster 2) in the dimensions gait and activity. The third cluster (cluster 1) was characterized by high activity and low extent of gait. The odds of being female and frail was significantly increased for cluster 1. Additionally, the odds of having a walking aid as women compared to men was increased, too.

The correlation analyses between the frailty level of our cohort (exclusively self-reported), showed moderate negative associations with the gait parameter 'STEP95' (cadence-based). Additionally, weak to moderate negative correlations were found between the activity parameter 'MADmedian' (MAD-based) and both scores. The difference between the two frailty scores was that we excluded the criteria 'muscle strength' and 'weight loss' for the reduced version (0:3) to examine whether the explained variance increased when we omitted these parameters, which may not be directly measurable with a wrist-worn sensor. In general, however, both scores revealed comparable results. A more direct comparison between the objective physical activity data and the subjective frailty components was done by separate analyses of variance. Both, the parameter 'STEP95' and the dimension 'gait' showed differences with medium effects for the criteria 'weakness' and 'physical activity'. The upper limb related activity ('MADmedian' and 'activity') showed differences with a medium effect for the 'physical activity' item. These results seem to be consistent with the content of the questions. The 'physical activity' question includes all types of physical activity, regardless of whether the upper or lower limbs are affected. However, the 'weakness' question specifically asks about the ability to climb one or more flights of stairs. Furthermore, the dimension 'gait' showed additional small effects for the criterion 'weight loss' and 'exhaustion'. Our findings are consistent with previous studies stating that the level of activity (respectively inactivity) is associated with different frailty levels [18-21, 23, 24] and that especially gait (ambulation) related parameters seem to be more sensitive [18, 19]. In 2012, Theou and colleagues [18] presented a wide range of comparisons between different PA measures (e.g., accelerometer, heart rate (HR), electromyography (EMG), global positioning system (GPS), and Minnesota Leisure Time Physical Activity Questionnaire (MLTAPO)) with each other and with the Frailty Index (FI). They found that the FI was significantly correlated to all PA measures. For accelerometry, 'total steps' and 'total activity minutes' were most strongly correlated to FI [18]. Our study extends this body of evidence by showing that there is also a correlation, however only weak to moderate, between an exclusively self-reported frailty score, including five short and easy questions, and gait and activity-related parameters as assessed by accelerometry. Furthermore, for our parameters related to gait, a significant difference was found for almost all frailty criteria, suggesting that mobility might be the driving parameter related to frailty, although the relationship between frailty and behavior might be multimodal, as seen, for instance, in the relation with falls [36]. Still, about 60% of the variance of behavior and the FI frailty assessment [18] (mixed assessment) as well as approximately 75% of the comparison with the self-reported frailty questionnaire remains unexplained. In addition, it should be considered that the association between pedometry and self-reports may be due to the fact that the self-report explicitly asks for gait function. However, R² did not change when non-PA questions were removed, indicating a generalizability of ambulation (via pedometry) to other domains.

The debate about the relationship between objective and subjective activity assessments in older adults is well known (e.g., [13, 37, 38]). The lack of complete agreement could indicate insufficient validity of self-reports or objective assessments, or (alternatively) low sensitivity of self-reports and objective measures [39]. This may include various aspects, such as detail of the questionnaire, extent of supervision, or the length of the recall period. Questionnaires may cover periods from one to seven days, or even up to several months. Answers are dependent on the subjects' age, their living environment as their health/behavioral reference (e.g., when an old Page 13 of 17

person compared him/herself with the younger neighbor), and the context of questioning [40]. In contrast to self-reports, objective assessments using wearable sensors can provide accurate documentation of daily activities such as walking, standing, sitting, and lying down [24, 25], which in turn, may allow to identify frailty-specific patterns in peoples' natural environment [23]. Different levels of frailty may be characterized by differences in daily PA patterns, such as fragmented walking distances (e.g., due to exhaustion, declining strength, or walking indoors instead of outdoors) or lower PA complexity [23]. However, in addition to the simple comparison of objective and subjective measures, cluster analyses might contribute to the validation of self-reports as a new approach and, in this sense, this may lead to a better understanding of what the self-report measures assess.

Based on the behavioral data (acceleration data), our cluster analysis resulted in three clusters that differed in terms of their upper extremity pronounced activity level and extent of gait (ambulation). Cluster 2 appeared to represent the most active group showing the highest extent of ambulation and activity, followed by cluster 1 (high activity and low extent of ambulation) and the least active cluster 3 (low activity and low extent of ambulation). Participants allocated to cluster 2 did not only show a different extent of gait and activity level, but also had a better self-rated health status (mean = 3.0; i.e., 'good') and less frequent use of walking aids. In contrast, participants in cluster 1 and cluster 3 showed a comparable use of walking aids. Therefore, the odds ratio of using walking assistive devices was significantly increased for cluster 1 and 3 compared to cluster 2. Yet, 33% of the participants classified into cluster 2 were categorized as frail and 45% as pre-frail. Our analyses of variance further revealed significant differences between the clusters and the frailty scores (both full and reduced version). Post hoc analyses showed that the clusters in which participants showed lower extent of ambulation also contained subjects with a higher frailty score (cluster 1 and cluster 3). This led to one robust group (cluster 2) and two frailty subtypes. However, for elderlies allocated to cluster 1, not only the risk of being frail was significantly increased, but also the probability of being female. Only the parameter 'gait' showed clear differences between all three clusters with a large effect. Consequently, cluster 1 contained the participants with the highest frailty scores, most of whom were female, and on average the oldest group. Interestingly, this finding seems to be consistent with the 'malefemale health-survival paradox, which states that women live longer than men, but with poorer health [41] as they usually experience more functional limitations, co-morbidities, and poorer self-rated health [42, 43]. Studies using the FI consistently show that women have higher

FI scores than men at all ages even though they tolerate a higher degree of frailty (lower mortality rate at any given FI score or age). Therefore, they can be seen as more frail (due to a poorer health status) and less frail (lower risk of mortality) at the same time [41]. Gender differences also seem to be reflected in activity behavior. In a study of Li et al. [44] PA was assessed by the CHAMPS (Physical Activity Questionnaire for Older Adults) and accelerometry for 7 consecutive days. They analyzed the data of 114 older adults (mean age 74.0 ± 6.0) and observed that preferences for level, type, and location of PA differed substantially between gender [44]. In addition, there is evidence based on sensor measures that men engage in more MVPA than women (e.g., [45, 46]), and that there might be also gender differences in the amount of time spent in lower intensity domains, such as sedentary and light activities [47]. Accordingly, even though men might achieve a greater amount of MVPA, they spend more time sedentary, whereas women may accumulate a greater number of light activities [17, 46, 47]. This fits quite well to the results of our cluster analysis showing that cluster 1 (most frail participants and 71% female) still performed activities connected to upper limb movements. Light housework (e.g., dusting, sweeping), or even cooking, body hygiene, and knitting, for example, may therefore have led to increased hand activity in women in our cohort. Additionally, potential gender issues may be present in the use of walking aids as well. There is evidence showing that predominantly women use walking aids, e.g., [48]. Consequently, this may have had an effect in the subjective frailty scoring, too. The frail group, based on the subjective frailty score, included 67% women and 72% walking aid users. However, for the results of the cluster analysis, there was no significant difference between cluster 1 and 3 regarding the use of walking aids.

Considering cluster 2 as the robust group - in terms of gait (ambulation) and upper limb PA, the differences between the two frail groups (1 and 3) remain to be discussed. Cluster 3 showed what the stereotype of frailty suggests: inactivity in both the gait (ambulation) and the upper limb PA dimension. The odds ratio analysis of each separate criterion revealed that especially participants within cluster 3 reported low PA and showed a trend towards increased weakness i.e., 'climbing stairs' and tendency towards low muscle strength i.e., 'lifting a heavy bag'. Cluster 1 was prone to both a high risk of low PA and weakness. Moreover, participants in cluster 1 showed a tendency towards exhaustion i.e., 'lack of energy'. Additionally, the parameter MADfrag, which reflects the relation of long and short activity bouts, and therefore displays the specific changes in intensities, was particularly low for people allocated to cluster 3. This is Page 14 of 17

in line with our previous study in which we found that higher frailty scores were associated with more monotonous behavior during two activities of daily living (gardening and tea task) [35]. To what extent the use of walking aids might be seen as a consequence of frailty or might lead to the classification as frail, could be answered by cluster 1. Participants in this cluster walked even less than the other frail group (cluster 3), while showing the same upper limb related activity rate as the robust group. This group (cluster 1) had walking aids in 80% of cases. Thus, assuming that pedometers have problems detecting steps in people using walkers [26], analyzing walking activity alone might not provide valid information about frailty. Additionally, the questions related to 'weakness' in the questionnaire used in our study (equivalent to 'walking speed' of the Fried frailty score [9]) was about difficulties going up one or several flights of stairs without resting. This tends to basically exclude people with walking aids as it becomes more difficult to climb stairs and consequently might result in a positive rating for this criterion. This is in line with existing evidence. Nunes et al. [15], for example, showed in their study that comparing the Fried frailty criteria with a self-reported frailty guestionnaire, 'decreased walking speed' showed a rather low specificity of 31.4%. Therefore, gait-related self-reported information may be misleading when it comes to frailty. Barreto and colleagues [25] investigated a self-reported frailty screening tool at baseline and one year later. Their analysis showed that frail individuals were older, predominantly female, had more co-morbidities, a greater decline in physical function, suffered more often from chronic pain, and reported decreased health status. Furthermore, they stated that frailty is a single entity, different from co-morbidity and physical limitation [25]. The question that arises from the train of thoughts is whether a person remains active, regardless of physical or neurological impairments that might impair walking. Although the values of the metabolic equivalent of task (MET) differs between gait and upper limb related activities, motor function of upper extremity has been identified as an important predictor of, e.g., disability [49]. In general (in terms of METs), lower body activities should have higher energy expenditure in comparison to upper body activities because they involve major muscle groups and the whole body mass is moving (instead of just an arm). Therefore, it could be meaningful to investigate changes in the different categories (ambulation and upper body activity), as changes in physical behavior may represent the first sign of frailty. This leads to the idea of a parameter for early detection of frailty. If we assume that cluster 1 is self-classified as frail solely due to ambulatory impediments, more specific actigraphy assessments of everyday behavior could help to get more information on

the overall activity level of the person as well as to differentiate between frailty and possible frailty-biases (e.g., using walking assistive devices or questions, which disadvantage people with walking aids). This could ultimately help to identify causes and mechanisms of what we consider physical frailty. However, in our study, the number of robust older adults was far less than the pre-frail and frail older adults. This might be due to the fact, that the frailty classification was solely based on the self-estimation of the individuals. Consequently, the participant may have considered themselves in a worse condition than they are.

This study has several strengths, but also limitations that need to be addressed and therefore, results should be interpreted with caution. First, we intended to increase the compliance and wear time of the smartwatch by using the wrist of choice of the participants [24, 26]. This further allows for continuous data collection and the capturing of more commonly performed tasks of daily living [26], including gait activity. This resulted in significant group differences between placement on the left or right wrist between cluster 1 and cluster 2. However, this may not have been of relevance, as these clusters differed in the extent of ambulation (gait), but not in the amount of hand-related activity. It is possible that this is a consequence of wearing the watch in a balanced proportion on the non-dominant or dominant hand between both groups, or more bimanual hand activity [50]. While this is solely based on speculation, as we had no information about hand dominance, activity in cluster 1 might have been overestimated due to more frequent measurement on the dominant hand compared to cluster 2. With regard to future studies, we recommend to assess handedness and define where the sensor should be worn. Second, while most clinical tests are geared towards measuring maximum physical performance (capacity), the use of wearables in everyday life, in contrast, is aimed at recording actual (submaximal) behavior. However, individuals' submaximal behavior and its relation to capacity could deviate. This is usually the case unless the capacity is greatly reduced and thus no longer different from actual everyday behavior. Therefore, the interpretation of the actual behavior remains difficult. In addition, accelerometry (in the proposed form) is not able to detect the movement of non-body masses (e.g., carrying groceries) and could therefore underestimate the energy expenditure. Third, devices worn on the wrist are known to be susceptible to interference with the use of assistive devices such as walkers [26, 51], which is increasingly the case in older age. In this context, especially the use of rolling walkers leads to a rather stationary wrist, and it is still unclear how much movement is actually registered by the device [26]. Although we assessed whether

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participants used an assistive device, we did not further subdivide the assistive devices (e.g., walking sticks or rolling walkers). For future studies, the simultaneous use of hip or ankle pedometers and wrist-worn bands might be an attractive solution, since wearables are becoming smaller and cheaper. If such instruments were combined, this could also provide more insights into the importance of energy consumption during certain activities. Another limitation refers to the smartwatch itself. As we had some major issues with the charging process and data collection, some participants were not able to handle the smartwatch independently and dropped out of the study. Consequently, the dropout rate was around 40%, which is quite high. This also affected the wear time of the watch drastically and we had to adapt the valid measurement hours to decrease data loss and the burden for the participants. The current wear time recommendation for valid accelerometer measurements is \geq 10 hours/ day for 6-9 days (e.g., [28]). Since we had issues with the frequent charging process of the watch, we adapted the amount of valid measurement hours down to \geq 8 hours to decrease the burden for the participants. However, since we had an extended wearing period of at least 10 days for 90% of the sample, this might still achieve good reliability in capturing PA. Another limitation which needs to be discussed is the use of a convenience sample and therefore the lack of generalizability. Due to the potential bias of the sampling technique, subgroups might be underrepresented, e.g., those who were not interested in the topic (public dissemination). In this regard, care managers were involved in the recruitment process to reach out for people in nursing homes as well. For future research, we would strongly recommend the use of devices with higher battery life and greater robustness towards unintentional adjustment of measurement setting.

Conclusion

This multicentric cross-sectional study showed that simple correlation analyses of smartwatch derived parameters (based on MAD and steps) and a self-reported frailty score leave up to 75% variances unexplained. However, cluster analysis showed a meaningful differentiation between three clusters based on the extent of gait (ambulation) and upper limb PA during everyday life. Interestingly, especially one group (cluster 1) had a higher risk of self-reported frailty, being older, female, and dependent on walking aids, despite showing hand activity. To summarize, while subjective frailty assessments may be a simple first screening approach, older women using walking aids appear to classify themselves as frail more frequently, despite still being physically active. Therefore, selfreports may be particularly biased in older women and, thus, actigraphy or the use of additional sensors may be necessary to get comprehensive information about their physical status.

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Abbreviations

Appleviau	015
MAD	Mean amplitude deviation
MADmean	Mean MAD
MADstd	Standard deviation of MAD
MADrel	Relative MAD
MADmedia	n Median MAD
MAD95	95th percentile of MAD
MADfrag	Fragmentation rate of MAD
STEP95	95th percentile of cadence
STEPmean	Average number of steps per 5 s
PA	Physical activity
HR	Heart rate
EMG	Electromyography
GPS	Global positioning system
R	Robust
Р	Pre-frail
F	Frail
OR	Odds ratio
CI	Confidence interval
BMI	Body mass index
MLTPAQ	Minnesota Leisure Time Physical Activity Questionnaire
MVPA	Moderate to vigorous physical activity
FI	Frailty Index
CHAMPS	Physical Activity Questionnaire for Older Adults
MET	metabolic equivalent of task

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Availability of data and material

For ethical reasons, it is not possible to make the data publicly available. Therefore, all datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

Conceptualization, J.H., R.K. and S.S.; methodology, P.G. and S.S.; software, C.S. and P.G.; validation, P.G. and S.S.; formal analysis, P.G. and S.S.; investigation, R.K. and S.S.; resources, J.H.; data curation, R.K., C.S., and S.S.; writing-original draft preparation, S.S.; writing-review and editing, S.S., P.G., J.H.; visualization, P.G. and S.S.; supervision, J.H.; project administration, J.H. and C.S.; funding acquisition, J.H. All authors have read and agreed to the published version of the manuscript.

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Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Medical Faculty of Technical University of Munich (reference number 101/19s). Written informed consent was obtained from all subjects. The study was conducted according to local regulatory requirements and laws and the ethical principles for medical research involving human subjects detailed in the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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3.4 Further related publications

The listed papers are not central to this cumulative dissertation; however, they address relevant topics and will be mentioned in the discussion.

- Gulde, P., Vojta, H., Schmidle, S., Rieckmann, P., & Hermsdörfer, J. (2023). Going beyond PA: Assessing sensorimotor capacity with wearables in multiple sclerosis—a cross-sectional study. Journal of NeuroEngineering and Rehabilitation, 20, 123. https://doi.org/10.1186/s12984-023-01247-z
- Gulde, P., Vojta, H., Schmidle, S., Rieckmann, P., & Hermsdörfer, J. (2024). Outside the Laboratory Assessment of Upper Limb Laterality in Patients With Stroke: A Cross-Sectional Study. Stroke, 55(1), 146–155. https://doi.org/10.1161/STROKEAHA.123.043657.

Chapter 4

General Discussion

General Discussion

4. General Discussion

Life expectancy and the global proportion of elderly individuals are increasing (World Health Organization, 2002). As a result, millions of elderly individuals worldwide are affected by the frailty syndrome, which significantly increases the likelihood of adverse health outcomes (Hoogendijk et al., 2019). Therefore, there is a pressing need to develop methods capable of identifying those who are most likely to need support services or face health crises. This is crucial for effectively and efficiently addressing upcoming challenges, such as rising demands for community resources, hospitalizations, and placements in nursing homes (Bandeen-Roche et al. 2023; Morley et al. 2013). The following section provides a summary of the conducted research, followed by a more concise discussion of task capacity, behavior and self-report, relevant for a more comprehensive understanding of frailty. It subsequently provides insights into the application of findings from the conducted studies to the concept of physical frailty.

4.1 Summary

This present thesis aimed to acquire insights into the physical frailty syndrome and its impact on the performance of daily activities, as prerequisite of independent living. Our focus was on examining specific activities of daily living (ADL) and exploring how engagement in daily life relates to self-reported frailty. All three studies emphasized the significance of the upper extremity, as essential aspect of the performance of instrumental ADL (i-ADL). In study I & II, we explored the feasibility of using the IMU of a smartwatch for evaluating the performance of complex ADL in relation to the level of frailty. Additionally, we examined the extent to which kinematic parameters remained consistent across various tasks (Schmidle et al., 2020, 2022). The results demonstrated the feasibility of utilizing an upper limb kinematic approach in complex, naturally paced ADL measured with a wrist-worn device. Furthermore, it revealed that while trail duration may not be a suitable parameter for measuring ADL performance in older individuals, individuals with higher frailty levels exhibited slower, more monotonous movements with a generally reduced agility in upper limb movements. There was no interaction between task and frailty level, and notably, agility and smoothness showed the highest correlation coefficients between both tasks. Study III aimed to explore the association between sensor-based daily activity measures (i.e., engagement in uncontrolled ADL performance), such as walking and upper limb activity, and self-reported frailty among a cohort of elderly individuals. To deepen our understanding of this relationship, we additionally analyzed behavioral patterns and validated the self-reports through clustering methods (Schmidle et al., 2023). The findings supported the idea of altered ADL behavior with regards to frailty showing differences between the level of self-reported frailty and activity levels in daily living. Particularly older women rated themselves in a worse condition, as especially the upper limb activity profile would indicate.

4.2 Integrated findings

The following section provides a comprehensive discussion on task capacity and behavior and self-reports.

General Discussion

4.2.1 Task performance

We observed variations in motor performance between individuals with and without frailty, resulting in altered performance of activities of daily living (Schmidle et al., 2020, 2022). In general, the frail elderly demonstrated more monotonous behavior compared to those less frail, explicitly differentiating between robust participants and those categorized as pre-frail or frail, with no discernible differences in trial duration (TD). All parameters but one showed clear differences between both tasks (i.e., gardening task and tea task), probably attributable to variations in task complexity and demands (Wood, 1986). Measures of agility and smoothness showed the highest inter-task correlation. Particularly noteworthy was the absence of differences in overall TD for both tasks across different levels of frailty (Schmidle et al., 2020, 2022). This contrasts with previous literature indicating increased TD in similar ADL tasks within the context of neurological conditions like spinal cord injury, stroke, and dementia, as well as in the aging population (Alt Murphy et al., 2011, 2012, 2013; De Los Reyes-Guzmán et al., 2016; Gulde et al., 2017, 2018, 2019; Gulde & Hermsdörfer, 2015; K. Kim et al., 2014; Thrane et al., 2018). The lack of the anticipated increase in TD can be attributed to various potential factors: a) the absence of cognitive aspects, such as decreased attention and working memory, which may often lead to increased execution times (Gulde et al., 2017, 2019; Gulde & Hermsdörfer, 2017), b) no examination of accuracy and errors, and c) task execution at maximum performance capacity in terms of execution speed, even though participants were introduced to perform the task at a natural pace (Schmidle et al., 2020, 2022). This implies that while those individuals classified as robust may have performed at a moderate proportion of their capacity (e.g., 50 %), the individuals considered frail were already operating close to their maximum capacity (e.g., 90 %). Apart from the fact that we explicitly excluded individuals with MMSE scores below 24 points, the absence of cognitive factors aligns with the general concept of physical frailty, which is distinct from definitions that encompass additional factors, such as cognitive frailty (Fried et al., 2021). Incorporations of cognitive aspects may obscure notable differences, illustrated by the findings that 22 % of individuals with Alzheimer's disease showed no physical frailty syndrome (Bilotta et al., 2012). This notion is strengthened by clinical experience involving older individuals who display physical robustness despite cognitive frailty and vice versa (Fried et al., 2021). Moreover, disparities in TD may not arise if accuracy is not considered (Demaree et al., 1999), and motivational factors such as thoroughness could also influence the outcome (Schmidle et al., 2022). However, clear differences in kinematic parameters reflecting motor performance (rather monotonous behavior in individuals with frailty) among the groups across different levels of frailty were identified. This is noticeable considering that the tasks were conducted at a natural pace without intending to challenge the individuals' performance limits. In a previous study we investigated the effect of instructed execution speed on the motor performance during two ADL tasks (tea task and letter task), comparing a group of young participants, older adults, and retirees (Gulde et al., 2019). The results showed that the group of retirees (mean age 71 years) were not able to decrease their TD or any other kinematic parameters. This leads to the assumption that our study participants (total mean age 82 years) were already acting at their capacity limits (Suominen, 2011) as other laboratory studies have shown this for muscle function (Hortobágyi et al.,

2003) and walking (Pincheira et al., 2017), explaining the low behavioral variance (Gulde et al., 2019). In walking, for example, the rise in energy expenditure during walking speed variations in older individuals predominantly stems from increased energy expenditure across all examined muscles. When walking at speeds either faster or slower than the energetically optimal pace, older individuals exhibit a greater rise in EE in the muscles compared to younger individuals. This leads to an increased energetic penalty when walking at non-optimal speeds. Leading to the speculation that both younger and older individuals prefer to walk at a pace that minimizes muscle energy costs, with the optimal pace being lower in older individuals. Moreover, it seems that older individuals have a narrower range of economical speeds due to larger increases in energy cost at speeds faster or slower than optimal (Pincheira et al., 2017). Hence, relying on solely time-based assessments may not provide comprehensive insights into the characteristics of movements and their root causes of changes and employing kinematic analysis to quantify movement characteristics can be essential for assessing the extent of frailty (Panhwar et al., 2019).

To conclude on the aspect of task performance (Schmidle et al., 2020, 2022):

- Trial duration in natural executed i-ADL tasks seems not to be an appropriate parameter to assess motor performance in older individuals with and without frailty.
- A higher frailty score is associated with slower, more monotonous movements, and an overall lower intensity and agility during the i-ADL performance.
- By emphasizing natural behavior over maximum speed instruction, individuals with frailty can be distinguished from robust participants with adequate kinematic measures, which presents significant potential for transitioning the assessment into the real-world contexts of individuals (e.g., pattern recognition).

This raises the question: how does the observed increase in monotonous upper limb related motor performance correlate with daily activity behavior, and does it align with self-reported physical frailty, considering that self-reports are frequently utilized for initial screening purposes?

4.2.2 Behavior & self-report

In general, the correlations between our cohort's self-reported frailty level and the derived components gait and activity were weak to moderate, showing stronger correlations with the gait dimension. This result aligns with prior research indicating that activity levels (or lack thereof) are linked to various levels of frailty (Del Pozo-Cruz et al., 2017; Galán-Mercant & Cuesta-Vargas, 2015; Razjouyan et al., 2018; Schwenk et al., 2015; Theou et al., 2012; Wanigatunga et al., 2022), particularly highlighting the sensitivity of gait-related parameters (Razjouyan et al., 2018; Theou et al., 2012). Considering that particularly the rating of physical frailty is highly dependent on gait function (Fried et al., 2001), there is a risk of mobilitybias when estimating an individual's status. In 2012, Theou and colleagues investigated different objective and subjective PA assessment tools across levels of frailty, assessed with the frailty index (FI), using for example electromyography (EMG), a global positioning system (GPS), and a subjective questionnaire (Minnesota Leisure Time Questionnaire - MLTQ). The key finding of this study was that the number of steps and the duration of activity recorded by accelerometers showed a stronger correlation with frailty compared to the other measured variables. However, approximately 60 % of the variance of behavior and the FI assessment remained unexplained. After accounting for the effect of age, about 45 % of the variance in the FI can be attributed to the percentage of time spent in activities measured by the combination accelerometer, EMG, GPS, and MLTQ. Comparisons among the PA tools revealed significant correlations between accelerometers and the other PA measures. However, correlations were not significant when the other PA measures were compared to each other (Theou et al., 2012), highlighting the relevance of accelerometry. In our study, the self-report of physical frailty and activity shared only 25 % variance, leaving 75 % unexplained. Therefore, to enhance our comprehension of how objective measures of daily activity correspond to self-reported physical frailty, we conducted an additional analysis by clustering behavioral patterns to validate the self-reports, particularly aiming to differentiate between upper and lower limbs and address the risk of mobility-bias. Based on the behavioral (acceleration) data, our cluster analysis identified three distinct clusters characterized by varying levels of upper limb activity and gait. Cluster 2 emerged as the most active one, considered as the robust group, exhibiting the highest degree of ambulation and upper limb activity. Additionally, they reported a higher self-rated health status and showed reduced reliance on walking aids than the other clusters. Cluster 3 represented the contrasting end of the activity spectrum and reflected characteristics that correspond to the stereotype of frailty: low levels of both upper limb activity and ambulation. The variations in different intensities were particularly low among individuals assigned to cluster 3 (Schmidle et al., 2023). This corresponds with our results from study I and II, indicating that individuals with higher frailty scores show a more monotonous behavior (Schmidle et al., 2020, 2022). Most interestingly, cluster 1 displayed a heterogeneous activity profile, with low rates of ambulation and a high degree of upper limb activity. Conversely, cluster 1 and 3 demonstrated similar self-rated health statuses, multimorbidity rates, and frequency of walking aid utilization. Among the elderly individuals grouped into cluster 1, not only was the risk of self-reported frailty increased, but also the probability of being female. Notably, only the parameter "gait" exhibited distinct differences across all three clusters, with a substantial effect. As a result, cluster 1 comprised participants with the highest frailty scores, a majority of whom were female, and on average, the oldest group. Two factors may address the deviation of cluster 1 from the others: a) the "male-female health-survival paradox", stating that women live longer than men but tend to experience greater levels of co-morbidity and disability (Gordon et al., 2017) and b) gender-related differences in activity behavior (Li et al., 2017). While significant variability in frailty assessment is observed depending on the tool utilized, females consistently exhibit higher frailty scores compared to men regardless (e.g., (Theou et al., 2014, 2015)). Interestingly, irrespective of age or frailty level, older women experiencing frailty demonstrate better survival rates compared to men (Park & Ko, 2021). Frailty and its progression are influenced by various factors across multiple domains, which may have different effects depending on the individual's sex (Park & Ko, 2021). Emerging evidence highlight these

sex-specific differences in frailty and its determinants suggest that the differences observed between women and men are likely attributed to a combination of biological (e.g., chronic disease, changes in immunity and endocrinology), psychosocial (e.g., social vulnerability, indicated for example by the marital status), and behavioral (e.g., coping strategies) factors (Gordon & Hubbard, 2020). In the behavioral level, several contributing factors, such as coping mechanisms (e.g., problem-solving strategies) and sex-specific differences in stress perception (potentially explaining differences in women's behavior around health issues, including illness perception, self-rated health, and health care utilization) may elucidate variances in women's behavior (Park & Ko, 2021). Therefore, individuals of cluster 1 may have rated their level of frailty in a worse condition as their activity profiles indicate (Schmidle et al., 2023). In general, sex differences may be also seen in activity behavior, with evidence suggesting that the preferences for the level, type, and location of physical activity may vary significantly between sexes (Li et al., 2017). For example, men seem to participate in more moderate-to-vigorous physical activity (MVPA) than women (e.g., Hagströmer, Oja, and Sjöström 2007), and sex discrepancies can be also seen in the duration of lower intensities, such as sedentary and light activities (Martin et al., 2014). During aging, elderly men may substitute higher-intensity with sedentary behavior rather than engaging in light-intensity activity, leading to reduced activity time throughout the day. Conversely, the level of light activity may remain relatively consistent for women across all age groups. Elderly women seem to sustain activity at this intensity level for a greater duration throughout the day, including the evening hours (Martin et al., 2014). Therefore, tasks such as light housework (e.g., dusting, sweeping) (Li et al., 2017), cooking, and knitting could have contributed to heightened hand activity among women in our study cohort.

To conclude on the aspects of behavior and self-report (Schmidle et al., 2023):

- There is limited agreement between self-reported physical frailty and the activity profile.
- Self-estimation of physical frailty might be influenced by biases, especially among older women.
- Mobility and upper extremity activity should be equally weighted in the assessment of frailty as individuals with gait impairments may be disproportionately categorized as frail.

Taking together the identified results of the conducted studies included in this dissertation, the next chapter provides important considerations of the gained knowledge and its transfer to the concept of physical frailty.

4.3 Transfer of knowledge to the concept of physical frailty

As outlined in the introduction, there is still an ongoing debate about a universal definition of frailty and therefore how frailty is generally understood (Dent et al., 2019; Morley et al., 2013). At the same time, current methods for measuring frailty continues to have limitations, which restrict their application in clinical practice (Cesari et al., 2014). Consequently, efforts are made to assess frailty more easily by, for instance, utilizing a single modality to measure it as a quantifiable physical parameter (Panhwar et al., 2019). As such, accelerometry is increasingly preferred for movement assessment due to several advantages (Godfrey et al., 2008). However, despite the huge potential of such devices, so far, research has predominantly focused on mobility in relation to physical frailty (Vavasour et al., 2021), leaving unanswered questions regarding the potential and relevance of upper limb performance. Combining the outcomes of this dissertation, utilizing a wearable-based approach to assess upper limb performance, has not only demonstrated differences in performance in terms of frailty levels but has also added to the discussion on how we define frailty (Schmidle et al., 2020, 2022, 2023). Increasing the understanding of the concept of physical frailty and, subsequently, using a comprehensive assessment may not only help us to understand frailty better but also lays the foundation for effective action.

The following paragraphs highlight the significance of utilizing upper limb performance in the context of frailty, particularly using wearables.

4.3.1 Upper limb performance

In general, the assessment of lower limb function is central to the concept of physical frailty (Fried et al., 2001), making it unsuitable for individuals with mobility impairments (Toosizadeh et al., 2015). This is particularly evident in two of the five frailty criteria. The question about "low physical performance", for example, encompasses all forms of physical activity, where gait function is key (e.g., walking, mowing the lawn, raking, hiking, and jogging). The question about "weakness", on the other hand, explicitly assesses gait speed (Fried et al., 2001) (or respective in the used questionnaire, the ability to ascend one or more flights of stairs (Schmidle et al., 2023)). Consequently, if, for example a person is bound to a wheelchair or using walking aids, the individual is prone to get 2 positive rated criteria in the frailty scoring, which means the categorization of "pre-frailty". Therefore, primarily considering lower limb activity might disadvantage individuals with walking impairment (Schmidle et al., 2023). However, it may be important to reflect on whether an individual continues to engage in physical activity, notwithstanding potential physical or neurological impairments that could impact the ability to walk (Schmidle et al., 2023). Therefore, the difference of upper and lower limb activity should be briefly discussed, since upper limb performance proofed to differentiate between frailty levels (Lee et al., 2018; Toosizadeh et al., 2015, 2016, 2017) and demonstrated variances in behavioral patterns (Schmidle et al., 2023). First, activities related to the upper or lower body differ in terms of the metabolic equivalent of task (MET). The MET can be used to compare different activities in terms of energy consumption. As such, activities can be grouped in four main categories: sedentary behavior (i.e., 1.0-1.5 METs), light-intensity (1.6-2.9 METs), moderate-intensity (3.0-5.9 METs), and vigorous intensity (≥ 6.0 METs) (Ainsworth et al., 2011). Typically, lower body activities should exhibit higher energy expenditure in terms of METs compared to upper body activities. This is because lower body movements involve major muscle groups and the movement of the entire body mass, rather than just an arm. Yet, simply using the hands actively as opposed to not using them at all can already result in a variance in METs. Hence, given that less intense activities, like preparing meals, may contribute to over 80 % of daily activity in older adults (Buman et al., 2010), assessing upper limb activity seem to hold significant promise. Secondly, the measurement of lower limb related PA has been discussed to be

influenced by seasonal aspects (e.g., summer vs. winter) (Hamilton et al., 2008; Kimura et al., 2015). A study of Hamilton et al. (2008) investigated whether step counts from a sample of adults living in the UK vary between summer and winter. They found clear differences in ambulatory activity, with levels notably lower during winter compared to summer (Hamilton et al., 2008). Considering upper limb activity, it is somewhat more difficult to make a statement. Nevertheless, an attempt can be made to consider seasonal aspects, particularly in relation to food intake, which encompasses food preparation as well. In a systematic review and meta-analysis, Stelmach-Mardas and colleagues (2016) observed variations in energy intake across seasons. However, the substantial decline in energy intake during winter/summer among Spanish men, for example, can primarily be explained by shifts in the energy density of food (Stelmach-Mardas et al., 2016). Although speculative, there is a possibility that upper limb activity is less influenced by seasonal effects. However, if this is not the case, nonetheless, variations might be less important in terms of METrelated differences. Lastly, differences can be drawn between the upper and lower limb activity in terms of fine and gross motor control. Therefore, while fine motor skills involve the use of small muscles, particularly evident in the hands and fingers for tasks requiring precision and control, lower limbs are typically more often involved in movement that require more force and less precision, such as walking or jumping (Muratori et al., 2013). Assessing upper limb related activity provides the possibility to further differentiate between tasks primarily focusing on fine motor control or tasks covering more aspects of gross motor control, as this was the case for the differentiation between the gardening and the tea task in study II (Schmidle et al., 2022). Furthermore, grip strength and manual dexterity of upper extremity has been identified as an important predictor of dependency (e.g., Gill et al. 2009; Ostwald et al. 1989).

Overall, this leads to the idea of utilizing kinematic parameters of the upper limb for early detection of physical frailty. Hence, it could be valuable to individually examine changes in different categories, such as ambulation and upper limb activity, as changes in physical behavior may serve as an (initial) indicator of frailty (Schmidle et al., 2023), and may occur in varying degrees.

4.3.2 Wearable-based approach

We observed discrepancies between the self-report of physical frailty and the activity profile (Schmidle et al., 2023). This aligns with a well-known debate regarding the relationship between objective and subjective assessments in older adults (Jørstad-Stein et al., 2005; Prince et al., 2008, 2020), indicated by various factors such as inadequate validity of self-reports or objective assessments, or alternatively, low sensitivity of self-reports and objective measures (Gulde & Rieckmann, 2022). In frailty, this debate holds significant relevance, as various assessment tools yield different prevalence data (Collard et al., 2012). Assessing self-reported PA is easy to measure, yet it is susceptible to variations in health status, depression, and fatigue, all of which are prevalent among older individuals with frailty (Rikli, 2000). Furthermore, light to moderate activities, which are crucial for older adults with frailty, pose the greatest challenge for measurement (Washburn, 2000). Based on a systematic review, low physical activity is one of the most frequently altered criteria (Theou et al., 2015). The original Fried assessment (Fried et al., 2001) of PA utilizes the 18-item

PA questionnaire (short version of the MLTQ). However, it focuses on moderate-to-vigorous physical activities (MVPA), not related to older adults (Drey et al., 2011) and shows floor effects (Theou et al., 2012). Therefore, the appropriateness of the MLTQ for the general geriatric population has been questioned (Ziller et al., 2020). The method of physical activity assessment and the choice of cut-points for low physical activity has shown to considerably impact frailty phenotype prevalence (14.9-31.9 %) (Ziller et al., 2020). Interestingly, the mean of different tools of self-reported PA ranged from 130 to 600 minutes MVPA, with particularly the MLTQ (18- and 6-item version) showing no significant differences between the levels of frailty. PA measured with an accelerometer using the Freedson cut point (Freedson et al., 1998) showed an average of 26 minutes MVPA for individuals with frailty. When using the Copeland & Esliger cut point (Copeland & Esliger, 2009), a mean of 500 min/week were measured. However, for both cut points, clear differences were found between the levels of frailty (Ziller et al., 2020). Evidence indicates that objective measures of PA, such as those derived from accelerometers, have been proven to show a stronger correlation with frailty compared to subjective questionnaires (Theou et al., 2012). With wearable sensors becoming increasingly compact and unobtrusive, using a composite of parameters reflecting high-frequency components of arm movements (for upper body activity during sedentary periods) and intensity components extracted from leg movement could be synergistically integrated to generate a significantly more precise prediction of physical activity related EE (Chen & Bassett, 2005).

Arguably, the most attractive feature of wearable sensors is that they offer the opportunity to conduct clinical investigations in real-world environments (Deutsch & Burgsteiner, 2016; Lee et al., 2018; Razjouyan et al., 2018; Toosizadeh et al., 2015; Wile et al., 2014). Therefore, they provide the chance to go beyond classical PA measures (David et al., 2021; Gulde et al., 2023, 2024). As such, wearables can evaluate volume (the amount of activity accumulated), intensity (the rates of activity-related [local] energy expenditure when active), and movement quality (the efficiency/smoothness of movements) (Gulde et al., 2024). In frailty, it is questioned whether solely time-based assessments may provide comprehensive insights into the characteristics of movements and their root causes of changes (Panhwar et al., 2019). This concern seems to be valid, as assessing complex i-ADL in individuals with frailty revealed that a time-based measure did not differ between the frailty levels (Schmidle et al., 2020, 2022). Still exploring the motor performance of i-ADL appears to be particularly interesting as, due to their complexity, impairments in i-ADL typically manifest before b-ADL and i-ADL are seen as a potential frailty marker (Nourhashémi et al., 2001).

By using wearables, data recording can be done in a continuous way and moreover, evaluating individuals within their home environment (including surrounding community) would provide externally valid information regarding sensorimotor capacity, including its fluctuations and changes, as an additional dimension to classical PA assessments (Gulde et al., 2023). This approach would be particularly attractive, given that the evaluation of frailty continues to face challenges in its integration into clinical practice (e.g., cumbersome and time consuming) (Cesari et al., 2014), and may not correctly identify physical frailty due to its

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dependence on subjective patient-reported data (Park et al., 2021). In addition, in the case of the physical frailty syndrome, there appears to be a correlation between motor capacity (evaluated in the laboratory) and mobility performance in the daily routines of pre-frail and frail elderly individuals (Jansen et al., 2019). Therefore, assessing the performance of daily activities in individuals at risk of frailty seems promising, particularly given the assumption that individuals with frailty may already be functioning at their maximum performance capacities (Schmidle et al., 2022).

4.4 Limitations & methodological considerations

The generalizability of the overall findings warrants careful consideration. In study I & II, the small sample size especially with regards to the differentiation between the levels of frailty, is noteworthy (Schmidle et al., 2020, 2022). Additionally, the cohort study III, relied on a convenience sample. Hence, because of the sampling methods employed, certain subgroups could be inadequately represented (for instance, individuals not interested in the topic might not have been reached through public dissemination efforts) (Schmidle et al., 2023). Furthermore, none of our studies utilized the original Fried score (Fried et al., 2001) for assessing physical frailty, due to practicability reasons. For example, in study III, the population of robust older adults was notably smaller compared to pre-frail and frail individuals. This disparity could stem from the frailty categorization relying solely on self-assessment. As a result, participants might have perceived themselves as being in a poorer condition than they are (Schmidle et al., 2023). If the primary object is solely to screen for high risk, such justifications may suffice. If the goal is to delay or prevent frailty itself though, rather than just treating individuals considered at risk, then validity of the approach also becomes a crucial factor to consider (Bandeen-Roche et al., 2023).

Activity counts, based on accelerometry, capture a wide range of movements, but they struggle to fully differentiate between functional and non-functional movements because of their high sensitivity and low specificity. Therefore, additionally using gyroscopic data seem to be a promising approach to further specify functional and non-functional movements of the upper limb (David et al., 2021; Leuenberger et al., 2017; Subash et al., 2022). As such, data derived from gyroscopes may reduce the "cross-talk" with gait, a phenomenon frequently observed with accelerometric assessments (David et al., 2021; Leuenberger et al., 2017). Additionally, since the orientation of the forearm is crucial for ADL performance, gyroscopic data becomes particularly relevant (Leuenberger et al., 2017). Furthermore, wrist-worn devices are prone to interfere when used alongside assistive devices like walkers (Larsen et al., 2020; Schrack et al., 2016). Particularly, the use of rolling walkers often results in a rather stationary wrists, raising uncertainties about the device's ability to accurately capture activity (Schrack et al., 2016). Hence, in future research, employing both hip or ankle pedometers along with wrist-worn IMUs could present an appealing approach, giving the shrinking size and decreasing costs of wearables. Additionally, combining these devices could offer additional insights into energy expenditure during specific activities, as changes in activity may occur in varying degrees between the upper and lower limb (Schmidle et al., 2023). However, because we faced some technical challenges due to, for example, frequent recharging of the smartwatch, we strongly

recommend using devices with extended battery life and greater robustness towards unintentional changes to measurement settings in future research, to increase independent handling and decrease potential dropouts (Schmidle et al., 2023).

Conclusion & outlook

5. Conclusion & outlook

So far, there has been insufficient research on the relevance of upper limb performance in relation to physical frailty. The results of the three studies encompassing this dissertation show that wrist-worn devices have the potential to 1) capture kinematic parameters relevant to differentiate motor performances with regards to physical frailty in instrumental activities of daily living (i-ADL) (Schmidle et al., 2020, 2022), 2) provide information on the activity level of the upper limb during daily living, as a promising indicator of i-ADL engagement (Schmidle et al., 2023), and 3) validate self-reports of physical frailty, as especially objective and subjective methods may lack agreement (Schmidle et al., 2023). These findings have significant impact on the general research focus on physical frailty, as until now, extensive investigations have been made on lower limb functions. This thesis contributes to the broader understanding of the physical frailty syndrome and the utilized wrist-worn approach demonstrates potential in addressing the following aspects:

- Identifying differences in i-ADL performance using wrist-worn sensors within and outside the laboratory setting, thereby moving towards real-world applications.
- Providing a cost-effective approach for clinicians to conduct kinematic analyses.
- Exploring various body locations for assessing upper and lower limb performance separately, considering their potentially equally weighted significance in the context of physical frailty.
- Using wearables as validation method for self-reported frailty assessments.
- Addressing sex differences in activity behavior, such as the type of activity engaged in.
- Addressing potential frailty-biases, including those that may disadvantage individuals with walking impairments or result in distorted self-perceptions when using questionnaires.

To advance the field, we stress to further investigate the importance of the upper limbs when assessing everyday life performances in individual with frailty. Considering the promising potential to record data in uncontrolled settings using small sensors, a frailty prediction model integrated into a smartwatch could offer a significant clinical application. To address this, it may be valuable to conduct a more comprehensive investigation into the correlation between task capacity and performance, specifically highlighting upper limb function. Following this, longitudinal studies could be carried out on both upper and lower limbs, as changes in PA could be indicative of the natural progression of physical frailty. Further incorporating gyroscopic data could enhance the distinction between upper and lower body movements, offering valuable insights into forearm positioning, which is deemed to be crucial for ADL performance (Leuenberger et al., 2017). Particularly, the use of digital biomarkers of physical frailty could serve as a promising automated method for identification (Park et al., 2021). This is because the monitoring of alterations in the physical and behavioral characteristics of the population over time, may play a significant role in this assessment (Khusainov et al., 2013; Park et al., 2021).

Affidavit

I hereby confirm that the dissertation "Wearable-based analysis of everyday life performances in individuals with frailty in advanced age" is the result of my own work and that I have only used sources or materials listed and specified in the dissertation.

Munich 30th of April 2024

Stephanie Schmidle
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Appendix

Appendix 1 – Questionnaire for assessing physical frailty (Fried et al., 2001), according to (Kunadian et al., 2016). Translated into German.

Frailty Assessment

ID:_____

Ungewollter Gewichtsverlust

 $BMI: ___ < 18.5 kg/m^2 \quad ja \ nein$

Körperliche Ausdauer/Energie

1. Fühlen Sie sich energetisch/ voller Energie?

Ja Nein

2. Wie oft in den letzten vier Wochen haben Sie tagsüber im Bett gelegen?

Jeden Tag Jede Woche Manchmal Nie

Niedrige körperliche Aktivität

- 1. Wie oft üben Sie leichte körperliche Aktivität aus?
 - > 3x pro Woche 1-2x pro Woche 1-3x im Monat So gut wie nie/ Nie
- 2. Wie oft üben Sie gemäßigte körperliche Aktivität aus?
 - > 3x pro Woche 1-2x pro Woche 1-3x im Monat So gut wie nie/ Nie
- 3. Wie oft üben Sie intensive körperliche Aktivität aus?
 - > 3x pro Woche 1-2x pro Woche 1-3x im Monat So gut wie nie/ Nie

Handkrafttest

Durchschnitt von 3 Versuchen: _____ kg

TUG

 \geq 19 Sekunden ja nein

Fried Score: _____ robust pre-frail frail

Appendix 2 – Questionnaire study III (Schmidle et al., 2023) including questions on physical frailty (Fried et al., 2001), in accordance with (Romero-Ortuno, 2011). Translated into German.

Anamnesebogen

Name: ID: Institution: Kontaktinformation:

Persönliche Information Geburtsdatum: Geschlecht: Gewicht: Körpergröße:

Anamnese

<u>Chronische Erkrankungen</u> Leiden Sie an einer dieser Krankheitsbilder?

- 1. Schlaganfall
- 2. Parkinson
- 3. Alzheimer
- 4. Multiple Sklerose
- 5. Epilepsie
- 6. Bluthochdruck
- 7. Asthma Bronchiale
- 8. Arthritis
- 9. Diabetes Mellitus

Medikamente

Nehmen Sie Medikamente gegen Schwindel? Ja / nein

Nehmen Sie Medikamente für Ihren Blutdruck? Ja / nein

Persönliche Gesundheitswahrnehmung

Wie würden Sie selbst Ihren Gesundheitszustand einstufen?

- 1. Hervorragend
- 2. Sehr gut
- 3. Gut
- 4. Mittelmäßig
- 5. Schlecht

Verglichen mit Ihrem Gesundheitszustand vor einem Jahr, wie würden Sie diesen aktuell einschätzen?

- 1. Viel besser
- 2. Etwas besser
- 3. Gleich
- 4. Etwas schlechter
- 5. Viel schlechter

In den letzten zwei Wochen war mein Leben mit Ereignissen/Dingen gefüllt, die mich Interessieren

- 1. Die ganze Zeit
- 2. Die meiste Zeit
- 3. Mehr als die Hälfte der Zeit
- 4. Weniger als die Hälfte der Zeit
- 5. Zu manchen Zeitpunkten
- 6. Zu keinem Zeitpunkt

Fühlen Sie sich zuhause sicher?

- 1. Nein, gar nicht
- 2. Etwas
- 3. Mittelmäßig
- 4. Ziemlich
- 5. Sehr

Fühlen Sie sich außerhalb Ihres Zuhauses sicher?

- 1. Nein, gar nicht
- 2. Etwas
- 3. Mittelmäßig
- 4. Ziemlich
- 5. Sehr

Lebenssituation

Wohnsituation

Leben Sie alleine? Ja / nein Wenn nein, mit wem leben Sie zusammen?

Leben Sie in der Stadt, Vorstadt oder auf dem Land?

- 1. Ländlich
- 2. Stadt nah
- 3. In der Stadt

<u>Umkreis</u>

Wir sind interessiert daran, welche Orte Sie in den letzten drei Tagen besucht haben

In den letzten drei Tagen: Waren Sie in anderen Räumen als Ihrem Schlafzimmer? Ja / nein Waren Sie in einem Bereich in unmittelbarer Nähe Ihres Zimmers, wie zum Beispiel Ihrer Veranda oder dem Flur? Ja / nein

Waren Sie an Orten in Ihrer unmittelbaren Nachbarschaft außerhalb des Grundstücks, wie Garten und Garage? Ja / nein

Waren Sie außerhalb der Straße in der Sie wohnen innerhalb ihrer Nachbarschaft, wie im Supermarkt oder bei der Apotheke? Ja / nein

Waren Sie an Orten außerhalb Ihrer Stadt? Ja / nein

Professionelle Pflege

Beziehen Sie eine Pflegestufe? Ja / nein

Informelle Pflege

Erhalten Sie Unterstützung von Angehörigen? Ja / nein

<u>Gehhilfe</u>

Benutzen Sie eine Gehhilfe innerhalb oder außerhalb des Hauses? Ja / nein Wenn ja, für Draußen / Drinnen

Überwachungssystem

Haben Sie ein Überwachungs- oder Alarmsystem Zuhause / im Seniorenheim? Ja / nein

Frailty Syndrom

Bericht der Institution:

Erschöpfung

Hat es Ihnen in den letzten Monaten an Energie gefehlt Dinge auszuführen, die Sie gerne tun?

Ja / nein

Unbeabsichtigter Gewichtsverlust

Wie würden Sie Ihren Appetit bewerten?

- 1. Appetitsverlust
- 2. Keinen Appetitsverlust
- 3. Ich bin mir nicht sicher

Essen Sie aktuell mehr oder weniger als normalerweise?

- 1. Weniger
- 2. Mehr
- 3. Weder noch

Muskelkraft

Haben Sie Schwierigkeiten Dinge, wie zum Beispiel einen vollen Einkaufskorb mit einem Gewicht von mehr als 5kg, anzuheben?

Ja / nein

<u>Schwäche</u>

Fällt es Ihnen schwer ein Stockwerk hochzusteigen, ohne zu pausieren? Ja / nein

Fällt es Ihnen schwer mehrere Stockwerke hintereinander hochzusteigen, ohne zu pausieren?

Ja / nein

Körperliche Aktivität

Wie häufig nehmen Sie an Aktivitäten teil, die eine moderate Anstrengung von Ihnen abverlangen (z.B. Gartenarbeit, putzen, das Auto säubern oder einen Spaziergang machen)

- 1. Mehrmals pro Woche
- 2. Ein bis dreimal pro Woche
- 3. Einmal pro Woche
- 4. Kaum bzw. gar nicht

<u>Stürze</u>

<u>Sturzereignisse</u> Sind Sie in den letzten 12 Monaten gestürzt? Ja / nein

Wenn ja, wie häufig?

Sturzursache

Wieso sind Sie gestürzt?

- 1. Gestolpert
- 2. Ausgerutscht
- 3. Gleichgewichtsverlust
- 4. Kollaps/Zusammenbruch
- 5. Plötzlicher Kraftverlust der Beine
- 6. Schwindel

Verletzungen

Aus wie vielen Ihrer Stürze resultierte eine Fraktur/ein Bruch?

Information zum Experiment

Smartwatch Code:_____

User-account Oolware:______Automatischer Alarm an: Ja / nein Telefonnummer der Kontaktperson im Falle eines Alarms:______ Position der Uhr: An welchem Arm wird die Uhr getragen? R / L

Appendix 3 – Study reprint permission (study I)

Monday, April 29, 2024 at 14:23:05 Central European Summer Time

 Betreff:
 Published HCII 2020 paper, thesis

 Datum:
 Montag, 29. April 2024 um 14:19:45 Mitteleuropäische Sommerzeit

 Von:
 Ronan Nugent

 An:
 Stephanie Schmidle

Hello Stephanie,

Thank you for your contribution to our program, we note the HCII 2020 paper: "Frailty Assessment in Daily Living (FRAIL) – Assessment of ADL Performance of Frail Elderly with IMUs", S. Schmidle et al., HCII 2020, Late Breaking Papers, Part II, CCIS Vol. 1294 (https://link.springer.com/chapter/10.1007/978-3-030-60703-6_12).

As we discussed, it's fine for Springer Nature if you reproduce this in your thesis.

Thank you for your checking with us, and good luck in your defence.

Best regards, Ronan

(Ronan Nugent, Editorial Director, Springer Computer Science)