Alma Mater Studiorum – Università di Bologna

DOTTORATO DI RICERCA IN

Ingegneria Biomedica, Elettrica e dei Sistemi (IBES) – Curriculum in Bioingegneria

Ciclo XXXI

Settore Concorsuale: 09/G2

Settore Scientifico Disciplinare: ING-INF/06

INSTRUMENTED CLINICAL SCALES TO PROMOTE OBJECTIVE MEASURES OF PHYSICAL CAPABILITY IN CLINICAL ASSESSMENT AND REHABILITATION MEDICINE

Presentata da: Alice Coni

Coordinatore Dottorato

Prof. Daniele Vigo

Supervisore

Prof. Lorenzo Chiari

Co-Supervisore

Fabio La Porta MD, Ph.D

Esame finale anno 2019

ABSTRACT

Ageing is usually combined with a decline of physical and cognitive capacity, which implies a significant economic cost in terms of health care and social assistance. Early detection of people at risk of developing age-related Physical Capability (PC) decline is crucial for primary prevention. Instrumenting Physical Performance (PP) tests and continuous monitoring of daily Physical Activity (PA) by means of wearable inertial sensors allow the extraction of many objective measures, which could help in detecting the age-related physical decline. However, little use is made in everyday clinical practice, because of the lack of standardization, redundancy of information and the need for normative data. A Factor Analysis approach allows to identify a smaller number of empirically defined and statistically independent factors representing distinct domains. This technique can be used to obtain a model of the older adults' PC and provide a uniform and standard clinical interpretation of those measures.

The main goal of this thesis was the design of a general model for providing an objective and comprehensive functional assessment tool, being able to also explore the relationships among instrumented scores, clinical scores and specific impairments and diseases. More than 500 community-dwelling adults participating in three different EU studies (PreventIT [1], InCHIANTI [2] and PRE.C.I.S.A [3]) underwent a battery of PP tests, wearing an inertial sensor at L5. The battery included the assessment of postural sway in Quiet Standing (QS), walking, Chair Stand test (CST) and Timed Up and Go test (TUG) and the collection of a set of health-related measures. Age and gender relationships have been investigated. Exploratory Factor Analysis (EFA) was used to define a conceptual model based on the set of sensor-based measures extracted. One-week continuous monitoring of daily PA activity has also been recorded from a subset of 171 participants of the InCHIANTI Study. PA measures included the percentage of sedentary, active, and walking time, the duration and intensity (METs) of the activities, as well as the gait and turning characteristics. The outcomes of both the sensor-based assessments of PP and daily PA were consistent with the conventional clinical outcomes. Instrumented functional testing showed the potential to i) advance the quality of current mobility assessments; ii) enhance our understanding of an individual's true PC; and iii) disclose subtle changes in PC that would otherwise remain undetected.

In conclusion, the development and implementation of an easy to use, objective and comprehensive tool for the assessment of the individuals' PC has demonstrated to be feasible. This tool enriches the conventional clinical outcomes, allowing to objectively measure several mobility skills that would otherwise remain undetected and foster the achievement of the early detection of the age-related functional decline, facilitating the design of interventions and rehabilitation strategies.

"Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it" - Plátōn (428 – 348 B.C.)

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my Supervisor Prof. Lorenzo Chiari, for the support and guidance during all my PhD at the Alma Mater Studiorum - Università di Bologna.

My gratitude also goes to my Co-Supervisor Dr. Fabio La Porta, my colleagues Marco Colpo and Sabato Mellone, and all the researchers of the Personal Health System Lab. and Biolab of the Department of Electrical, Electronic and Information Engineering (DEI) for the insight and expertise that greatly assisted my research.

A special thank goes to Prof. Mirjam Pijnappels, Jeanine M. Van Ancum, Nini H Jonkman and all the MOA team for the exciting opportunity to work with them during my visiting research period at the Vrije Universiteit of Amsterdam.

I would like to acknowledge Prof. Jochen Klenk and Martina Mancini who carefully revised the thesis giving valuable comments.

A particularly warm thank to all the participants and assessors of the InCHIANTI, PreventIT and PRE.C.I.S.A studies for their essential collaboration to the data collection.

Last but not least, I would like to thank my family and friends for the precious love received.

TABLE OF CONTENTS

1.	Inti	RODU	CTION	1
	1.1.	Рну	SICAL CAPABILITY AS A MEASURE OF HEALTHY AGEING AND WELLBEING	. 1
	1.1.	1.	HEALTHY AGEING	. 1
	1.1.	2.	PHYSICAL ACTIVITY AND PHYSICAL CAPABILITY	. 1
	1.1.	3.	CONVENTIONAL SELF- AND OBJECTIVE ASSESSMENT OF PHYSICAL CAPABILITY	2
	1.1.4	4.	SENSOR-BASED MEASURES OF PHYSICAL CAPABILITY	2
	1.2.	RES	EARCH PROJECT AND AIMS	3
	1.3.	The	SIS OUTLINE	5
2. DI	CON SCRIMI	MPARI INATI	ISON OF STANDARD CLINICAL AND INSTRUMENTED MEASURES OF PHYSICAL PERFORMANCE IN NG FUNCTIONAL STATUS OF HIGH FUNCTIONING PEOPLE AGED 61-70 YEARS OLD	N . 7
	2.1.	Inte	RODUCTION	7
	2.2.	Met	THODS	7
	2.2.	1.	POPULATION	7
	2.2.2	2.	DEMOGRAPHIC MEASURES	8
	2.2.	3.	OUTCOME	8
	2.2.4	4.	STANDARD CLINICAL PHYSICAL PERFORMANCE TESTS	8
	2.2.:	5.	INSTRUMENTED PHYSICAL PERFORMANCE TESTS	8
	2.3.	STA	TISTICAL ANALYSIS	9
	2.4.	RES	ULTS	10
	2.5.	Disc	CUSSION	16
	2.6.	CON	ICLUSIONS	18
3.	THE	E INCI	HIANTI-FARSEEING PROJECT	19
	3.1.	Inte	RODUCTION	19
	3.2.	Met	THODS	20
	3.2.	1.	POPULATION	20
	3.2.2	2.	HEALTH-RELATED MEASURES	21
	3.2.	3.	PHYSICAL PERFORMANCE TESTS	21
	3.2.4	4.	STATISTICAL ANALYSIS	22
	3.3.	RES	ULTS	22
	3.3.	1.	SENSOR-BASED PHYSICAL PERFORMANCE MEASURES	22
	3.3.2	2.	ANALYSIS OF AGREEMENT	22
	3.3.	3.	INFLUENCE OF AGE AND GENDER ON SENSOR-BASED PHYSICAL PERFORMANCE MEASURES 2	23
	3.4.	Disc	CUSSION	28
	3.4.	1.	ANALYSIS OF AGREEMENT	28
	3.4.2	2.	INFLUENCE OF AGE AND GENDER ON SENSOR-BASED PHYSICAL PERFORMANCE MEASURES 2	28

3.5.	CON	ICLUSIONS	
3.6.	Тне 30	INSTRUMENTED TIMED UP AND GO TEST: AN EXPLORATORY FACTOR ANALYSIS A	PPROACH
3.0	5.1.	BACKGROUND AND AIM	
3.0	5.2.	Methods	
3.0	5.2.1.	POPULATION	30
3.0	5.2.2.	INSTRUMENTED TUG	30
3.0	5.2.3.	STATISTICAL ANALYSIS	
3.0	5.3.	RESULTS	
3.0	5.4.	DISCUSSION	
3.0	5.5.	CONCLUSIONS	
4. A	Senso	R-BASED CONCEPTUAL MODEL FOR PHYSICAL CAPABILITY ASSESSMENT	
4.1.	Dev	VELOPMENT OF THE CONCEPTUAL MODEL	
4.	1.1.	POPULATION AND METHODS	
4.2.	Infi	LUENCE OF AGE, GENDER, BODY COMPOSITION AND COGNITION: RESULTS	
4.2	2.1.	QS FACTOR MODEL	40
4.2	2.2.	7MW FACTOR MODEL	41
4.2	2.3.	CST FACTOR MODEL	41
4.2	2.4.	TUG FACTOR MODEL	
4.2	2.5.	CORRELATION ANALYSIS	44
4.3.	DIS	CUSSION	46
4.3	3.1.	CONVENTIONAL OUTCOME	47
4.3	3.2.	IADL	48
4.3	3.3.	CES-D	
4.3	3.4.	PA	
4.3	3.5.	FALLN	49
4.3	3.6.	HAND	49
4.3	3.7.	PWR	50
4.3	3.8.	TMTA	50
4.3	3.9.	SPPB	50
4.4.	Infi	LUENCE OF THE OVERALL PERFORMANCE: RESULTS	
4.4	4.1.	QS FACTOR MODEL	
4.4	4.2.	7MW FACTOR MODEL	
4.4	4.3.	CST FACTOR MODEL	
4.4	4.4.	TUG FACTOR MODEL	
4.4	4.5.	CORRELATION ANALYSIS	
4.5.	DIS	CUSSION	
4.5	5.1.	CONVENTIONAL OUTCOME	

4.5.2.	IADL	59
4.5.3.	CES-D	59
4.5.4.	PA	59
4.5.5.	FALLN	59
4.5.6.	HAND AND PWR	60
4.5.7.	TMTA	60
4.5.8.	SPPB	60
4.6. Rei	FINEMENT OF THE CONCEPTUAL MODEL: FINAL VERSION	61
4.6.1.	POPULATION AND METHODS	61
4.6.2.	RESULTS	62
4.6.2.1.	QS FACTOR MODEL	64
4.6.2.2.	7MW FACTOR MODEL	65
4.6.2.3.	CST FACTOR MODEL	65
4.6.2.4.	TUG FACTOR MODEL	66
4.6.2.5.	LINEAR REGRESSION ANALYSIS	68
4.6.3.	DISCUSSION	
4.6.3.1.	CONVENTIONAL OUTCOME	
4.6.3.2.	IADL	
4.6.3.3.	FALL-HISTORY	
4.6.3.4.	CES-D	
4.6.3.5.	PA	74
4.6.3.6.	SPPB	74
4.6.3.7.	HAND	
4.6.3.8.	PWR	75
4.6.3.9.	TMTA	75
4.6.3.10	CASE STUDIES	
4.7. Co	NCLUSIONS	77
5. THE PRI	E.C.I.S.A STUDY: APPLICATION OF THE SENSOR-BASED CONCEPTUAL MODEL	
5.1. OU	TLINE OF THE STUDY AND DESCRIPTION OF THE POPULATION	
5.2. ME	THODS	
5.3. Res	SULTS	79
5.4. Dis	CUSSION	80
5.4.1.	CASE STUDIES	81
5.5. Co	NCLUSIONS	82
6. SENSOR-	BASED PA MEASURES FOR THE ASSESSMENT OF USUAL PERFORMANCE	83
6.1. BA	CKGROUND AND AIM	83
6.2. ME	THODS	
6.2.1.	POPULATION	84

	6.2.2.	INSTRUMENTED MEASURES	84
	6.2.3.	STATISTICAL ANALYSIS	84
6	5.3. Re	SULTS	84
6	5.4. DI	SCUSSION	87
6	5.5. Co	DNCLUSIONS	89
7.	FINAL F	REMARKS AND FUTURE DIRECTIONS	90
8.	Appeni	DIX A: SENSOR-BASED MEASURES COMPUTED FROM THE INSTRUMENTED PHYSICAL	
Per	RFORMAN	CE TESTS	93
9.	BIBLIO	GRAPHY	98

LIST OF TABLES

TABLE 2.1 DESCRIPTION OF THE PREVENTIT POPULATION 11
TABLE 2.2 COLLINEARITY ANALYSIS OF THE 30CST INSTRUMENTED MEASURES 12
TABLE 2.3 COLLINEARITY ANALYSIS OF THE TUG INSTRUMENTED MEASURES 13
TABLE 2.4 UNIVARIABLE AND MULTIVARIABLE ANALYSIS OF THE 30CST INSTRUMENTED MEASURES
TABLE 2.5 UNIVARIABLE AND MULTIVARIABLE ANALYSIS OF THE TUG INSTRUMENTED MEASURES . 15 $$
TABLE 2.6 BOOTSTRAPPING VALIDATION OF THE 30CST AND TUG MODELS 15
TABLE 2.7 SENSITIVITY ANALYSIS 16
TABLE 3.1 Factor analysis of the instrumented TUG features and statistical analysis. 33
TABLE 4.1 DEMOGRAPHIC AND FUNCTIONAL PROFILES OF THE GROUPS WHO UNDERWENT THE FOUR
TEST
TABLE 4.2 SENSOR-BASED MEASURES CONTRIBUTING TO EACH FACTOR OF THE FIRST VERSION OF THE
CONCEPTUAL MODEL, FOR EACH INSTRUMENTED TEST
TABLE 4.3 FACTOR LOADINGS OF THE FIRST VERSION OF THE QS CONCEPTUAL MODEL40
TABLE 4.4 FACTOR LOADINGS OF THE FIRST VERSION OF THE 7MWT CONCEPTUAL MODEL41
TABLE 4.5 FACTOR LOADINGS OF THE CST CONCEPTUAL MODEL
TABLE 4.6 Factor loadings of the first version of the TUG conceptual model43
TABLE 4.7 CORRELATION ANALYSIS BETWEEN DOMAINS OF THE CONCEPTUAL MODEL AND RESIDUALS
OF THE HEALTH-RELATED MEASURES44
TABLE 4.8 CORRELATION ANALYSIS BETWEEN DOMAINS OF THE FIRST VERSION OF THE CONCEPTUAL
MODEL
TABLE 4.9 CORRELATION ANALYSIS BETWEEN RESIDUALS OF THE HEALTH-RELATED MEASURES46
TABLE 4.10 Factor loadings of the second version of the 7 mWT conceptual model52
TABLE 4.11 FACTOR LOADINGS OF THE SECOND VERSION OF THE CST CONCEPTUAL MODEL
TABLE 4.12 ACTOR LOADINGS OF THE SECOND VERSION OF THE TUG CONCEPTUAL MODEL
TABLE 4.13 CORRELATION ANALYSIS BETWEEN DOMAINS OF THE SECOND VERSION OF THE
CONCEPTUAL MODEL AND HEALTH-RELATED MEASURES

TABLE 4.14 CORRELATION ANALYSIS BETWEEN DOMAINS OF THE SECOND VERSION OF THE CONCEPTUAL MODEL 57
TABLE 4.15 CORRELATION ANALYSIS BETWEEN HEALTH-RELATED MEASURES 58
TABLE 4.16 DEMOGRAPHIC AND FUNCTIONAL PROFILES OF EACH SUBGROUP UNDERTAKING THE FOUR FUNCTIONAL TESTS 61
TABLE 4.17 SENSOR-BASED MEASURES CONTRIBUTING TO EACH FACTOR OF THE THIRD VERSION OF THE CONCEPTUAL MODEL, FOR EACH INSTRUMENTED TEST
TABLE 4.18 FACTOR LOADINGS OF THE THIRD VERSION OF THE QS conceptual model64
TABLE 4.19 FACTOR LOADINGS OF THE THIRD VERSION OF THE 7MWT CONCEPTUAL MODEL
TABLE 4.20 FACTOR LOADINGS OF THE THIRD VERSION OF THE CST CONCEPTUAL MODEL 66
TABLE 4.21 FACTOR LOADINGS OF THE THIRD VERSION OF THE TUG CONCEPTUAL MODEL
TABLE 4.22 LINEAR REGRESSION ANALYSIS BETWEEN DOMAINS 69
TABLE 4.23 LINEAR REGRESSION ANALYSIS BETWEEN DOMAINS AND HEALTH-RELATED MEASURES $.70$
TABLE 4.24 LINEAR REGRESSION ANALYSIS BETWEEN HEALTH-RELATED MEASURES
TABLE 5.1 DESCRIPTION OF THE PRE.C.I.S.A. POPULATION 79
TABLE 6.1 SPEARMAN'S CORRELATION COEFFICIENT BETWEEN FEATURES AND HEALTH-RELATED VARIABLES
TABLE 6.2 LOADINGS OF THE FACTOR ANALYSIS OF THE MEAN VALUES DATASET
TABLE 6.3 LOADINGS OF THE FACTOR ANALYSIS OF THE EXTREME VALUES DATASET 86
TABLE 8.1 SENSOR-BASED FEATURES EXTRACTED FROM THE QS TEST
TABLE 8.2 SENSOR-BASED FEATURES EXTRACTED FROM THE 7MW TEST 95
TABLE 8.3 SENSOR-BASED FEATURES EXTRACTED FROM THE CST TEST 96
TABLE 8.4 SENSOR-BASED FEATURES EXTRACTED FROM THE TUG TEST

LIST OF FIGURES

FIGURE 1.1 FLOWCHART OF THE RESEARCH APPROACH
FIGURE 2.1 SENSITIVITY ANALYSIS: DISCRIMINATIVE ABILITY (AUC AND DELONG TEST) OF STANDARD
CLINICAL, INSTRUMENTED AND COMBINED MODELS OF THE 30CS I AND TUG TEST [50]
FIGURE 3.1 DISTRIBUTION OF THE PARTICIPANTS ASSESSED IN THE 4TH WAVE OF THE INCHIANTI COHORT STUDY
FIGURE 3.2 BLAND-ALIMAN PLOTS COMPARING THE DIFFERENCE BETWEEN THE SENSOR-BASED
MEASURES AND THE STOPWATCH MEASURES FOR THE TOTAL DURATION (SECONDS) OF THE 7-
METER WALK TEST (A), 5-TIMES REPEATED CHAIR STAND TEST (B) AND TIMED UP AND GO TEST
(C). THE RED LINES REPRESENT THE MEAN VALUE OF THE DIFFERENCES BETWEEN MEASURES
(SENSOR-BASED VS. STOPWATCH) AND THE BLUE LINES REPRESENT THE LIMITS OF AGREEMENT
$(\pm 1.96 \text{ STANDARD DEVIATIONS}).$ 23
Figure 3.3 Trend with age of the sensor-based measures computed from the QS test $\dots 24$
Figure 3.4 Trend with age of the sensor-based measures computed from the 7MW test 25
FIGURE 3.5 TREND WITH AGE OF THE SENSOR-BASED MEASURES COMPUTED FROM THE CST TEST 26
Figure 3.6 Trend with age of the sensor-based measures computed from the TUG test $\dots 27$
FIGURE 3.7 DOTS REPRESENT THE PREDICTED VALUES OF THE FACTORS. THICK LINE REPRESENTS THE
SECOND ORDER POLYNOMIAL CURVE FITTING OF THE FACTOR WITH AGE. BOXPLOTS SHOW THE
DISTRIBUTION OF THE VALUES IN THE SIX AGE GROUPS DEFINED IN TABLE 3.1 [68] 32
FIGURE 4.1 FLOWCHART OF THE CONCEPTUAL MODEL DEVELOPMENT PROCESS; N IS THE NUMBER OF
SENSOR-BASED MEASURES AND FACTORS OR DOMAINS OF EACH INSTRUMENTED TEST
FIGURE 4.2 FLOWCHART OF THE THIRD VERSION OF THE CONCEPTUAL MODEL DEVELOPMENT PROCESS
FIGURE 4.3 RADAR PLOTS OF THREE CASE STUDIES. THE BLACK LINES REPRESENT THE MEDIAN, 25TH
AND 75TH PERCENTILE OF THE OLDER ADULTS' FACTOR SCORES. THE DARK GREY AREA
REPRESENTS EXTREME VALUES (VERY HIGH VALUES ABOVE THE 75 TH PERCENTILE AND VERY LOW
values under the 25^{1H} percentile). Favourable values of the scores, below the 75^{TH}
PERCENTILE, REFLECTED GOOD PERFORMANCES IN THE DOMAINS

Figure 5.1 Graphical representation of the scores of the PRE.C.I.S.A study participants. The black lines represent the median, 25^{TH} and 75^{TH} percentile of the InCHIANTI

FIGURE 5.2 SHOWS THREE CASE STUDIES. THE BLACK LINES REPRESENT THE MEDIAN, 25th and 75th percentile of the InCHIANTI population, used as a reference. The coloured lines represent the scores of the three groups of PRE.C.I.S.A. study (Parkinson, Stroke and 65+). The dark grey area represents extreme values (very high values above the 75th percentile and very low values under the 25th percentile). Favourable values of the scores, below the 75th percentile, reflected good performances in the domains......81

LIST OF ABBREVIATIONS AND ACRONYMS

7MW	7-meter Walk Test
10MW	10-meters Walking Test
30CST	30-sec Chair Stand Test
7MW1	First domain of the 7MW factor model
7MW2	Second domain of the 7MW factor model
7MW3	Third domain of the 7MW factor model
7MW4	Fourth domain of the 7MW factor model
7MW5	Fifth domain of the 7MW factor model
А	Accelerometer
ADL	Activities of Daily Living
AP	Antero-Posterior
AUC	Area Under the Receiver Operating Curve
BMI	Body Mass Index
CES-D	Center for Epidemiologic Studies Depression Scale
CF	Centroidal Frequency
CI	Confidence Interval
CST1	First domain of the CST factor model
CST2	Second domain of the CST factor model
CST3	Third domain of the CST factor model
CST4	Fourth domain of the CST factor model
CST5	Fifth domain of the CST factor model
CST6	Sixth domain of the CST factor model
DISPL	Displacement
E.V.	Explained Variance
EA	Ellipse Area
EFA	Exploratory Factor Analysis
F50	Median frequency
F95	Frequency bandwidth
FALLN	number of falls in the last year declared during the assessment
FD	Frequency Dispersion
G	Gyroscope

HAND	Hand-Grip strength
HFS	High Functional Status
IADL	Instrumental Activities of Daily Living
IMUs	Inertial Measurement Units
LLFDI	Late-Life Function and Disability Instrument
М	Mean
METs	Metabolic Equivalents
ML	Medio-Lateral
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
MV	Mean Velocity
NI	Not Included in the model
NJS	Normalized Jerk Score
NM	Number of medications
OR	Odds Ratios
PA	Physical Activity
PC	Physical Capability
PCI	Phase Coordination Index
PP	Physical Performance
PWR	Lower extremity muscle power measured using the Nottingham leg extensor Power Rig
QS1	First domain of the QS factor model
QS2	Second domain of the QS factor model
QS3	Third domain of the QS factor model
QS4	Fourth domain of the QS factor model
Reg	Regularity
RMS	Root Mean Square
SA	Sway Area
SD	Standard Deviation
SE	Spectral Entropy
SP	Sway Path
SPs	Smartphones SP
SPPB	Short Physical Performance Battery

Sts	Sts: Sit to Stand
stS	stS: Stand to Sit
SW	Stopwatch
TMTA	Trail Making Test A
TUG	Timed Up and Go test
TUG1	First domain of the TUG factor model
TUG2	Second domain of the TUG factor model
TUG3	Third domain of the TUG factor model
TUG4	Fourth domain of the TUG factor model
TUG5	Fifth domain of the TUG factor model
TUG6	Sixth domain of the TUG factor model
TUG7	Seventh domain of the TUG factor model
TUG8	Eighth domain of the TUG factor model
V	Vertical
VHF	Very High Functional Status
VIF	Variance Inflation Factor

1. INTRODUCTION

1.1. PHYSICAL CAPABILITY AS A MEASURE OF HEALTHY AGEING AND WELLBEING

1.1.1. HEALTHY AGEING

The number of older people is constantly increasing worldwide. In the European Union, 19% of the whole population was aged over 65 in 2017 and this percentage will increase to 29.1% by the year 2080 [4]. This will lead to the transition towards a much older population structure, which will affect the social and health care systems of every country. Significant challenges must be faced to meet the rising needs of an ageing population. Ageing is usually combined with a decline of physical and cognitive capacity, which implies a significant economic cost in terms of health care and social assistance. A public-health response to the ageing phenomenon should act to reduce the losses associated with older age and reinforce recovery, adaptation and psychosocial growth [5]. For these reasons, it is of the utmost importance to foster an active and healthy ageing and monitor effectively the population's health status. In accordance with a recent resolution of the World Health Organization and on the evidence of the world report on ageing and health, a comprehensive global strategy and action plan on ageing and health has been developed [6].

1.1.2. PHYSICAL ACTIVITY AND PHYSICAL CAPABILITY

Since healthy ageing and wellbeing are becoming the main goals of modern societies, the focus of researches on ageing has moved to the design of intervention strategies, aiming to reduce the risk of developing age-related disability and disease [7]. One of the most important approaches to delay the morbidity associated with ageing is to increase Physical Activity (PA) among older people. To raise awareness of relationships between PA and health in older adults, better methods are needed to facilitate monitoring in clinics, at home or in a community setting [8]. A high number of biomarkers of healthy ageing have been suggested in the literature [9,10]. The most widely recognized by the scientific community is Physical Capability (PC) [11]. By definition, PC includes muscle strength and physical performance against the ability to perform daily physical tasks, for instance: maintain balance, rising from a chair or walking, which involve physiological functions of several body systems [12]. The subdomains engaged in performing the activities of daily living include balance, locomotion and strength and are strongly associated with quality of life, disability [13,14] and may be predictive for subsequent health outcomes and mortality in community-dwelling populations [10,15,16].

1.1.3. CONVENTIONAL SELF- AND OBJECTIVE ASSESSMENT OF PHYSICAL CAPABILITY

PC is conventionally assessed by questionnaires and clinical rating scales based on self-reports, which assess functional limitations or ability to perform activities of daily living (ADL). These tools aim to measure latent variables and this implies that they are subjective, may have poor reliability, validity and responsiveness and they may suffer from ceiling and floor effect [17,18]. To overcome the above limitations and improve validity and reproducibility, objective and standardized tests of PC, also called Physical Performance tests (PP), were introduced. PP tests require good balance and strength, and they need the good function of the musculoskeletal, cardiovascular, respiratory, and nervous systems. Poor PP, like poor capacity to maintain the static balance with different feet position and eyes open/closed, slow walking speed, or poor abilities to stand from a chair and sit back down again a set number of times, may predict subsequent health outcomes in community-dwelling populations [15]. It is also associated with greater risk of subsequent disability in terms of restrictions in activities of daily living [19]. During the clinical assessment of PC, a set of different PP tests are often administered together, such as the Short Physical Performance Battery (SPPB) which includes measures of balance, gait and chair rise and foresees the computation of a total performance score. This score has been demonstrated to predict mortality and institutionalization across a broad spectrum of functional status [20,21]. PP tests are also able to accurately capture the change of PC with ageing, reflecting the loss of functioning of the body systems engaged. Recently, Ferrucci et al. showed the shape of the decline of walking speed and other measures of lower extremity performance over time. They also showed that early decline in mobility is detectable and may guide strategies for prevention targeted to individuals and populations [22].

1.1.4. SENSOR-BASED MEASURES OF PHYSICAL CAPABILITY

Many tools have been developed to objectively measure physical capability and obtain more detailed information in addition to the simple total time to perform the test. These techniques include photogrammetry, kinematic and kinetic analyses, video motion-capture, electromyography, force plate analysis. These tools employ sophisticated biomechanical methods and produce highly accurate functional parameters for clinical research, however, they are costly, cumbersome, time-consuming, and they require access to specialized equipment and a dedicated laboratory set-up. Furthermore, in-lab measurements of movements may not accurately reflect subjects' functional capability in the daily living environment. This has given rise to the development of wearable sensors, which are small and light, non-invasive and less expensive than the lab-based instruments. They allow to objectively monitor human movements, not only in clinics but also in the free-living home environment. Inertial

Measurement Units (IMUs) contain accelerometers and gyroscopes and have become accessible regarding measurement accuracy, size, cost and energy consumption [23]. IMUs have proven to be a reliable method to monitor a range of different movements, like gait [24], postural sway [25], turnings, and Sit-to-Stand/Stand-to-Sit transitions [26,27]. They allow to extract a high number of task-specific measures, like the complexity of the motor control (19); step length, walking speed, cadence [28,29], coordination index [30], gait regularity, symmetry [31] and smoothness [32]; turnings and Sit-to-Stand/Stand-to-Sit range and smoothness [33,34]. It has been proven that these measures are associated with similar effect sizes to age-related changes in physical performance in middle-aged to older adults [35]. Furthermore, it has been shown that balance and gait represent independent control systems for mobility and not all balance and gait measures deteriorate the same way with age [36]. Inertial sensors have also shown to be appropriate in monitoring daily physical activity (PA) levels. In a recent study, an inertial sensors-based PA classification system developed with older adults as the target population has been presented and validated [37]. Thanks to the diffusion of integrated inertial sensors into objects of daily living like smartphones and smartwatches, continuous activity monitoring will also likely goes beyond clinical outcome assessment to support remote health [38].

1.2. RESEARCH PROJECT AND AIMS

Early detection of people at risk of developing age-related PC decline is crucial for primary prevention. Objective measures of PC can provide a better understanding of the functional decline process with age and hence may become a useful tool for designing preventive and intervention strategies. However, little use is made of these measures as yet in everyday clinical practice. This is probably due to the lack of standardization and the need for normative data and longitudinal data. Furthermore, larger and high-quality trials are needed for validating the sensor-based approach. A high number of sensor-based measures can be derived from the PP tests, which bring redundant information (high covariance among measures) and sometimes their unclear clinical meaning makes the interpretation of the results difficult. It would be advisable to create consensus in the clinical and research community on a minimum, recommended set of PP tests from which extract the sensorbased measures, to standardise these outcome tools, popularise their valuable use and increase comparability between studies [38]. Hence, there is need to reduce the dimension of the set of the sensor-based measures computed, without compromising selectivity. One suggested approach is to group measures into latent factors, using an Exploratory Factor Analysis (EFA) approach. EFA is a multivariate statistical method widely used in the social, health, biological, and, sometimes, physical sciences to describe variability among correlated variables. It enables to identify a smaller number of

empirically defined and statistically independent factors representing distinct domains. EFA is based on the common factor model, which assumes that each observed variable is influenced by underlying common factors and unique factors. Unique factors are related to measurement error and variation in the data. Variables that are highly correlated are likely to be influenced by the same factor, while those that are relatively uncorrelated are likely influenced by different factors [39]. The respective factor loading represents the strength of this relationship, which can be used to mapping the factors into domains with a clear conceptual meaning. The conceptual interpretation of the discovered latent factors could provide a simplified framework to the starting dataset. The so defined latent factors and their clinical interpretation constitute the conceptual model and may be used to transform datasets containing high number of correlated sensor-based measures into health-related relevant domains. Such an approach has been widely adopted to characterize gait of both community-dwelling older adults and people at risk of falling, and affected by Dementia and Parkinson's Disease [40–46]. These studies developed and validated a conceptual gait model from a set of instrumented temporal gait parameters extracted from a computerized walkway with embedded pressure sensors (GaitRiteTM). However, these conceptual gait models make use of only temporal parameters and the omission of measures like step/stride regularity, jerk and RMS acceleration might lead to a loss of useful information. Indeed, as an example, a recent study showed that not all information about impaired PD gait can be captured through measuring spatiotemporal information [47]. Furthermore, these additional measures showed to be related to different heath conditions during dynamic and static balance assessment [48,49]. Such an approach can be used to obtain a model of the older adults' PC and provide a uniform and standard clinical interpretation, which could contribute to facilitate the adoption of the sensor-based assessment in everyday clinical practice.

The main goal of this thesis is the design of a general model for providing an objective and comprehensive functional assessment tool, being able to also explore the relationships among instrumented scores, clinical scores and specific impairments and diseases.

The research project has been carried out in close collaboration with medical doctors, physiotherapists, and patients to obtain an assessment tool usable in the everyday clinical practice, which meets the needs and expectations of clinicians and patients. The objectives of the research project were:

O1.Definition of a standardised functional assessment protocol, based on wearable inertial sensors, to be used for both healthy and pathological subjects; to properly validate existing and novel algorithms and methods for signal processing and feature extraction in both healthy

and pathological people; and to define normative values taking into account the effect of age, gender, weight, and height.

- O2.Reduction of the redundancy of information derived from the large number of features extracted for the raw signals by means of the exploratory factor analysis; to provide a uniform clinical interpretation of single and aggregated features/factors; to verify the association of single and aggregated features/factors with well-established clinical assessment tools for investigating physiological and pathological conditions.
- O3.Computation of summary scores from the proposed methods and models, in order to obtain a model for objective physical capability assessment of both healthy and pathological people.
- 1.3. THESIS OUTLINE

This thesis is structured into six additional chapters. Figure 1.1 summarises the research approach.



Figure 1.1 Flowchart of the research approach

- Chapter 2 compares standard clinical with instrumented measures of physical performance in their ability to distinguish between different levels of functional status in a very healthy cohort of young older adults. It shows that both clinical and instrumented measures, recorded through a smartphone, can discriminate early functional decline in healthy adults aged 61–70 years, supporting the assumption that an early intervention strategy based on the instrumented measures of physical performance is feasible (O1).
- **Chapter 3** firstly, investigates the agreement between standard clinical and sensor-based measures of time. Secondly, describes the influence of age and gender on a set of instrumented PP measures in a large cohort of healthy community dwelling adults. Finally, it describes an EFA approach to find latent structure of the TUG test, suggesting that the instrumented measures of physical performance are a feasible tool for assessing the functional decline in the general population (O1).
- Chapter 4 describes the development process for designing a sensor-based model for PC assessment using an EFA approach. A battery of PP tests was instrumented and a set of sensor-based measures were extracted. The aims of this chapter were i) reduce the redundancy of information derived from the large number of features extracted for the raw signals; ii) provide a uniform clinical interpretation of the new latent variables (domains); iv) verify the association of these new variables with well-established clinical assessment tools for investigating physiological and pathological conditions (O2). In this chapter, the different stages of the conceptual mode development and validation are described.
- **Chapter 5** shows the application of the model to a different cohort of older adults, which also included people with neurological conditions, such as Parkinson's disease and Stroke. It shows also how the model could be adopted in clinical practice (O2 and O3).
- **Chapter 6** describes how the individuals' usual performance can be objectively measured through daily PA monitoring. The association between mean and extreme values of PA and gait characteristics derived from daily living activities and well-established clinical tools were also explored for quantifying motor and cognitive impairments in a cohort of community-dwelling older adults (O3).
- **Chapter 7** discusses the main results and the limitations of the thesis. It also highlights the extension of the work that can be the object of future research.

2. COMPARISON OF STANDARD CLINICAL AND INSTRUMENTED MEASURES OF PHYSICAL PERFORMANCE IN DISCRIMINATING FUNCTIONAL STATUS OF HIGH FUNCTIONING PEOPLE AGED 61-70 YEARS OLD

Some contents of this chapter are taken from: Coni Alice, et al. "Comparison of Standard Clinical and Instrumented Physical Performance Tests in Discriminating Functional Status of High-Functioning People Aged 61–70 Years Old." Sensors 19.3 (2019): 449 [50].

2.1. INTRODUCTION

As discussed before, age-related functional and cognitive decline have negative consequences for quality of life. Early identification of people at risk of functional decline is essential for targeting preventive and/or protective interventions. Questionnaires as the Late-Life Function and Disability Instrument (LLFDI) [51] have shown to be useful in assessing one's ability to carry out activities of daily living. Physical performance is one domain of physical function and it could be objectively measured with sensor-based PP test. Although the standard clinical outcomes of these PP tests are commonly used to assess older people or patient populations, their potential ability to detect slight changes in functional status for an early detection of functional decline is not clear. To investigate the potential of inertial sensors in assessing functional status in young older adults (aged 60–70 years), data from the baseline of the H2020 PreventIT project [52] were analysed. PreventIT [1] is a threearmed feasibility randomised trial including a total of 189 participants, with two behaviour change exercise programmes and a control group. The goal of the PreventIT project is the reduction of the overall risk of functional decline and to empower people to improve their quality of life adopting a healthy and active lifestyle to reduce pressure on caregivers and the health care system. This project targets mobility decline in particular, as it is related to falls, frailty, depression, inactivity and cognitive impairment, and is important for independence in daily life and quality of life.

The aim of this study was to assess whether standard clinical and instrumented measures of PP can distinguish between older adults with a High and Very High Functional Status, stratified by the LLFDI [53].

2.2. Methods

2.2.1. POPULATION

The PreventIT study is a multi-centre trial with three centres in Trondheim (Norway), Amsterdam (The Netherlands), and Stuttgart (Germany). People were invited by a random draw from local registries. Participants were included if they were i) aged between 61-70 years, ii) retired for more than six months, iii) home-dwelling, iv) able to read newspaper or text on smartphone, v) able to walk 500 m without walking aids, vi) without cognitive impairments (Montreal Cognitive Assessment,

MoCA>24 points [54]), and vii) they were excluded if they participated in exercise classes more than once a week or did sport for more than 150 minutes per week.

2.2.2. DEMOGRAPHIC MEASURES

During the assessment, participants filled questionnaires about: age, gender, Body Mass Index (BMI), Physical Activity (PA), hand grip strength (HAND), and cognitive status (Montreal Cognitive Assessment, MoCA).

2.2.3. Outcome

The function component of the Late Life Function and Disability Instrument (LLFDI) was used to measure the functional status of participants. The LLFDI indeed assesses function and disability, assessing the poor ability to perform specific physical tasks encountered in daily routines. The function component evaluates self-reported difficulty to perform 32 activities in daily living consisting of three dimensions: upper extremity, basic lower extremity and advanced lower extremity. Questions are phrased, "How much difficulty do you have doing a particular activity without the help of someone else and without the use of assistive devices?" with a rating scale from 5 to 1 (the higher the scoring category, the less difficulty the person has in doing activities). The overall function raw score is obtained adding the scores of all the 32 items [55]. As no validated cut-off has been described in literature to distinguish between people with different levels of functional status, we dichotomized the scaled scores (ranged 0 to 100) of the function domain of the LLFDI based on the median value to classify the people in our cohort as high (HFS) and very high (VHFS) functional status.

2.2.4. STANDARD CLINICAL PHYSICAL PERFORMANCE TESTS

Participants performed two physical performance tests under two instruction sets given by the assessor: the 30-sec Chair Stands Test (30CST) and the Timed Up and Go test (TUG) Test. During the 30CST, participants started seated and, on the command "go", they stood up and sat down for 30 seconds as quickly as they could, and the number of repetitions was recorded. During the TUG, participants started seated on a chair, on the command "go", they rose from the chair, walked three meters ahead at a comfortable and safe pace, made a 180° turn, walked back to the chair and sat down again. The total number of repetitions performed during the 30CST and the stopwatch-based total time needed to perform the TUG test were recorded by assessors according to the standard clinical protocol.

2.2.5. INSTRUMENTED PHYSICAL PERFORMANCE TESTS

Participants wore a smartphone at the lower back, attached with an elastic belt, while they performed the 30CST and TUG tests. The smartphone-based system used to instrument these two PP tests was

developed within the FARSEEING project [56]. A custom Android application [27] running on smartphones (Galaxy SII or Galaxy SIII, Samsung) was used for recording the following tri-axial inertial signals: Antero-Posterior (AP), Medio-Lateral (ML) and Vertical (V). These signals were then processed using MATLAB [57] to extract a set of instrumented measures [58].

Signals recorded during the 30CST were segmented into two sub-phases: Sit-to-Stand and Stand-to-Sit transitions. The AP acceleration signal and the angular velocity about the ML axis were used to identify postural transitions [33]. Twenty-one instrumented measures were extracted from the 30CST test [33,49,59], including durations, measures of movements' intensity (e.g. Root Mean Square, RMS) and smoothness (e.g. Normalized Jerk Score, NJS [m]) in AP, ML and V direction. The measures were computed for each Stand-to-Sit/Sit-to-Stand transition and then averaged over the Sit-to-Stand/Stand-to-Sit sub-phases (see Table A.3).

The TUG consists of four sub-phases: Sit-to-Walk, Walk, 180Turn, Turn-to-Sit. The AP acceleration and the angular velocity on the ML axis were used to identify postural transitions and the walking phase, and the angular velocity around the V axis was used to identify turns [33]. Walking measures were derived from the AP, ML and V signals, excluding postural transitions and the turning phase, and concatenating the two episodes of straight walk [60]. Twenty eight measures were extracted from the TUG test [28,31,33,49,59,61,62] including durations, intensity and smoothness of each sub-phase, as well as the mean and maximum angular velocity during the turns and the number of steps performed while walking and turning (see Table A.4).

2.3. STATISTICAL ANALYSIS

Statistical analyses were performed in R for Windows version 3.4.3 [63].

Four logistic regression models were fitted and the Areas Under the ROC Curve were compared to assess the performances of 30CST and TUG standard clinical and instrumented outcome measures in distinguishing between HFS and VHFS.

For each test, firstly a univariable logistic regression with the standard clinical measure as input (number of repetitions for 30CST, total time in s for TUG) was fitted. Secondly, a multivariable logistic regression with the instrumented measures was fitted. Then, for each test, the discriminative ability of the resulting models was assessed by comparing the Area Under the Receiver Operating Curve (AUC). We used the DeLong test to assess differences between AUC of the different models [64]. Lastly, a bootstrapping method with backward step-down variable deletion (R function 'validate', package 'rms') was applied to internally validate each model and assess the impact of outliers. The instrumented measures were pre-processed with the same procedure for both 30CST

and TUG. The NJS for all the sub-phases in AP, ML and V direction, which are not normally distributed, were log-transformed and all the instrumented measures were normalized to compare measures by z-scores (using the R function "scale"). The linearity of each instrumented measure was assessed by fitting a restricted cubic spline function (using the R function "rcs" with three knots at 0.1, 0.5, 0.9 quantiles) in the logistic regression model. Usually, in order to avoid overfitting, the assessment of multicollinearity is recommended before fitting the multivariable logistic regression on the dataset. Furthermore, the validity of the multivariable logistic regression model becomes problematic when the ratio of the numbers of subjects per variable inserted in the model is lesser than 10 [65]. We addressed these issues by following the next steps. Firstly, the multicollinearity between instrumented measures was assessed, using the R function "imcdiag". To detect and deal with multicollinearity i) the Variance Inflation Factor (VIF) was computed on the entire dataset; ii) the instrumented measure with highest VIF was selected and removed from the dataset; iii) the VIF was computed on the new subset of measures. The procedure was repeated until no collinearity was found (i.e. all the elements in the VIF vector were below 10). Starting from the obtained subset of instrumented measure, we selected those measures that better discriminate between participants with HFS and VHFS (p-value ≤ 0.15) fitting one univariable logistic regression for each instrumented measure.

The resulting subset of sensor-based measure was entered into a stepwise backward multivariable logistic regression. The instrumented measures with p-value ≤ 0.05 were selected to fit the final model.

At last, a sensitivity analysis was conducted for both the 30CST and TUG tests in order to compare the discriminative ability in distinguishing between HFS and VHFS of the following three models: i) standard clinical model, obtained from the standard clinical measure (30CST number of repetitions or TUG duration); ii) instrumented model, obtained from the selected subset of instrumented measures; and iii) combined model, obtained by including the instrumented 30CST number of repetitions or TUG duration in the instrumented model. The multicollinearity between all the instrumented measures included in the combined model was beforehand assessed.

2.4. Results

Among the participant recruited, 160 (mean age 66.3 \pm 2.4 years, 87 females) strong (HAND 33.41 \pm 11.19 kg), whit a moderate level of declared physical activity (90% declared a PA level \geq 3) performed the two instrumented PP tests (see Table 2.1). The population was divided into two groups: HFS (range [44.33 71.33]) and VHFS (range [72 100]), based on the median value of the LLFDI

score. The between-group demographics reported in Table 2.1 shows that the VHFS group was significantly stronger (HAND) and faster during the PP tests with respect to the HFS group.

Table 2.1 Description of the PreventIT population

	Total population	HFS	VHFS
	N = 160	N = 78	N = 82
Gender, Female	87 (54.38%)	52 (66.67%)	35 (42.68%)
Age, years	66.29 (2.40)	66.13 (2.44)	66.45 (2.37)
Height, cm	170.94 (9.35)	169.32 (9.86)	172.49 (8.63)
Weight, kg	79.49 (15.61)	79.97 (16.35)	79.04 (14.95)
Handgrip strength*, kg	34.41 (11.19)	31.06 (10.75)	37.61 (10.71)
Gait speed*, m/s	2.05 (0.46)	1.82 (0.41)	2.27 (0.40)
30CST* , number of repetitions	13.41 (3.29)	12.36 (3.13)	14.40 (3.14)
TUG duration*, s	8.70 (1.60)	9.25 (1.85)	8.17 (1.10)
PA >=3	144 (90%)	71 (91.03%)	73 (89.02%)
Falls, number >=2	23 (14.38%)	15 (19.23%)	8 (9.76%)
MoCA, points	27.08 (1.85)	27.06 (1.89)	27.09 (1.83)
Medications, number >=4	44 (27.50%)	29 (37.18%)	15 (18.29%)
LLFDI, points, median [range]	72.31 [44.33 100]	65.57 [44.33 71.33]	79.35 [72.31 100]

Values are presented as mean \pm SD or number (%) unless otherwise indicated.

ACRONYMS: 30CST: 30-sec Chair Stand test; HFS: High Functional Status; LLFDI: Late-Life Function and Disability Instrument; MoCA: Montreal Cognitive Assessment; PA: declared physical activity level; TUG: Timed Up and Go test; VHFS: Very High Functional Status. *HFS and VHFS significantly different (p-value<0.01)

Twenty-one and twenty-nine instrumented measures were computed from the 30CST (Table A.3) and TUG (Table A.4) respectively. To avoid multicollinearity, 6 and 4 instrumented measures were excluded from the original dataset of the 30CST and TUG respectively (Tables 2.2 and 2.3).

Table 2.2 Collinearity analysis of the 30CST instrumented measures

	First step		Last step	
	VIF	detection	VIF	detection
Mean Sit-to-Stand RMS A AP	5.79	0	3.30	0
Mean Sit-to-Stand RMS A ML	6.01	0	2.91	0
Mean Sit-to-Stand RMS A V	4.68	0	2.45	0
Mean Sit-to-Stand NJS A AP	20.26	1	6.06	0
Mean Sit-to-Stand NJS A ML	18.54	1	-	-
Mean Sit-to-Stand NJS A V	17.02	1	-	-
Mean Sit-to-Stand RMS G AP	3.28	0	2.85	0
Mean Sit-to-Stand RMS G ML	4.27	0	3.88	0
Mean Stand-to-Sit RMS A AP	7.51	0	2.78	0
Mean Stand-to-Sit RMS A ML	7.31	0	3.16	0
Mean Stand-to-Sit RMS A V	4.14	0	2.09	0
Mean Stand-to-Sit NJS A AP	29.03	1	2.44	0
Mean Stand-to-Sit NJS A ML	27.97	1	-	-
Mean Stand-to-Sit NJS A V	19.68	1	-	-
Mean Stand-to-Sit RMS G AP	4.38	0	3.73	0
Mean Stand-to-Sit RMS G ML	5.34	0	3.86	0
Mean Duration Sit-to-Stand	11.18	1	4.84	0
SD Duration Sit-to-Stand	5.70	0	5.27	0
Mean Duration Stand-to-Sit	17.27	1	-	-
SD Duration Stand-to-Sit	4.26	0	3.77	0
Instrumented number of repetitions	24.75	1	-	-

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; G=Gyroscope; ML: Medio-Lateral; RMS: Root Mean Square; SD: Standard Deviation; NJS: Normalized Jerk Score; V: Vertical; VIF: Variance Inflation Factor

Table 2.3 Collinearity analysis of the TUG instrumented measures

	Firs	t step	Las	tstep			
	VIF	detection	VIF	detection			
Sit-to-Walk Duration	11.44	1	6.20	0			
180Turn Duration	12.11	1	6.90	0			
Turn-to-Sit Turning Duration	9.43	0	9.35	0			
Turn-to-Sit Duration	37.85	1	9.36	0			
Walk Duration	79.06	1	7.67	0			
Sit-to-Walk RMS A AP	2.91	0	2.90	0			
Sit-to-Walk RMS A ML	2.91	0	2.83	0			
Sit-to-Walk RMS A V	18.24	1	2.31	0			
Sit-to-Walk NJS A AP	10.17	1	9.97	0			
Sit-to-Walk NJS A ML	8.11	0	8.02	0			
Sit-to-Walk NJS A V	7.58	0	6.75	0			
Turn-to-Sit RMS A AP	2.77	0	2.36	0			
Turn-to-Sit RMS A ML	4.54	0	2.98	0			
Turn-to-Sit RMS A V	24.83	1	-	-			
Turn-to-Sit NJS A AP	10.57	1	9.08	0			
Turn-to-Sit NJS A ML	12.85	1	-	-			
Turn-to-Sit NJS A V	8.31	0	6.43	0			
180Turn Mean Velocity	8.65	0	8.23	0			
Turn-to-Sit Turning Mean Velocity	9.82	0	9.70	0			
180Turn Maximum Velocity	3.74	0	3.41	0			
Turn-to-Sit Turning Maximum Velocity	6.01	0	5.97	0			
180Turn NJS G V	3.58	0	3.39	0			
Turn-to-Sit Turning NJS G V	4.39	0	4.34	0			
Walk RMS A AP	3.66	0	3.11	0			
Walk RMS A ML	2.71	0	2.52	0			
Walk RMS A V	18.69	1	-	-			
180Turn Number of Steps	2.46	0	2.41	0			
Walk Number of Steps	6.88	0	6.43	0			
Instrumented TUG total duration	132.41	1	-	-			
ACRONYMS: A: Accelerometer: AP: Antero-Posterior: G-Gyroscope: MI · Medio-Lateral: NIS: Normalized Jerk Score: RMS							

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; G=Gyroscope; ML: Medio-Lateral; NJS: Normalized Jerk Score; RMS: Root Mean Square; SD: Standard Deviation; V: Vertical; VIF: Variance Inflation Factor

Discriminative ability of each instrumented measure, expressed as odds ratio (OR) determined by univariate logistic regression, is reported in Tables 2.4 and 2.5. Three and two instrumented measures were selected by the univariable analyses (p-value ≤ 0.15) for the 30CST and TUG respectively. Discriminative ability of the subset of variables, expressed as odds ratio (OR) determined by stepwise backward multivariate logistic regression, is reported in Tables 2.4 and 2.5. Three instrumented measures for the 30CST ("mean Stand-to-Sit G RMS ML", "mean Duration Sit-to-Stand" and "SD Duration Sit-to-Stand") and two for the TUG ("Walk duration", "Last turn maximum velocity") showed a significant discriminative ability (p-value ≤ 0.05).

Table 2.4 Univariable and multivariable analysis of the 30CST instrumented measures

	Univariable logistic regression			Stepwise backward multivariable logistic regression		
	OR	95% CI	p-value	OR	95% CI	p-value
Mean Sit-to-Stand RMS A AP	1.04	[0.76-1.41]	0.820			
Mean Sit-to-Stand RMS A ML	1.22	[0.89-1.68]	0.224			
Mean Sit-to-Stand RMS A V	1.12	[0.82-1.53]	0.473			
Mean Sit-to-Stand NJS A AP ¹	0.80	[0.58-1.09]	0.157			
Mean Sit-to-Stand RMS G AP	1.01	[0.74-1.38]	0.928			
Mean Sit-to-Stand RMS G ML	1.14	[0.83-1.56]	0.413			
Mean Stand-to-Sit RMS A AP	1.03	[0.76-1.40]	0.852			
Mean Stand-to-Sit RMS A ML	1.14	[0.83-1.56]	0.415			
Mean Stand-to-Sit RMS A V	1.12	[0.82-1.53]	0.487			
Mean Stand-to-Sit NJS A AP ¹	0.67	[0.49-0.94]	0.019			
Mean Stand-to-Sit RMS G AP	0.90	[0.66-1.23]	0.503			
Mean Stand-to-Sit RMS G ML	0.78	[0.57-1.08]	0.131	0.71	[0.49 0.98]	0.045
Mean Duration Sit-to-Stand	0.59	[0.41-0.84]	0.004	0.69	[0.48 0.98]	0.041
SD Duration Sit-to-Stand	0.65	[0.47-0.92]	0.014	0.62	[0.41 0.89]	0.014
SD Duration Stand-to-Sit	0.82	[0.60-1.13]	0.226			

Bolded p-values indicate statistically significant univariable and multivariable discriminative ability (≤ 0.15 and ≤ 0.05 respectively).

ACRONYMS: A: accelerometer; AP: Antero-Posterior; G: gyroscope; NJS: Normalized Jerk Score; ML: Medio-Lateral; RMS: Root Mean Square; SD: Standard Deviation; V: Vertical. ¹log transformed feature

Table 2.5 Univariable and multivariable analysis of the TUG instrumented measures

	Univariable			Stepwise backward multivariable logistic regression		
	OR	95% CI	p-value	OR	95% CI	p-value
Sit-to-Walk Duration	0.96	[0.70-1.31]	0.786			
180Turn Duration	0.80	[0.58-1.11]	0.185			
Turn-to-Sit Turning Duration	0.62	[0.44-0.88]	0.008			
Turn-to-Sit Duration	0.70	[0.50-0.97]	0.032			
Walk Duration	0.54	[0.36-0.79]	0.002	0.59	[0.38-0.86]	0.010
Sit-to-Walk RMS A AP	1.20	[0.87-1.65]	0.258			
Sit-to-Walk RMS A ML	1.04	[0.76-1.43]	0.787			
Sit-to-Walk RMS A V	1.89	[0.69-5.18]	0.213			
Sit-to-Walk NJS A AP ¹	1.18	[0.86-1.63]	0.303			
Sit-to-Walk NJS A ML ¹	1.16	[0.84-1.60]	0.364			
Sit-to-Walk NJS A V ¹	1.28	[0.90-1.82]	0.173			
Turn-to-Sit RMS A AP	0.96	[0.71-1.31]	0.805			
Turn-to-Sit RMS A ML	1.25	[0.91-1.72]	0.164			
Turn-to-Sit NJS A AP1	0.94	[0.69-1.28]	0.703			
Turn-to-Sit NJS A V ¹	0.82	[0.60-1.13]	0.223			
180Turn Mean Velocity	1.18	[0.86-1.62]	0.301			
Turn-to-Sit Turning Mean Velocity	1.60	[1.14-2.25]	0.007			
180Turn Maximum Velocity	1.38	[1.00-1.91]	0.051			
Turn-to-Sit Turning Maximum Velocity	1.66	[1.17-2.35]	0.004	1.50	[1.05-2.18]	0.031
180Turn NJS G V ¹	0.87	[0.63-1.19]	0.386			
Turn-to-Sit Turning NJS G V1	0.76	[0.55-1.06]	0.104			
Walk RMS A AP	1.35	[0.95-1.92]	0.098			
Walk RMS A ML	1.26	[0.92-1.74]	0.155			
180Turn Number of Steps	0.95	[0.70-1.31]	0.764			
Walk Number of Steps	0.58	[0.40-0.85]	0.005			

Bolded p-values indicate statistically significant univariable and multivariable discriminative ability (≤ 0.15 and ≤ 0.05 respectively).

ACRONYMS: A: accelerometer; AP: Antero-Posterior; G: gyroscope; ML: Medio-Lateral; NJS: Normalized Angular Jerk Score; RMS: Root mean square; V: Vertical; ¹log transformed feature.

The internal validation of each of the models was assessed by applying a bootstrapping method with backward step-down variable deletion (Table 2.6). The original AUC and optimism-corrected AUCs were in the same range (with differences less than 0.04), indicating confirmation of the internal validity of the models.

	30C	ST	TUG		
	AUC original	AUC corrected	AUC original	AUC corrected	
Standard clinical	0.682	0.684	0.684	0.685	
Instrumented	0.680	0.654	0.650	0.627	
Combined	0.661	0.630	0.684	0.670	

Discriminative ability of the six fitted models is presented in Figure 2.1. Standard clinical, instrumented and combined models of the 30CST showed moderate discriminative ability with an AUC of 0.68 (95%CI 0.60-0.76) and 0.69 (95%CI 0.61-0.77) respectively, p-values 0.97 (standard clinical-instrumented), 0.74 (instrumented-combined), 0.48(standard clinical-combined). The discriminative ability of standard clinical, instrumented and combined models of the TUG was similar: AUC of 0.68 (95%CI 0.60-0.77), 0.65 (95%CI 0.56-0.73) and 0.69 (95%CI 0.60-0.77) respectively, p-values 0.26 (standard clinical-instrumented), 0.94 (instrumented-combined), 0.12 (standard clinical-combined).



Figure 2.1 Sensitivity analysis: discriminative ability (AUC and DeLong test) of standard clinical, instrumented and combined models of the 30CST and TUG test [50]

		AUC	95% CI	<i>p</i> -Value of the DeLong test	,
30CST	Standard clinical	0.68	[0.60-0.76]	Standard clinical—Instrumented	0.97
	Instrumented	0.68	[0.60-0.76]	Instrumented—Combined	0.74
	Combined	0.69	[0.61–0.77]	Standard clinical—Combined	0.48
TUG	Standard clinical	0.68	[0.60-0.77]	Standard clinical—Instrumented	0.26
	Instrumented	0.65	[0.56-0.73]	Instrumented—Combined	0.94
	Combined	0.69	[0.60-0.77]	Standard clinical—Combined	0.12

Table 2.7 Sensitivity analysis

2.5. DISCUSSION

This study aimed to compare the discriminative ability of standard clinical with instrumented measures of physical performance in distinguishing between High and Very High Functional Status (HFS, VHFS) in a relatively fit and healthy population of community-dwelling adults aged 61-70 years. The 30CST number of repetitions and TUG duration (the standard clinical as well as the

instrumented) showed moderate discriminative ability. These two types of measurement showed similar performances in the univariable logistic regressions, suggesting that the prediction of minor functional status differences is possible in our fit and healthy population either by the standard clinical protocol or the instrumented measures. Instrumented physical performance tests allow us to collect a number of additional measures beyond the total 30CST repetition or TUG duration. These measures could have the potential to add more detailed information about the participants' functional status.

Three of the 30CST instrumented measures were entered as input to fit the final model "mean Duration Sit-to-Stand", "SD Duration Sit-to-Stand" and "mean Stand-to-Sit G RMS ML". The 30CST, by definition, is a measure of lower limbs strength and endurance. The time needed to stand up from a sitting position represents the dynamic balance and the lower limbs strength. It is an index of the power generated from muscles to stand up against gravity. The shorter the duration, the higher the strength. The standard deviation (SD) of the duration is a measure of variability, therefore higher the SD, the higher is the difference between the duration of this task among the repetitions. Indeed, high SD of the standing duration could be related to fatigue and weakness. The Stand-to-Sit G RMS in ML direction is a measure of the intensity of the forward trunk rotation while sitting. The sitting phase requires dynamic balance and lower limbs strength to control the lowering of the body to the seated position. A more intense trunk rotation during the Stand-to-Sit phase could be related to less muscle strength, as demonstrated in a recent study for the Sit-to-Stand phase [66].

The final model of the TUG included two instrumented measures: "Walk duration" and "Last turn maximum velocity". The duration of the straight walk is a predictor of health status in old age [22]. Indeed, gait speed is traditionally used as a predictor for clinical outcomes, e.g. an older adult with gait speed lower than 1 m/s was considered at risk of falling. The turn before sitting involves cognition, motor planning and visual capacities in preparation for sitting. Difficulty turning is associated with mild cognitive impairment in old age [67]. The De-Long test (Table 2.7) was not significant, suggesting that these two types of measurement have a similar discriminative ability. Yet, in contrast to the conventional clinical measures, with the instrumented measures it is possible to objectively measure the participants' capacities while performing specific tasks, like walking, turning or sitting. Furthermore, the discriminative ability increased, albeit not significantly, when the conventional clinical and instrumented measures have been combined.

The first limitation of this study is the homogeneous population, characterized by a very skewed distribution of the LLFDI scores, which may have led to a decrease in the discriminative ability. The second limitation was the lack of literature for validated cut-off for discriminating between different LLFDI levels. A valid cut-off score can be helpful to identify people at risk of developing functional decline. This aspect might be the subject of future studies. Lastly, the ratio between the sample size

and the number of instrumented measures required the performance of a feature selection, before fitting the stepwise backward logistic regression and this might have led to a loss of information. Despite these limitations, instrumented 30CST and TUG measures proofed to be comparable to the standard clinical measures, with moderate discriminative ability, in detecting slight differences of LLFDI even in this homogeneous population. In summary, high power of the lower limbs muscle, low duration and variability of the Sit-to-Stand transition, high gait speed and good ability in performing the turn before sitting, have shown a moderate ability in discriminating between HFS and VHFS. It is reasonable to assume that the detection of differences in the functional status would also be possible in less fit and homogeneous population of older adults. However, procedures for the reduction of the high number and redundancy of instrumented measures and the influence of age, gender and biometric measures on the instrumented measures need to be investigated.

2.6. CONCLUSIONS

In a relatively fit and healthy population of adults aged 61-70 years, standard clinical and instrumented measures distinguish between HFS and VHFS, with moderate discriminative ability. This result supports the hypothesis that an early identification of risk of the age-related functional decline can be achieved. This corroborates the assumption that an early intervention strategy based on the instrumented measures of physical performance is feasible.

3. THE INCHIANTI-FARSEEING PROJECT

Some contents of this chapter are taken from: Coni Alice, et al. "Influence of age and gender on sensor-based functional measures: A factor analysis approach" [68].

3.1. INTRODUCTION

The decline of gait stability and postural control with age is probably due to the age-related loss of function of the musculoskeletal, cardiovascular, respiratory, and nervous systems and the reduction in the ability to detect and process proprioceptive and sensorial information. To understand these mechanisms, the InCHIANTI study (Invecchiare nel Chianti, ageing in the Chianti area), a longitudinal study of the factors contributing to the decline of mobility in late life, was designed by the Laboratory of Clinical Epidemiology of the Italian National Research Council on Aging, (INRCA, Florence, Italy) in a partnership with the local administrators and the primary care physicians of Greve in Chianti and Bagno a Ripoli, two small towns in the countryside of the Tuscany area where Chianti wine is produced. The data collection started in September 1998 and was completed in March 2000. The main goals of this study were: i) understand the risk factors influencing the loss of walking ability; ii) identify physiologic subsystems critical for walking; and iii) identify measures that clinicians can use to understand the causes of walking difficulties in older adults. The study protocol, selection of participants and information collected are presented elsewhere [69].

As previously described, standard clinical outcomes of the PP tests (i.e. 7MW, CST and TUG total duration) recorded with stopwatches (SW) are extensively used as a screening tool in older age. Sensor-based measures computed from the PP tests might be sensitive markers of age-related changes in PC providing possible insights into underlying determinants [22,35]. In a sensor-based assessment, it is possible to provide automatic algorithms for an objective and comprehensive picture of the person's PC which goes well beyond a simple temporal measure obtained with a stopwatch. Indeed, with the instrumented version of the PP tests it is possible to automatically extract the standard clinical outcome and other additional more detailed information. To deeper investigate these aspects, the PP tests were instrumented by means of a smartphone (SP) starting from the 4th wave of the InCHIANTI study (Follow up 4, 2013-2015).

In Chapter 2 it was shown that in a relatively fit and healthy population of adults aged 61-70 years, standard clinical and sensor-based measures of PP are useful for an early identification of risk of agerelated functional decline. A recent work showed that sensor-based measures of balance and gait are affected by age in a healthy community-dwelling cohort [36]. Thus, further investigation of the influence of age, gender and biometric measures on these measures is needed. In this section of the thesis, the agreement between standard clinical and sensor-based measures of time was firstly investigated, then the functional decline associated with ageing and gender-related differences were explored in a large group of community-dwelling persons.

3.2. Methods

The assessment provides for the collection of i) several health-related measures used to assess the participants' functional profile, inertial signals collected from ii) a battery of PP tests and iii) long-term PA monitoring at home. Sensor-based PP tests included the assessment of postural sway in Quiet Standing (QS), the 7-meter Walk test (7MW), the 5-times Repeated Chair Stand test (CST), and the Timed Up and Go test (TUG). Methods used for task segmentation and task-specific measures computation are based on state-of-the-art methods to characterize postural sway [25,70], walking [28,31], postural transitions [33,49,59] and turnings [61,62]. The time taken to complete the 7MW, CST and TUG tests was also recorded with a stopwatch following the standard clinical protocol. The daily PA was also recorded through a custom Android application designed to provide measures representative of the participants' motor profile. PA measures included the percentage of sedentary, active, and walking time, the duration and intensity (METs) of the activities, as well as the gait and turning characteristics. The algorithms used for the signal processing and instrumented measures computation are part of the system developed within the FARSEEING project [71].

3.2.1. POPULATION

Four hundred community-dwelling participants (213 females), aged (71.95 \pm 15.86, range 35-100 years old) were recruited from the fourth wave of the InCHIANTI cohort study (Figure 3.1). Participants performed the battery of PP tests wearing a smartphone (SP) on the lower back (L5) by means of an elastic case waist belt.



Figure 3.1 Distribution of the participants assessed in the 4th wave of the InCHIANTI cohort study.
3.2.2. HEALTH-RELATED MEASURES

The health-related measures collected during the assessment included the Mini-Mental State Examination (MMSE, measure of the participant's cognitive status, range from 0 to 30), Instrumental Activities of Daily Living [72] (IADL, i.e. the number of instrumental activities in which the person requires help, e.g. preparing meals, performing housework, getting to places outside of walking distance, managing medications, etc., range from 0 to 8), Center for Epidemiologic Studies Depression Scale [73] (CES-D, a questionnaire used to assess depressive symptoms range from 0 to 60), Physical Activity [74] (PA, declared level of physical activity assessed through a questionnaire, range from 1 to 7), the number of falls in the last year declared during the assessment (FALLN), Hand-Grip strength test [75] (HAND, kg stronger hand), the lower extremity muscle power measured using the Nottingham leg extensor Power Rig [76] (PWR, watt), the Trail Making Test A [77] (TMTA, a neuropsychological test that assesses various cognitive abilities, including visual-conceptual, visuospatial, and visual-motor tracking, seconds) and the Short Physical Performance Battery, a measure of mobility function [13] (SPPB, range from 0 to 12).

3.2.3. PHYSICAL PERFORMANCE TESTS

QS: participants stand for 30 seconds with their arms at their side, feet hip-width apart, wearing shoes, with their eyes closed [21]. The assessors evaluate the participants' ability to perform the test; the standard clinical outcome is dichotomous (i.e. able/not able).

7MW: participants walk 7 meters at a comfortable and safe pace. The start and stop locations are marked on the floor [69]. The standard clinical outcome of this test is the total time recorded with a stopwatch. Older persons with gait speed, calculated as 7 meters divided for the total duration of the test, slower than 1 m/s are usually considered at high risk of adverse health outcomes [78].

CST: participants start seated on a chair with arms folded across the chest and with their back against the chair's backrest. On the command "go", they stand up and sit down 5 times as quickly as they can [79]. The conventional outcome is the total time taken to perform the test, recorded with a stopwatch.

TUG: participants start seated on a chair with their back against the chair's backrest. On the command "go", they rise from the chair, walk 3 meters ahead at a comfortable and safe pace, turn around a coloured cone on the floor, walk back to the chair and sit down again [80]. The conventional outcome is the total duration of the tests, recorded with a stopwatch. Older adults who took 13.5 seconds or longer to perform the TUG are classified with high risk for falls [81].

3.2.4. STATISTICAL ANALYSIS

Bland-Altman plots were used to investigate the agreement between standard clinical and sensorbased measures of time. Polynomial curve fitting was used to investigate the influence of age on the sensor-based measures computed from the battery of PP tests. t-Test was performed to investigate gender-related differences. All the analyses were performed using MATLAB [57].

3.3. Results

3.3.1. SENSOR-BASED PHYSICAL PERFORMANCE MEASURES

QS: in total, 23 sensor-based measures were extracted from i) the acceleration in ML and AP directions, including measures in the time and frequency domains, and ii) the estimated displacement of the body centre of mass (13), computed in the time domain to quantify the amount and direction of sway (Table A.1).

7MW: in total, 19 sensor-based measures were extracted from the acceleration in ML, AP and V direction to describe temporal gait parameters and measures of smoothness, regularity, and coordination (15,18) (Table A.2).

CST: this test was segmented into Sit-to-Stand and Stand-to-Sit transitions [26]. The AP acceleration and the angular velocity about the ML axis are used to identify postural transitions [33]. Overall, 31 task-specific sensor-based measures are extracted from acceleration and angular velocity in AP, ML and V direction to quantify mean values and standard deviations across repetitions of relevant parameters of the two sub-phases (Table A.3).

TUG: this test consists of four sub-phases: Sit-to-Walk, Walk, 180Turn, Turn-to-Sit. Overall, 38 task-specific sensor-based measures are extracted, including measures of gait, turning and postural transitions (Table A.4).

3.3.2. ANALYSIS OF AGREEMENT

The Bland-Altman plots (Figure 3.2) compare the SP to the SW in timing the 7MW, CST and TUG tests. The red lines represent the mean value of the differences between measures (SP vs. SW) and the blue lines represent the limits of agreement between the two measures. Limits of agreement between the SP- and SW-based durations of 7MW, CST and TUG were [-0.46 3.08] s and [-0.13 5.09] s and [-0.68 3.04] s, respectively.



Figure 3.2 Bland-Altman plots comparing the difference between the sensor-based measures and the stopwatch measures for the total duration (seconds) of the 7-meter Walk test (a), 5-times Repeated Chair Stand test (b) and Timed Up and Go test (c). The red lines represent the mean value of the differences between measures (sensor-based vs. stopwatch) and the blue lines represent the limits of agreement (±1.96 standard deviations).

3.3.3. INFLUENCE OF AGE AND GENDER ON SENSOR-BASED PHYSICAL PERFORMANCE MEASURES

Figures 3.3, 3.4, 3.5 and 3.6 show the trend with age of a representative subset of the sensor-based measures computed from the QS, 7MW, CST and TUG tests respectively. Black lines represent the general population, pink and blue lines represent females and males respectively. Eight age groups (ranging from 35 to 100 years) are reported in the x-axis. For each age group, the filled circles represent the median value and the dotted lines represent the 10th and 90th percentile. The green dots represent significant gender differences (p-value<0.05).



Figure 3.3 Trend with age of the sensor-based measures computed from the QS test



Figure 3.4 Trend with age of the sensor-based measures computed from the 7MW test



Figure 3.5 Trend with age of the sensor-based measures computed from the CST test



Figure 3.6 Trend with age of the sensor-based measures computed from the TUG test

3.4. DISCUSSION

3.4.1. ANALYSIS OF AGREEMENT

The Bland-Altman plots reported in Figure 3.2, show the analysis of agreement between standard clinical (i.e. SW-based) and SP-based 7MW, CST and TUG tests. The SP-based overestimated the duration of the tests determined by the SW during 7MW, CST and TUG. The visual inspection of signals recorded by means of SPs suggested that the values out of the limits of agreement were due to human errors. The positive bias between SPs and SW could be due to the accuracy of the operators to press the start and stop button at the beginning and the end of the participants' movement. The algorithm running on the SPs are more accurate than SW in the detection of the beginning and end of the movements and hence in timing the test. In conclusion, SPs agreed sufficiently with SW in timing the 7MW, CST and TUG tests.

3.4.2. INFLUENCE OF AGE AND GENDER ON SENSOR-BASED PHYSICAL PERFORMANCE MEASURES

Among all the possible features that can be extracted from a wearable inertial sensor, features that have been already clinically investigated in the literature, and that showed their reliability and validity, were computed from the instrumented PP tests. Figure 3.3.a shows the trend with age of the sensor-based features computed from the QS test. The trend appears flat until 75 years, then the abilities to maintain the static balance clearly worsen. In general, there is no significant gender difference in younger age. The differences became more pronounced when the performances start to decrease, in accordance to the findings of Riva et al., which showed a significant difference between women and men in the older subjects (75–84 years), as a consequence of less effective proprioceptive control [82].

Figure 3.3.b shows the trend with age of the sensor-based features computed from the 7MW test. Total duration, Cadence and coordination (Phase Coordination Index, PCI) showed a decline after plateau. The linear decline starts above 75 years; women tend to have a lower speed and it might be due to the lower mean height. Cadence (number of steps per minute) increases on equal distance walked meaning that steps are shorter, and the higher PCI indicates a more asymmetric walk. RMS in AP, ML and V directions showed a linear deterioration with age. These results are consistent with the results reported in two recent studies, demonstrating the decline of walking speed and other gait measures during time [22,36].

Figure 3.3.c shows the trend with age of the sensor-based features computed from the CST test. The total time required to perform the test can be considered as an index of lower limbs strength, high values are associated with loss of functional capacity and muscle strength. Women tend to have lower Range and RMS values (particularly above 75), but there are no substantial gender-related differences in the total duration of the test. Range and RMS in V direction are associated with the muscular strength of the lower limbs. Hence, women tend to have lower values with respect to men. Low values of these parameters could be associated with frailty, sarcopenia, and pathological conditions. Compensatory strategies may help women to overcome the poorer lower limbs muscle strength and complete the test with a similar time with respect to men.

Figure 3.3.d shows the trend with age of the sensor-based features computed from the TUG test. The TUG total duration is widely clinically used to assess the older adults' health status. As we expected, measures of time (Total/sub-phases durations) worsen with age, indicating the progressive loss of functional capacities. As in the CST test, the RMS in V direction of the Sit-to-Walk decrease with age. The intensity of the movements while standing can be related to the muscle strength needed to lift up the body weight, and to the motor planning for the gait initiation. Figure 3.3 also shows the increased difficulties of turns (increased duration and NJS). The increased difficulties in performing this complex task may reflect the reduced physical and cognitive function.

3.5. CONCLUSIONS

The agreement between standard clinical and sensor-based measures of time was firstly investigated. SPs agreed sufficiently with SW in timing the 7MW, CST and TUG tests, suggesting that sensor-based measures can provide a better understanding of the functional decline process with age and hence becoming a useful tool for designing intervention strategies. Thus, SPs can substitute the SW in timing the tests, giving the possibility to compute a high number of reliable measures from the inertial signals in addition to this conventional outcome. However, the added value of the additional information obtained from wearable sensors needs further investigations.

Many sensor-based measures extracted from the four PP tests exhibited a significant association with age. As expected, speed/time related features clearly worsen with aging, but many other sensor-based measures showed a significant decrease: postural control and stability, coordination of walking, cadence, weight shift ability, worsen with ageing as well as features which can be related to the muscle weakness and dynamic balance.

This preliminary study provides evidence that a sensor-based assessment can be a feasible and effective tool for assessing the functional decline in the general population. Standardization is important in order to remove, as far as possible, the effect of confounders. These results highlight the

importance of considering the influence of age, gender and other variables, like body composition (weight and height) in studies that make use of sensor-based PP measures.

3.6. THE INSTRUMENTED TIMED UP AND GO TEST: AN EXPLORATORY FACTOR ANALYSIS APPROACH

3.6.1. BACKGROUND AND AIM

From a motor point of view, after the age of 50, approximately 1–2% of muscle mass is lost per year. The loss in body mass density, which is related to muscle weakness, is greater in women compared to men aged 60 years and older [83]. Ageing implies not only a loss in musculoskeletal functioning but also a decline in vision, reaction time, peripheral and vestibular sensations: all of which can reduce upper body stability [84]. Among the PP tests, the Timed Up and Go (TUG) is one of the most widely used, since it allows to assess balance, locomotion, and the ability to turn in the elderly. Instrumenting the TUG with inertial sensors enables the computation of several task-specific measures, which may enrich the conventional clinical outcome. The purpose of this study was to investigate the functional decline associated with ageing by means of a factor analysis, in order to classify domains of an instrumented TUG in a group of community-dwelling elderly people. Gender-related differences were also investigated.

3.6.2. Methods

3.6.2.1. POPULATION

A subsample of the InCHIANTI cohort study, 239 community-dwelling elderly persons (128 females, 80.85 ± 6.67 years old, range 65-93), was assessed. Participants performed a TUG test instrumented by means of a waist-worn smartphone.

3.6.2.2. INSTRUMENTED TUG

The Android smartphone application used for managing the embedded inertial sensors (tri-axial accelerometer and gyroscope) is an outcome of the FARSEEING project [71]. Samsung Galaxy SII and SIII were used as sensing units. Signal processing and features extraction algorithms were implemented in MATLAB [57]. The TUG was segmented into four sub-phases: Sit-to-Walk, Walk, 180Turn, and Turn-to-Sit and the sensor-based features were computed for each sub-phase as already described in section 3.3.1.

3.6.2.3. STATISTICAL ANALYSIS

A second order polynomial curve fitting with respect to age was applied to the extracted features. Subjects with one or more features outside the 99.9% confidence interval were excluded from the analysis in order to remove outliers due to performance errors and/or physical impairments.

Factor analysis was performed using R for Windows, version 3.4.3 [63] in order to reduce the large number of variables in the dataset and for underlining the structure in the relationships between features. Varimax rotation was used to derive orthogonal factor scores. Sensor-based measures with factor loading higher than 0.5 were considered relevant. The number of factors to retain was selected using the scree plot. Pearson's Correlation analysis was used for investigating the association between latent factors and age. The sample was divided into six age groups spanning 5 years (from [65-69] to [90-95]). A univariate Generalized Linear Model (GLM) was used to test the effects of the age group and the gender. SPSS [85] was used for GLM with age groups as fixed effects and gender as a covariate.

3.6.3. RESULTS

The final sample included 214 elderly persons (115 females, 80.77 ± 6.75 years old, range 65-93) since 25 outliers were identified. Characteristics of the age groups are reported in Table 3.1. Factor Analysis grouped 35 out of 38 features (Table 3.1) into six factors, accounting for 70% of the total variance. Taking into account the features in each group the factors were labelled as follows (Table 3.1): "Global Fitness", "Turning Ability", "Smoothness of the Sit-to-Walk", "AP Dynamics of the trunk during postural transitions", "ML Weight Shift during postural transitions", "Smoothness of the Turn-to-Sit". Correlation with age, multiple comparisons among age groups, and GLM results are reported in Table 3.1. Significant correlations were found between age and "Global Fitness", "Turning Ability", and "AP Dynamics of the trunk during postural transitions" (Figure 3.8).



A) Predicted values for the factor 1 labelled as "Global Fitness".

B) Predicted values for the factor 2 labelled as "Turning Ability".

C) Predicted values for the factor 4 labelled as "Antero-Posterior Trunk Dynamics during Postural Transitions".

 $\frac{65}{65}$ $\frac{70}{70}$ $\frac{75}{70}$ $\frac{80}{75}$ $\frac{85}{80}$ $\frac{90}{95}$ $\frac{95}{90}$ Figure 3.7 Dots represent the predicted values of the factors. Thick line represents the second order polynomial curve fitting of the factor with age. Boxplots show the distribution of the values in the six age groups defined in Table 3.1 [68]

Table 3.1 Fa	ctor analysis o	f the instrumer	nted TUG feature	s and statistical	analysis

		Total Duration TtS Duration Gait Duration Range V Acc. StW Peak velocity 180T Peak Velocity TtS N. of Steps Range AP Acc Gait Range ML Acc Gait Range V Acc Gait RMS AP Acc Gait RMS ML Acc Gait	Duration 180T Duration TtS Mean Velocity 180T Mean Velocity TtS NJS 180T NJS TtS N. of Steps 180T	StW Duration NJS AP Acc StW NJS ML Acc StW NJS V Acc StW	Range AP Acc StW RMS AP Acc StW Range AP Acc TtS RMS AP Acc TtS	Range ML Acc StW RMS ML Acc StW Range ML Acc TtS RMS ML Acc TtS	NJS AP Acc TtS NJS ML Acc TtS NJS V Acc TtS
Factors		Global Fitness	Turning Ability	Sit-to-Walk Smoothness	AP Trunk Dynamics during Postural Transitions	ML Weight Shift during Postural Transitions	Turn-to-Sit Smoothness
Explained Va	ariance	21%	16%	9%	9%	8%	8%
Cumulative V	/ariance	21%	37%	46%	55%	63%	71%
		General	LISED LINEAR MODE	ELS AND CORRELATIO	N ANALYSIS (p value))	
Age Group *	Gender	0.522	0.002	0.541	0.410	0.337	0.376
Age Group		0.870	0.003	0.752	0.493	0.440	0.402
Gender		0.007	0.494	0.351	0.307	0.618	0.003
Correlation w	vith Age	< 0.001	< 0.001	0.107	0.011	0.490	0.589
		Mu	ULTIPLE COMPARISO	ONS BETWEEN AGE GI	ROUPS (p value)		
Age Group	Vs AG 2	0.059	0.504	0.487	0.660	0.988	0.772
1	Vs AG 3	0.002	0.251	0.420	0.405	0.636	0.657
[65-69]	Vs AG 4	< 0.001	0.152	0.932	0.088	0.636	0.997
N = 23	Vs AG 5	<0.001	< 0.001	0.226	0.083	0.586	0.993
15 F.	Vs AG 6	<0.001	<0.001	0.210	0.007	0.994	0.957
Age Group	Vs AG 1	0.059	0.504	0.487	0.660	0.988	0.772
2	Vs AG 3	0.311	0.088	0.964	0.746	0.655	0.488
[70-74]	Vs AG 4	0.007	0.041	0.361	0.340	0.668	0.729
N = 16	Vs AG 5	<0.001	< 0.001	0.063	0.299	0.641	0.748
10 F.	Vs AG 6	<0.001	< 0.001	0.073	0.036	0.995	0.831
Age Group	Vs AG 1	0.002	0.251	0.420	0.405	0.636	0.657
3	Vs AG 2	0.311	0.088	0.964	0.746	0.655	0.488
[75-79]	Vs AG 4	0.088	0.977	0.271	0.524	0.897	0.573
N = 22	Vs AG 5	0.001	0.026	0.033	0.453	0.276	0.599
14 F.	Vs AG 6	<0.001	0.005	0.050	0.053	0.667	0.652
Age Group	Vs AG I	<0.001	0.152	0.932	0.088	0.636	0.997
4	Vs AG 2	0.007	0.041	0.361	0.340	0.668	0.729
[80-84]	VS AG 3	0.088	0.977	0.271	0.524	0.897	0.573
N = 90	Vs AG 5	0.017	0.001	0.104	0.815	0.159	0.994
43 F.	VS AG 6	<0.001	0.001	0.154	0.074	0.084	0.951
Age Group	VS AG 1	<0.001	<0.001	0.220	0.085	0.580	0.995
ر 100_83]	VSAU 2 VsAU 2	<0.001 0.001	0.001	0.005	0.299	0.041	0.748
N = A7	VSAU 3	0.001	0.020	0.104	0.455	0.270	0.099/
27 F	VSAC 4	0.017	0.219	0.104	0.013	0.139	0.958
Age Group	Vs AG 1	<0.017	<0.001	0.210	0.122	0.994	0.957
6	Vs AG 2	< 0.001	<0.001	0.073	0.036	0.995	0.831
[90-95]	Vs AG 3	< 0.001	0.005	0.075	0.053	0.667	0.652
N = 16	Vs AG 4	< 0.001	0.005	0.154	0.074	0.684	0.951
6 F.	Vs AG 5	0.019	0.219	0.711	0.122	0.645	0.958
ACRONYM	S · M · Media	-I steral: AP: Anter	Dostarior: V. Varti	cal: Ve AG: Versue A	an Group: StW: Sit to	Walls TtS: Turn to	Sit: 180T.

180Turn; RMS: Root Mean Square; Acc: Acceleration; N.: Number; F.: females; NJS: Normalised Jerk Score

3.6.4. DISCUSSION

We aimed to investigate if an EFA of the instrumented TUG test is a suitable tool for the detection of the age-related functional decline. Gender-related differences were also investigated. A significant number of features can be derived from the instrumented TUG. EFA grouped these features based on the shared information. The so obtained independent factors were then interpreted and labelled based on their clinical meaning. The influence of age and gender on the factors are reported in Table 3.1 and shown in Figure 3.4. As expected, the "Global Fitness" decreases with age. Although the effect of the age group is not significant, there is a significant correlation with age. It is clear, looking at the multiple comparisons, that the decrease of the "Global Fitness" is significant between subsequent age groups. The effect of gender is also significant, meaning that the decline is different between women and men. The total duration of the TUG, the standard clinical outcome of the test, is included in the "Global Fitness" factor, which is coherent with the usual interpretation of this variable. The "Turning Ability" also declines with ageing mainly above 80 years old (Figure 3.4) as also confirmed by the multiple comparisons. The ability to turn is essential for daily living activities, since almost every task performed during the day requires some amount of turning. The trend of this factor confirms how its contribution significantly influences the functional decline. The significant interaction between gender and age group suggests that the decline of the "Turning Ability" is different between women and men. The "AP Trunk Dynamics during Postural Transitions" is significantly correlated with age (Figure 3.4) meaning that the AP trunk dynamics decreases with ageing with a relatively slow trend and no gender differences. The "Turn-to-Sit Smoothness" is significantly different between males and females with a generally higher smoothness in women with respect to men. The final two factors, the "Sit-to-Walk Smoothness" and the "ML Weight Shift during Postural Transitions" show neither age nor gender-related differences and could be interesting candidates for identifying frailty, motor impairment, and associations with the fall risk [86].

3.6.5. CONCLUSIONS

A TUG test, instrumented by means of a consumer electronic device like a smartphone, proves to be a suitable testing solution for quantitative movement analysis. A significant number of features can be derived from the signals of the embedded inertial sensors and those features can be grouped in factors with a clear clinical value allowing to investigate several mobility skills at once, well beyond the total duration, which is the only outcome of the clinical TUG. Statistical analysis provides evidence that a sensor-based assessment is a feasible and effective tool for assessing the functional decline in the general population. The reduction of the dimension of the dataset of sensor-measures extracted, without the loss of useful information can be achieved by means of Factor Analysis. The factors obtained might allow us to investigate several mobility skills, well beyond the standard clinical outcome of the test. The effect of body composition, cognition and polypharmacy on the sensor-based measures computed from the PP tests should also be investigated.

4. A SENSOR-BASED CONCEPTUAL MODEL FOR PHYSICAL CAPABILITY ASSESSMENT

Some contents of this chapter are taken from: Coni Alice, et al. "Factor Analysis model of the instrumented Timed Up and Go test for physical capability assessment" [87] Coni Alice, et al. "A Sensor-Based Conceptual Model for Physical Capability Assessment" [Submitted to sensors]

As previously described, EFA allows to discover the latent structure of the starting dataset, computing a few new variables called factors. It was previously shown how it could be applied to the instrumented TUG-. The underlined latent factors showed to be indicative of several mobility skills and to have the potential to describe the age-related functional decline. The same principle can be applied to the entire battery of sensor-based PP tests to obtain a general model for the objective PC assessment of older adults.

4.1. DEVELOPMENT OF THE CONCEPTUAL MODEL

4.1.1. POPULATION AND METHODS

A subsample of the InCHIANTI cohort study [2] was assessed within the framework of the EU FARSEEING project [71]. Participants were subjected to a battery of four PP tests performed in a fixed order, including the QS, 7MW, CST and TUG (see section 3.2.3 for more detailed description). The health status of the older adults was assessed by a number of health-related measures, including MMSE, IADL, CES-D, PA, FALLN, HAND, PWR, TMTA, and SPPB. See section 3.2.2 for more detailed information.

Robust linear regression was used to identify outliers and adjust for the effects of age, gender, height, weight, and cognitive status (indexed by the MMSE). An older adult was considered outlier if at least one of his/her sensor-based measure had a null weight in the robust linear regression model (MATLAB function "robustfit") [88]. One EFA was then performed on the residuals of each set of sensor-based measures to reduce the dimension of the dataset and to uncover the underlying relationships between sensor-based measures. Since the EFA is based on the assumption of normally distributed data, the jerk scores were log transformed and all the sensor-based measures were standardized to zero mean and unit variance before EFA. Varimax rotation was used to derive orthogonal factor scores. Sensor-based measures with factor loading greater than 0.5 as the absolute value were considered relevant. For each EFA, a scree plot (Parallel analysis) was used to determine the minimum number of factors to retain. We verified that each resulting factor structure explained at least 70% of the total variance [89]. Since the factor model was obtained excluding the outliers, their factor scores were lately predicted. Hence, all the participants were included in the subsequent statistical analysis. Each factor was interpreted using a priori knowledge on the sensor-based

measures that contribute to it and then mapped into a specific conceptual domain. Spearman's correlation analysis was used to investigate both the association between domains in the conceptual model and the associations between each domain and the residuals of the health-related measures. Signal processing and statistical analyses were performed using MATLAB [57]. Exploratory Factor Analysis was performed using R for Windows, version 3.4.3 [63]. Figure 4.1 shows the flowchart of the conceptual model development process.



Figure 4.1 Flowchart of the conceptual model development process; N is the number of sensor-based measures and factors or domains of each instrumented test.

4.2. INFLUENCE OF AGE, GENDER, BODY COMPOSITION AND COGNITION: RESULTS

Two hundred and seventy-three community-dwelling older adults (148 females, 80.8 ± 6.5 years old, range 65-98) performed the PP test in a fixed order, while wearing a smartphone at the lower back. Not all the participants were able to complete the whole battery of tests: Table 4.1 reports the demographic and functional profiles of each subgroup undertaking the four functional tests.

	POPULATIO QS		7mW	CST	TUG
	Ν	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
	Mean (SD)				
Age (years)	80.8 (6.5)	80.8 (6.5)	80.4 (6.5)	79.9 (6.4)	80.6 (6.4)
Weight (kg)	69.1 (13.3)	69.1 (13.2)	69.0 (13.4)	70.5 (12.9)	69.2 (13.4)
Height (cm)	159.1 (9.5)	159.1 (9.5)	159.4 (9.5)	159.9 (9.3)	159.1 (9.6)
IADL	1 (1.81)	1.00 (1.82)	0.81 (1.61)	0.70 (1.51)	0.88 (1.68)
MMSE	26.46 (3.11)	26.46 (3.13)	26.77 (2.77)	27.00 (2.48)	26.53 (3.07)
CES-D	13.96 (8.15)	14.00 (8.15)	13.39 (7.79)	13.42 (8.26)	13.61 (7.82)
PA	3.01 (1.02)	3.01 (1.02)	3.07 (1.01)	3.21 (1.04)	3.03 (1.01)
FALLN	0.58 (2.13)	0.59 (2.14)	0.53 (2.17)	0.38 (1.80)	0.56 (2.14)
SPPB	8.81 (2.94)	8.82 (2.95)	9.09 (2.66)	9.61 (2.12)	8.96 (2.74)
HAND (kg)	26.97 (9.09)	26.99 (9.10)	27.31 (9.15)	28.14 (9.08)	27.07 (9.03)
PWR (W)	87.24 (53.68)	87.10 (53.65)	89.47 (54.14)	92.92 (51.55)	88.00 (53.64)
TMTA	84.51 (56.51)	84.44 (56.72)	79.67 (49.96)	76.57 (49.81)	82.61 (54.42)
Sample size Tot (Females)	273 (148F)	271 (147F)	249 (129F)	202 (99F)	264 (142F)

 Table 4.1 Demographic and functional profiles of the groups who underwent the four test

ACRONYMS: SD: standard deviation; F: females; QS: Quiet Standing; 7mW: 7meters Walking test; CST: Repeated Chair Standing test; TUG: Timed Up and Go test; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; MMSE: Mini-Mental State Examination; CES-D: Epidemiologic Studies Depression Scale; FEAR: Survey of Activities and Fear of Falling in the Elderly; PA: Physical Activity; FALLN: declared number of falls; SPPB: Short Physical Performance Battery; HG. Hand-Grip strength test; PR. Power Rig; TMTA: Trail Making Test A

The results of the EFA performed on each PP test of the battery are shown in Table 4.2. Each factor was labelled and mapped into a specific domain based on the sensor-based measures that contribute to it.

Factors	Original Features	Factors	Original Features	Factors	Original Features	Factors	Original Features
	Quiet Standing		7-Meters Walk	Re	beated Chair Standing		Timed Up and Go
QSI	RMS A ML Range A ML SP ML DISPL SA DISPL EA DISPL MV ML DISPL	7MW1	Total duration Cadence RMS A AP RMS A V Range A AP Range A ML Range A V	CST1	Sts A Range V Sts A RMS V Sts G Range ML Sts G RMS ML stS A Range V stS A RMS V stS G Range ML stS G RMS ML	TUG1	180T Duration TtS Duration MV 180T MV TtS Peak Angular Velocity 180T Peak Angular Velocity TtS NJS 180T NJS TtS Number of Steps 180T
QS2	RMS A AP Range A AP SP AP DISPL SP Planar DISPL MV AP DISPL	7MW2	Step Reg AP Step Reg V Stride Reg AP Stride Reg ML Stride Reg V	CST2	stS JS AP stS JS ML stS JS V Total Duration Duration stS SD Duration stS	TUG2	Range Walk A AP Range Walk A ML Range Walk A V RMS Walk A AP RMS Walk A ML RMS Walk A V
QS3	F50 AP F95 AP CF AP NJS AP	7MW3	NJS AP NJS V NJS ML	CST3	stS A Range AP stS A Range ML stS A RMS AP stS A RMS ML	TUG3	StW Duration JS AP StW JS ML StW JS V StW
QS4	F50 ML F95 ML CF ML NJS ML	7MW4	Step Reg ML RMS A ML	CST4	Sts JS AP Sts JS ML Sts JS V Duration Sts	TUG4	TtS Duration JS AP TtS JS ML TtS JS V TtS
QS5	FD AP SE ML	7MW5	SD Cadence PCI	CST5	Sts A Range ML Sts A RMS ML Sts G Range AP Sts G RMS AP	TUG5	Range A ML StW RMS A ML StW RMS A ML TtS
IN	FD ML SE AP			CST	Sts A Range AP Sts A RMS AP	TUG	Range A AP StW RMS A AP StW Range A AP TtS
				IN	stS G Range AP stS G RMS AP SD Duration Sts	TUG 7	Range A V TtS RMS A V TtS
						TUG 8	Total Duration Walk Duration Number of Steps
						IN	Range A V StW RMS A V StW Range A ML TtS 180T Duration
ACI Ellij Tim	RONYMS: 180T: 180Tu pse Area; FD: Frequenc e-Normalized Jerk Score malized Jerk Score: PCI	rn; A: y Disp ; M: N	Accelerometer; AP: An ersion; F50: median fin fean; ML: Medio-Late	ntero-P requent ral; M	osterior; CF: Centroidal cy, F95: frequency bandy V: Mean Velocity; NI: N anularity: RMS: Root M	Freque width; (lot Incl	ency; DISPL: displacement; EA: G: Gyroscope; JS: Jerk Score; JS: uded in the model; NJS:

Normalized Jerk Score; PCI: Phase Coordination Index; Reg: Regularity; RMS: Root Mean Square; SA: Sway Area; SD: Standard Deviation; SE: Spectral Entropy; SP: Sway Path; StW: Sit to Walk; Sts: Sit to Stand; stS: Stand to Sit TtS: Turn to Sit; V: Vertical

4.2.1. QS FACTOR MODEL

Twenty-four outliers were identified by the robust linear regression. The factor analysis grouped 21 out of 23 sensor-based measures into 5 factors, accounting for 78% of the total variance (see Table 4.3). The resulting independent domains were labelled as: "Effectiveness of the balance control", "Dynamics of the postural sway in AP direction", "Reactivity and smoothness of the AP balance control", "Reactivity and smoothness of the ML balance control", and "Complexity of the balance control".

Domain	Effectiveness of the balance control	Effectiveness of the balance control Dynamics of the postural sway in AP direction		Reactivity and smoothness of the ML balance control	Complexity of the balance control		
Factor	QS1	QS2	QS3	QS4	QS5		
RMS A ML	0.74	0.19	-0.05	-0.37	0.15		
Range A ML	0.79	0.18	0.01	-0.27	0.05		
SP ML DISPL	0.93	0.21	0.08	-0.16	-0.23		
SA DISPL	0.72	0.48	-0.14	-0.16	0.24		
EA DISPL	0.60	0.43	-0.22	-0.26	0.39		
MV ML DISPL	0.92	0.19	0.05	-0.13	-0.24		
RMS A AP	0.32	0.59	-0.40	-0.12	0.41		
Range A AP	0.29	0.70	-0.28	-0.12	0.33		
SP AP DISPL	0.20	0.96	0.00	-0.03	-0.18		
SP Planar DISPL	0.42	0.88	0.02	-0.05	-0.21		
MV AP DISPL	0.16	0.93	-0.03	-0.03	-0.23		
F50 AP	-0.04	0.09	0.76	0.12	-0.38		
F95 AP	-0.03	-0.14	0.91	0.18	0.12		
CF AP	-0.05	-0.06	0.98	0.14	-0.04		
NJS AP	0.09	-0.14	0.83	0.13	0.32		
F50 ML	-0.17	-0.07	0.17	0.80	-0.20		
F95 ML	-0.24	-0.07	0.12	0.88	0.14		
CF ML	-0.22	-0.07	0.16	0.96	0.00		
NJS ML	-0.26	-0.04	0.14	0.84	0.24		
FD AP	0.01	-0.27	0.28	0.07	0.51		
SE ML	-0.15	0.06	-0.06	0.16	0.51		
FD ML	-0.02	0.00	-0.19	-0.20	0.45		
SE AP	0.12	-0.14	0.22	0.08	0.49		
CV %	19	37	53	69	78		

Table 4.3 Factor loadings of the first version of the QS conceptual model

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CF: Centroidal Frequency; CV: Cumulative Variance; DISPL: displacement; EA: Ellipse Area; FD: Frequency Dispersion; F50: median frequency, F95: frequency bandwidth; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; MV: Mean Velocity; NJS: Normalized Jerk Score; RMS: Root Mean Square; SA: Sway Area; SD: Standard Deviation; SE: Spectral Entropy; SP: Sway Path; V: Vertical

4.2.2. 7MW FACTOR MODEL

Eleven outliers were identified by the robust linear regression. The factor analysis grouped all 19 sensor-based measures into 5 factors, accounting for 74% of the total variance (see Table 4.4). The resulting independent domains were labelled as: "Global performance", "Gait regularity", "Gait smoothness", "ML weight shift control", and "Gait variability".

Domain	Global performance	Gait regularity	Gait smoothness	ML weight shift control	Gait variability
Factor	7MW1	7MW2	7MW3	7MW4	7MW5
Total duration	-0.64	-0.48	0.10	0.01	0.13
Cadence	-0.72	-0.21	0.65	-0.03	0.00
RMS A AP	0.88	0.21	0.27	0.10	-0.14
RMS A V	0.83	0.26	-0.01	0.07	-0.12
Range A AP	0.88	0.01	0.20	0.04	-0.11
Range A ML	0.60	-0.30	0.14	0.59	0.00
Range A V	0.81	-0.02	0.01	0.07	-0.04
Step Reg AP	0.13	0.69	0.20	0.01	-0.24
Step Reg V	0.20	0.74	-0.07	-0.16	-0.17
Stride Reg AP	-0.01	0.83	0.10	0.09	-0.21
Stride Reg ML	-0.03	0.61	-0.09	0.41	-0.01
Stride Reg V	0.19	0.85	-0.09	-0.08	-0.12
NJS AP	0.35	0.19	0.79	0.02	-0.12
NJS V	0.02	-0.03	0.69	-0.01	0.06
NJS ML	0.05	-0.07	0.55	0.57	0.04
Step Reg ML	-0.07	0.39	-0.08	0.52	-0.02
RMS A ML	0.60	-0.11	0.02	0.79	0.00
SD Cadence	-0.23	-0.36	0.09	-0.03	0.90
PCI	-0.09	-0.22	-0.05	0.03	0.85
CV %	25	45	56	65	74

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance, G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; PCI: Phase Coordination Index; Reg: Regularity; RMS: Root Mean Square; SD: Standard Deviation; V: Vertical

4.2.3. CST FACTOR MODEL

Twenty-six outliers were identified by the robust linear regression. The factor analysis grouped 28 out of 31 sensor-based measures into 6 factors, accounting for 77% of the total variance (see Table 4.5). The resulting independent domains were labelled as: "Range of motion", "Stand-to-Sit Impairment", "Effectiveness of the motor control during Stand-to-Sit", "Sit-to-Stand Impairment", "Lateral weight shift control during Sit-to-Stand", and "Sit-to-Stand forward bending".

	-			aam		
Table 4.5	Factor	loadings	of the	CST	conceptual	model
14010	1 40001	routingo	01 0110	~~ -	eoneep caa.	

			Effectiveness of		lataral waight	Sit to Stand
Domains	Range of	Stand to Sit	the motor	Sit to Stand	shift control Sit	forward
Domains	motion	Impairment	control Stand	Impairment	To Stand	bending
			To Sit		10 Stand	bending
Factors	CST1	CST2	CST3	CST4	CST5	CST6
Sts A Range V	0.85	0.17	0.08	0.29	0.20	-0.06
Sts A RMS V	0.84	0.14	0.01	0.28	0.20	-0.15
Sts G Range ML	0.86	0.09	0.03	-0.08	0.20	0.23
Sts G RMS ML	0.91	0.04	0.01	-0.16	0.16	0.08
stS A Range V	0.74	0.09	0.35	0.11	0.02	0.12
stS A RMS V	0.84	0.16	0.15	0.18	0.06	-0.09
stS G Range ML	0.70	-0.14	0.35	-0.03	-0.01	0.21
stS G RMS ML	0.84	-0.19	0.22	-0.15	0.04	0.08
stS JS AP	0.15	0.83	-0.02	0.18	0.00	-0.08
stS JS ML	0.09	0.93	0.05	0.20	0.01	-0.16
stS JS V	0.27	0.89	-0.10	0.17	-0.05	-0.11
Total Duration	0.06	0.78	-0.22	0.46	-0.04	-0.24
Duration stS	0.03	0.88	-0.28	0.28	-0.07	-0.17
SD Duration stS	-0.16	0.65	-0.02	-0.11	-0.04	0.00
stS A Range AP	0.20	-0.31	0.53	-0.08	0.10	0.31
stS A Range ML	0.07	0.00	0.94	0.06	0.15	0.13
stS A RMS AP	0.26	-0.42	0.51	-0.12	0.07	0.37
stS A RMS ML	0.06	-0.10	0.89	-0.02	0.32	0.02
Sts JS AP	0.16	0.34	-0.06	0.83	0.14	0.17
Sts JS ML	0.10	0.36	0.02	0.78	0.37	-0.25
Sts JS V	0.40	0.40	-0.06	0.76	0.09	-0.20
Duration Sts	0.10	0.52	-0.11	0.73	-0.02	-0.34
Sts A Range ML	0.07	-0.01	0.29	0.06	0.88	0.15
Sts A RMS ML	0.00	-0.05	0.30	0.00	0.88	0.05
Sts G Range AP	0.30	0.00	0.11	0.09	0.70	0.11
Sts G RMS AP	0.20	-0.06	0.16	0.05	0.68	0.12
Sts A Range AP	0.07	-0.24	0.16	-0.13	0.22	0.90
Sts A RMS AP	0.16	-0.27	0.17	-0.16	0.21	0.81
stS G Range AP	0.27	0.00	0.48	0.01	0.16	0.02
stS G RMS AP	0.17	-0.10	0.48	-0.05	0.25	0.01
SD Duration Sts	-0.26	-0.11	0.08	0.49	-0.12	-0.07
CV %	20	38	49	60	70	77

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; RMS: Root Mean Square; SD: Standard Deviation; Sts: Sit to Stand; stS: Stand to Sit; V: Vertical

4.2.4. TUG FACTOR MODEL

Twenty-one outliers were identified by the robust linear regression. The factor analysis grouped 34 out of 38 sensor-based measures into 8 factors, accounting for 72% of the total variance (see Table 4.6). The resulting independent domains were labelled as: "Turning Impairment", "Walking Intensity", "Sit-to-Walk Smoothness", "Turn-to-Sit Smoothness", "ML weight transfer ability", "AP weight transfer Impairment", "Weight lift difficulties", and "Shakiness".

	Turning Impairment	Walking Intensity	Sit to walk Smoothness	Turn to sit Smoothness	ML weight transfer ability	AP weight transfer Impair ment	Weight lift difficulties	Feebleness
	TUG1	TUG2	TUG3	TUG4	TUG5	TUG6	TUG7	TUG8
180T Duration	0.89	-0.22	0.00	0.04	-0.06	-0.05	0.01	0.13
TtS Duration	0.63	-0.18	0.08	0.05	0.00	-0.03	-0.01	0.24
MV 180T	-0.81	0.38	-0.09	-0.10	-0.04	0.01	0.07	-0.14
MV TtS	-0.63	0.34	-0.07	-0.10	-0.06	0.01	0.09	-0.13
Peak Angular Velocity 180T	-0.58	0.47	-0.04	-0.06	0.02	0.04	0.08	-0.17
Peak Angular Velocity TtS	-0.59	0.35	-0.10	-0.11	-0.04	0.03	0.15	-0.16
NJS 180T	0.91	0.07	-0.01	0.08	0.01	-0.04	0.01	-0.05
NJS TtS	0.60	0.04	-0.01	0.08	0.07	-0.03	0.04	0.04
Number of Steps 180T	0.78	-0.08	-0.11	-0.05	-0.07	-0.12	0.06	-0.07
Range Walk A AP	-0.17	0.64	-0.08	0.03	0.16	0.00	0.04	-0.13
Range Walk A ML	-0.06	0.76	0.00	0.00	0.07	0.01	0.09	-0.01
Range Walk A V	-0.21	0.83	-0.04	-0.04	0.00	0.12	0.04	-0.11
RMS Walk A AP	-0.28	0.67	-0.03	0.02	0.21	-0.02	0.07	-0.30
RMS Walk A ML	-0.07	0.82	0.00	0.00	0.06	0.03	0.12	-0.07
RMS Walk A V	-0.29	0.79	-0.08	-0.07	-0.01	0.04	0.05	-0.28
StW Duration	0.12	-0.16	0.87	0.01	-0.11	0.11	-0.02	0.21
JS AP StW	-0.02	-0.04	0.92	-0.02	-0.01	0.33	0.00	0.01
JS ML StW	0.05	0.00	0.89	0.01	0.36	0.04	-0.03	-0.01
JS V StW	-0.02	-0.01	0.94	-0.03	0.03	0.11	0.05	-0.04
TtS Duration	0.38	-0.29	0.04	0.51	0.01	0.00	-0.23	0.38
JS AP TtS	0.08	-0.01	-0.03	0.98	0.07	0.06	-0.01	0.02
JS ML TtS	0.14	-0.04	0.02	0.89	0.16	0.04	-0.03	0.04
JS V TtS	0.07	-0.01	-0.06	0.92	0.10	0.08	0.22	0.01
Range A ML StW	-0.01	0.12	0.11	0.05	0.96	-0.01	-0.01	-0.05
RMS A ML StW	0.04	0.02	0.02	0.08	0.93	-0.04	-0.04	0.02
RMS A ML TtS	0.18	0.02	0.08	0.06	0.55	-0.10	0.28	0.03
Range A AP StW	-0.14	0.00	0.27	-0.05	0.07	0.91	0.03	-0.03
RMS A AP StW	-0.12	-0.05	0.20	0.00	-0.04	0.93	0.04	-0.03
Range A AP TtS	-0.01	0.21	0.05	0.34	-0.07	0.50	0.30	0.00
Range A V TtS	-0.06	0.15	-0.03	0.15	0.14	0.13	0.91	-0.04
RMS A V TtS	-0.08	0.13	0.00	-0.11	0.16	0.18	0.86	0.03
Total Duration	0.46	-0.41	0.18	0.17	-0.06	0.03	-0.05	0.74
Walk Duration	0.57	-0.37	0.04	0.02	-0.08	-0.01	0.06	0.67
Number of Steps	0.08	-0.28	0.03	0.02	0.01	-0.05	0.01	0.70
Range A V StW	-0.26	0.29	0.13	-0.03	0.32	0.04	0.09	-0.16
RMS A V StW	-0.25	0.18	-0.15	0.09	0.42	0.11	0.08	-0.03
Range A ML TtS	0.12	0.10	0.06	0.19	0.45	-0.01	0.37	-0.02
180T Duration	0.01	0.19	0.05	0.24	-0.07	0.49	0.32	0.02
CV%	16	28	38	46	54	60	66	72

Table 4.6 Factor loadings of the first version of the TUG conceptual model

ACRONYMS: 180T: 180 Turn; A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; RMS: Root Mean Square; SD: Standard Deviation; StW: Sit to Walk; TtS: Turn to Sit; V: Vertical

4.2.5. CORRELATION ANALYSIS

The correlations between the domains of the conceptual model and the residuals of the health-related measures are reported in Table 4.7. The correlations between the domains of the conceptual model are reported in Table 4.8. The correlations between health-related measures are reported in Table 4.9. The main result is that higher-functioning (SPPB and TMTA) older adults who were more active (PA) and stronger (HG, PWR) performed better on the battery of PP tests.

Table 4.7 Correlation analysis between domains of the conceptual model and residuals of the health-related measures

		IADL	CES-D	ΡA	FALLN	HAND	PWR	TMTA	SPPB	'mW tot luration	rUG tot luration
Ineffectiveness of the Balance Control	QS1	.18	.09	02	.20	25	11	.00	.14	.09	.19
Dynamics of the Postural Sway in AP	QS2	.05	.04	.02	.09	09	.03	.02	.10	.03	.03
Reactivity and Smoothness of the AP Balance Control	QS3	07	08	.02	01	.06	01	.00	.13	.01	.01
Reactivity and Smoothness of the ML Balance Control	QS4	.03	06	12	02	07	03	01	.02	.02	.04
Complexity of the Balance Control	QS5	.01	07	.12	.16	.02	.04	04	08	.01	.01
Global Performance	7MW1	28	09	.31	05	.53	.17	.27	21	79	62
Gait Regularity	7MW2	15	12	.29	13	.29	.17	.13	06	45	36
Gait Smoothness	7MW3	.03	.04	.01	.13	11	.04	.08	.06	.09	.12
ML Weight Shift Control	7MW4	.14	05	.00	.04	08	17	.04	.04	.03	.04
Gait Variability	7MW5	07	.04	13	.15	13	12	12	03	.04	.10
Range of motion	CST1	05	.00	.00	04	05	.03	.00	.06	12	13
Stand to Sit Impairment	CST2	.20	.00	10	.01	38	11	20	.11	.28	.35
Effectiveness of the Motor Control Stand to Sit	CST3	.11	01	17	.04	.03	.12	.14	.13	.06	01
Sit to Stand Impairment	CST4	.12	.04	09	.05	38	12	06	.14	.28	.29
Lateral Weight Shift Control Sit to Stand	CST5	01	15	.05	.01	.06	.16	.19	.07	07	12
Sit to Stand Forward Bending	CST6	.00	11	.15	09	.28	.21	.20	.07	24	28
Turning Impairment	TUG1	.18	.08	13	.08	41	14	15	.15	.45	.57
Walking Intensity	TUG2	.03	06	.18	01	.19	.08	.13	06	24	34
Sit to Walk Smoothness	TUG3	.09	.00	03	02	06	02	07	.05	.07	.10
Turn to Sit Smoothness	TUG4	.08	.02	05	.09	16	03	09	01	.09	.14
ML Weight Transfer Ability	TUG5	.04	07	.01	.01	02	09	.00	.00	05	07
AP Weight Transfer Impairment	TUG6	.06	.02	06	.03	19	12	14	.14	.06	.14
Weight Lift Difficulties	TUG7	02	.15	.12	.02	06	01	.00	02	.01	05
Feebleness	TUG8	.29	.09	18	.18	50	18	18	.10	.58	.68

Correlation coefficients with a p-value < .05 are bolded

ACRONYMS: ADL: Activities of Daily Living; AP: Anteroposterior; CESD: Epidemiologic Studies Depression Scale; FALLN: declared number of falls; FEAR: Survey of Activities and Fear of Falling in the Elderly; HAND. Hand-Grip strength test; IADL: Instrumental Activities of Daily Living; ML: Medio-Lateral; MMSE: Mini-Mental State Examination; PA: Physical Activity; PR. Power Rig; SPPB: Short Physical Performance Battery; TMTA: Trail Making Test A; V: Vertical.

Table 4.8 Correlation Analysis between domains of the first version of the conceptual model			
	Table 4.8 Correlation Analysis	between domains of the first	st version of the conceptual model

	Ineffectiveness of the Balance Control	Dynamics of the Postural Sway in AP Direction	Reactivity and Smoothness of the AP Balance Control	Reactivity and Smoothness of the ML Balance Control	Complexity of the Balance Control	Global performance	Gait regularity	Gait smoothness	ML weight shift control	Gait variability	Range of motion	Stand to Sit Impairment	Effectiveness of the motor control Stand To Sit	Sit to Stand Impairment	Lateral Weight Shift Control Sit To Stand	Sit to Stand Forward Bending	Turning Impairment	Walking Intensity	Sit to walk Smoothness	Turn to sit Smoothness	ML weight transfer ability	AP weight transfer Impairment	Weight lift difficulties	Feebleness
	QS1	QS2	QS3	QS4	QS5	7MW1	7MW2	7MW3	7MW4	7MW5	CST1	CST2	CST3	CST4	CST5	CST6	TUG1	TUG2	TUG3	TUG4	TUG5	TUG6	TUG7	TUG8
QS1		.40	.07	.29	.46	06	08	.11	.17	.08	.07	.11	.09	.22	.12	10	.17	.02	01	.10	.12	.12	.04	.11
QS2	.00		.02	.12	.49	07	09	.09	.13	.03	.01	.04	.07	.20	.03	08	.16	.02	.03	12	05	.02	.03	.01
QS3	.24	.73		.05	02	.00	.19	.00	.00	04	.09	09	.02	.00	.00	.04	01	08	02	.03	03	.07	.03	09
QS4	.00	.04	.43		.06	06	02	01	08	.03	.01	01	.10	12	.01	.02	.03	.02	.06	.01	.00	.00	11	.05
QS5	.00	.00	.69	.33	10	10	.00	.17	.10	.04	.03	.14	.08	.13	02	.02	01	02	01	02	01	02	.13	.02
7MW1	.32	.30	.96	.36	.13	70	.02	03	.12	.00	.18	25	.05	22	.09	.19	32	.49	07	07	.13	.02	.06	39
7MW2	.22	.18	.00	.71	.99	.73	42	05	08	06	.09	13	13	02	13	.10	31	16	02	09	04	06	02	40
/MW3	.09	.14	.94	.84	.01	.63	.43	~ ~	.04	.17	.13	01	.13	.15	.20	09	.07	.08	.07	.09	02	.03	.06	.17
/MW4	.01	.04	.99	.20	.12	.06	.18	.00	1.0	.00	.08	.09	02	.07	.05	.13	.06	.37	.00	.05	.13	.05	.06	.13
CST1	.22	.05	.49	.03	.37	01	.34	.01	26	05	14	.07	.08	.07	07	24	.22	02	01	09	.01	04	.07	.14
CST2	.35	.07	.19	.04	.09	.01	.19	.07	.20	30	22	09	.08	.05	.03	.01	20	.00	.02	.00	.00	.40	.20	15
CST2	.14	33	.21	16	.05	.00	.00	.92	.21	.52	.22	88	.01	01	10	- 03	.19	15	.00	.08	.10	- 01	17	02
CST4	00	00	.02	.10	.23	00	.07	.00	36	34	48	.00	86	.01	- 05	05	14	- 16	.02	11	- 03	17	- 02	15
CST5	.09	.64	1.0	.07	.76	.00	.06	.01	.50	30	63	25	.01	45		.00	- 08	.26	.11	- 02	.03	.11	- 02	.08
CST6	.15	.2.7	.57	.77	.73	.01	.18	.20	.06	.00	.86	.31	.69	39	45	100	25	.29	.02	.01	.12	15	- 02	- 08
TUG1	.01	.01	.83	.63	.86	.00	.00	.30	.37	.00	.01	.01	.62	.06	.29	.00		.07	06	.03	.02	.12	06	.43
TUG2	.72	.71	.21	.81	.81	.00	.01	.19	.00	.76	.27	.06	.06	.02	.00	.00	.25		.00	.02	.06	.01	.00	.13
TUG3	.87	.63	.75	.31	.93	.26	.80	.25	.39	.93	.77	.99	.81	.11	.58	.78	.36	.98		01	10	21	.05	.02
TUG4	.11	.06	.60	.88	.72	.27	.18	.16	.41	.18	.95	.26	.60	.13	.74	.84	.64	.74	.82		.00	.00	.01	.10
TUG5	.06	.47	.66	.95	.83	.04	.58	.71	.04	.87	.44	.15	.20	.63	.10	.08	.75	.30	.12	.99		.10	03	.00
TUG6	.05	.74	.23	.94	.69	.78	.34	.67	.46	.50	.00	.13	.83	.01	.12	.03	.04	.82	.00	.95	.10		09	.08
TUG7	.53	.58	.64	.07	.04	.34	.74	.34	.38	.25	.00	.36	.02	.74	.82	.75	.35	.95	.40	.90	.59	.14		02
TUG8	.08	.82	.15	.39	.72	.00	.00	.01	.04	.03	.07	.00	.83	.03	.25	.28	.00	.03	.72	.10	1.0	.22	.76	
p-values a bolded	are repo	orted u	nder th	e main	i diago	nal an	d corre	lation	coeffic	ients a	ire rep	orted a	bove th	ie maii	n diago	onal. C	orrelat	ion co	efficier	nts with	n a p-v	alue <	.05 are	

ACRONYMS: AP: Anteroposterior; ML: Medio-Lateral; V: Vertical

	ADL	IADL	CES-D	FEAR	PA	FALLN	HAND	PWR	TMTB	TMTA	SPPB	7MW tot duration	TUG tot duration
ADL		0.30	0.05	0.20	-0.15	0.24	-0.09	-0.08	0.15	0.04	-0.27	0.14	0.14
IADL	0.00		0.04	0.16	-0.31	0.08	-0.16	-0.10	0.22	0.03	-0.47	0.35	0.33
CES-D	0.40	0.51		0.10	-0.13	0.26	-0.11	-0.14	0.15	0.14	-0.10	0.13	0.09
FEAR	0.00	0.00	0.08		-0.23	0.18	-0.03	-0.08	0.12	0.03	-0.22	0.22	0.23
РА	0.01	0.00	0.02	0.00		-0.08	0.21	0.16	-0.10	0.01	0.36	-0.35	-0.27
FALLN	0.00	0.15	0.00	0.00	0.15		-0.16	-0.07	0.09	0.10	-0.26	0.21	0.20
HG	0.11	0.01	0.07	0.60	0.00	0.01		0.33	-0.14	0.03	0.33	-0.27	-0.26
PR	0.20	0.09	0.02	0.19	0.01	0.28	0.00		-0.06	0.06	0.35	-0.34	-0.36
TMTA	0.01	0.00	0.01	0.04	0.10	0.12	0.02	0.33		0.62	-0.18	0.26	0.17
ТМТВ	0.63	0.74	0.07	0.65	0.86	0.19	0.68	0.41	0.00		0.01	0.07	0.07
SPPB	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.90		-0.66	-0.74
7MW tot	0.03	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.36	0.00		0.77
TUG tot duration	0.02	0.00	0.13	0.00	0.00	0.00	0.00	0.00	0.01	0.38	0.00	0.00	

Table 4.9 Correlation analysis between residuals of the health-related measures

p-values are reported under the main diagonal and correlation coefficients are reported above the main diagonal. Correlation coefficients with p-value < .05 are bolded

ACRONYMS: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; MMSE: Mini-Mental State Examination; CESD: Epidemiologic Studies Depression Scale; FEAR: Survey of Activities and Fear of Falling in the elderly; PA: Physical Activity; FALLN: declared number of falls; HAND: Hand-Grip Strength Test; PWR: Power Rig; TMTA: Trail Making Test A, SPPB: Short Physical Performance Battery

4.3. DISCUSSION

The aim of this work was to define a sensor-based conceptual model for the assessment of the older adults' physical capabilities. The EFA allowed reducing the dimension of each set of sensor-based measures computed from each PP test of the battery. One aspect to consider when performing EFA is the dimensionality of the starting dataset. It is common practice to have at least 5*N observations (i.e. participants), where N is the total number of measured variables (i.e. sensor-based measures). Our starting dataset includes 111 measures and this means that we needed more than 500 participants to perform one EFA after merging all the sensor-based measures. For this reason, one EFA for each PP test was performed. Since Varimax rotation was applied, the EFA model makes the assumption that the factors are independent. Hence, the factor scores of each functional test are expected to be uncorrelated. However, some correlations were observed between factors of the same functional test (see Table 4.7) because outliers were included in the factor analyses in this work. The correlation

analysis between domains and health-related measures was computed on the residuals obtained after removing the effect of age, gender, height, weight and MMSE from the health-related measures. Table 4.7 shows that we found several significant correlations between domains and conventional health-related measures. At the same time, small correlation coefficients (between ± 0.1 and ± 0.5) suggest that domains of the conceptual model and health-related measures carry partly related, but different, information and this leads us to hypothesize that the conceptual model enriches the outcome of conventional clinical tools for the evaluation of the physical capability.

In general, measures of strength (HAND and PWR) were related to domains that reflect the ability to walk, stand/sit from a chair and turn, but were not related to the postural sway. The standard clinical outcome, like the 7MW and TUG total duration or the SPPB score, were associated with the older adults' physical function and ability to execute the battery of PP tests.

Four of the domains were not correlated with any health-related measures (Table 4.7): the "Dynamics of the postural sway in AP direction" of the QS factor model, the "Range of motion" of the CST factor model, the "Sit to walk smoothness", and the "ML weight transfer impairment" of the TUG factor model. This could be due either to non-linear associations between domains and measures or to their association with other health-related measures that were not included in this study. For example, it has been proposed that "ML weight transfer impairment" may be associated with the risk of falling [90,91]. A more detailed description of these results is reported below.

4.3.1. CONVENTIONAL OUTCOME

As previously described, the 7MW and TUG total durations serve as the conventional clinical outcome measures of an older adult's PC. As expected, Table 4.8 shows that these two measures of time were significantly related to those domains that consist of measures of intensity (Range and RMS), velocity and duration of the movements ("Global performance", 7MW1, "Gait regularity", 7MW2, "Stand-to-Sit impairment", CST2, "Sit-to-Stand impairment", CST4 and "Sit-to-Stand forward bending", CST6, "Turning impairment", TUG1, "Walking intensity", TUG2 and "Shakiness", TUG8). Furthermore, only the total TUG duration was related to those domains related to transfer and turning ability, which requires good cognitive capacities to plan and coordinate postural transitions before sitting or walking, and good balance and coordination ("Ineffectiveness of the balance control", QS1, "Turn-to-Sit smoothness", TUG4, and "AP weight transfer impairment", TUG6). Indeed, Table 4.7 shows that these domains are related to each other and, in particular, the control of the static balance ("Ineffectiveness of the balance control", QS1, "Stath these domains are related to each other and, in particular, the control of the static balance ("Ineffectiveness of the balance control", QS1, "Turning impairment", TUG1, "AP weight transfer impairment", TUG6). On the other hand, no correlations between the conventional outcomes and measures related to the

dynamic postural control ("ML weight shift control", 7MW4 ,"Range of motion", CST1, "Effectiveness of the motor control during the Stand-to-Sit", CST3, "Lateral weight shift control during the Sit-to-Stand", CST5, "Weight lift impairment", TUG7), static postural control (almost all the factors of the QS factor model), smooth walking ("Gait smoothness", 7MW3 and "Sit-to-Walk smoothness", TUG3) and "Gait variability", 7MW5 were found. These results confirm that the stopwatch-based total time to complete the PP tests, is a good indicator of the older adults' health status since it is related to the older adults' impairments, but it does not give information on which physical domain is impaired (i.e. balance, strength or coordination).

4.3.2. IADL

Older adults who had a higher number of instrumental activities in which they required help (IADL), were also less confident, strong and fit ("Ineffectiveness of the balance control", QS1, "Global Performance", 7MW1, "Gait regularity", 7MW2, "Shakiness", TUG8), they showed higher impairments to lift the body weight ("ML weight shift control" (7MW4), "Stand to Sit Impairment" (CST2)) and turn ("Turning Impairment" (TUG1)). In addition, Table 4.7 confirms that these domains are indicative of the older adults' inabilities. Indeed, the higher the walking, turning and sitting ability ("Gait regularity" (7MW2), "Stand to Sit Impairment" (CST2), "Walking intensity" (TUG2), "Turning Impairment" (TUG1)), the lesser the "Shakiness" (TUG8) and the higher the "Global Performance" (7MW1).

4.3.3. CES-D

Table 4.8 shows that older adults who reported depressive symptoms (CES-D, cut-off: 16) had more difficulties during postural transitions ("Lateral weight shift control Sit to Stand" (CST5) and "Weight lift difficulties" (TUG7)). Table 4.7 shows that these two domains are not significantly correlated, thus, their contribution in lifting the body weight is independent. Postural transitions are commonly used as an index of the lower limbs muscle power. Older adults with depressive symptoms appear to be less confident and to have less dynamic postural control, which is reflected in a higher V acceleration while sitting and lower ML shift while standing. This result is in agreement with the study by Penninx et al. [90] in which depressive symptoms go together with developing a sedentary lifestyle and are associated with physical frailty.

4.3.4. PA

Table 4.8 shows that the older adults' declared physical activity (PA) was significantly related to domains that consist of measures of fitness, like intensity (range and RMS), duration, coordination, regularity and postural control ("Reactivity and smoothness of the ML balance control" (QS4),

"Complexity of the balance control" (QS5), "Global Performance" (7MW1), "Gait Regularity" (7MW2), "Gait Variability" (7MW5), "Effectiveness of the motor control Stand to Sit" (CST3), "Sit to Stand forward bending" (CST6), "Turning Impairment" (TUG1), "Walking Intensity" (TUG2) and "Shakiness" (TUG8)). Furthermore, most of these domains are also significantly related to the total 7MW and TUG durations (7MW1, 7MW2, CST6, TUG1, TUG2 and TUG8). These results confirm that measures including stopwatch timing, number of steps, gait regularity and coordination, and postural control, which are commonly used to assess older adults' PC, are also strongly related to their declared level of PA.

4.3.5. FALLN

The number of falls experienced during the 12 months preceding the assessment (FALLN), resulted related to poor performances during postural sway and locomotion ("Ineffective of the balance control" (QS1), "Complexity of the balance control" (QS5), "Gait regularity" (7MW2), "Gait smoothness" (7MW3), "Gait variability" (7MW5), "Shakiness" (TUG8). No association between FALLN and measures of strength and ability to transfer and turning (all the CST domains and domains related to postural transitions and turns of the TUG) where found. These results suggest that fell more who had a poorer static balance control and a more impaired locomotion. As shown in Table 4.7, the higher the "Shakiness" (TUG8), the poorer the walking ability ("Gait regularity" (7MW2), "Gait smoothness" (7MW3), "Gait variability" (7MW5). Furthermore, older adults with high "Gait smoothness" (7MW3) had also high "Complexity of the balance control" (QS5), high "Gait regularity" (7MW2) is related to high "Reactivity and smoothness of the AP balance control" (QS3), high "Ineffectiveness of the balance control" (QS1) and "Dynamics of the postural sway in AP direction" (QS2) are related to high "ML weight shift control" (7MW4) meaning that a good static postural control and walking ability participate together to the reduction of the falls number.

4.3.6. HAND

Older adults with more upper limbs strength (Hand-Grip strength test, HAND) showed better PC ("Global performance" (7MW1), "Gait regularity" (7MW2), "ML weight shift control" (7MW4), "Lateral weight shift control Sit-to-Stand" (CST5), "Sit-to-Stand forward bending" (CST6), "Turning Impairment" (TUG1) and "Shakiness" (TUG8)). Since the QS test aims to assess the abilities to maintain the static balance and it is not a direct indicator of the muscle strength, as expected, no associations between HAND and domains of the QS model were found. However, as reported in Table 4.7, some of the domains found significantly related to the and grip strength were also related to domains of the QS model (7MW2, 7MW4, TUG1), indicating that there is a secondary effect of the muscle strength in the ability to maintain the static balance. These results are consistent with the

findings of a previous study that highlights the association between grip-strength and future outcome in ageing adults [92].

4.3.7. PWR

Older adults with high PWR score had high muscle strength in the lower limbs. Table 4.8 shows that higher PWR score was related to better performance during gait, postural transitions and turns ("Global performance" (7MW1), "Stand-to-Sit impairment" (CST2), "Effectiveness of the motor control during the Stand-to-Sit" (CST3), "Lateral weight shift control Sit-to-Stand" (CST5), "Sit-to-Stand forward bending" (CST6), "Turning impairment" (TUG1), "Walking intensity" (TUG2), "AP weight transfer impairment" (TUG6), "Shakiness" (TUG8)), suggesting that the movements of the older adults with higher muscle power were more intense and faster, meaning that they were more fit and confident. As in the previous case, no direct association between measures of strength and QS domains were found.

4.3.8. TMTA

The Trail Making Test part A (TMTA) assesses psychomotor speed. The TMTA duration was related to domains that consist of sensor-based measures related to the older adults' cognitive capacities and motor control, like postural sway, locomotion and turns ("Ineffectiveness of the balance control", QS1, "Reactivity and smoothness of the AP balance control", QS3, "Global performance", 7MW1, "Turning impairment", TUG1, "AP weight transfer impairment", TUG6). The TMTA duration was not significantly associated with domains of the CST model, which are more indicative of strength, than cognition. These results are coherent with the literature: performance on the TMT is a strong, independent predictor of mobility impairment, accelerated decline in lower extremity function, and mortality in older community-living adults [77]. Attention and executive function are related to the cognitive control of gait, posture, and balance [93,94].

4.3.9. SPPB

The Short Physical Performance Battery (SPPB) score is a summary score which measures the older adults' PC. The higher the SPPB score, the better the adults' performance in walking, CST and TUG test. Almost all the domains in the conceptual model are related to this score ("Ineffectiveness of the balance control", QS1, "Global performance", 7MW1, "Gait regularity", 7MW2, "Gait variability", 7MW5, "Stand-to-Sit impairment", CST2, "Sit-to-Stand impairment", CST4, "Sit-to-Stand forward bending", CST6, "Turning impairment", TUG1, "Walking intensity", TUG2, "Turn-to-Sit smoothness", TUG4, "AP weight transfer impairment", TUG6, "Shakiness", TUG8). The domains related to the SPPB score are also related to the 7MW and TUG stopwatch duration. We can conclude

that SPPB is a good indicator of the older adults' health status, but since it is a summary score, it is not possible to know whether the impairments affect only balance, strength, coordination or a combination of these physical domains.

In conclusion, EFA allowed reducing the number of sensor-based measures and find domains with clear functional meaning. Correlation analysis suggested that domains underlying instrumented functional tests could provide quantitative information about several mobility skills, enriching the conventional clinical outcomes. Many significant associations between the domains of the conceptual model and the overall performance (measured by the total 7MW and TUG time) were found. These measures of time could influence the sensor-based measures, affecting the results. To overcome this limitation, the effect of the overall performance was removed from the sensor-based measures, in addition to the other confounders. Robust linear regression was hence used to remove the effects of age, gender, height, weight, cognitive status (indexed by the MMSE) and overall performance (e.g. the residuals of the sensor-based TUG measures were computed removing the effect of age, gender, height, weight, MMSE and total TUG duration). Since the outcome of the QS test is dichotomous (i.e. the participant was able/not able to perform the test), we could not remove the overall performance from the sensor-based measures computed from this test. The subsequent statistical analyses were already described in section 4.1.

4.4. INFLUENCE OF THE OVERALL PERFORMANCE: RESULTS

4.4.1. **QS** FACTOR MODEL

Since it is not possible to remove the overall performance of this test from the QS sensor-based measures, the QS factor model is the same as the model presented in section 4.2.1.

4.4.2. 7MW FACTOR MODEL

Eight outliers were identified by the robust linear regression. The factor analysis grouped all 18 sensor-based measures into 5 factors, accounting for 70% of total variance (see Table 4.10). The resulting independent domains were labelled as: "Global performance", "Gait regularity", "Gait smoothness", "ML weight shift control", and "Gait variability".

	Global performance	Gait regularity	Gait smoothness	ML weight shift control	Gait variability
	7MW1	7MW2	7MW3	7MW4	7MW5
Range A AP	0.85	-0.14	0.19	0.10	-0.05
RMS A AP	0.85	0.06	0.35	0.16	-0.10
RMS A V	0.78	0.12	-0.08	0.08	-0.05
Range A V	0.71	-0.18	-0.08	0.12	0.05
Stride Reg V	0.01	0.79	-0.06	-0.27	-0.06
Stride Reg AP	-0.10	0.77	0.18	-0.04	-0.23
Stride Reg ML	-0.01	0.71	-0.11	0.27	0.00
Step Reg V	-0.01	0.62	-0.01	-0.31	-0.15
Step Reg AP	-0.07	0.54	0.34	-0.05	-0.27
Step Reg ML	-0.05	0.52	-0.11	0.41	-0.01
NJS AP	0.28	0.06	0.89	0.07	-0.10
Cadence	-0.49	-0.04	0.77	-0.01	-0.07
NJS V	0.13	0.00	0.57	0.00	0.07
RMS A ML	0.51	-0.04	-0.06	0.85	0.04
NJS ML	0.00	-0.02	0.53	0.63	0.03
Range A ML	0.50	-0.28	0.06	0.69	0.03
SD Cadence	-0.09	-0.24	0.05	0.02	0.96
PCI	-0.02	-0.14	-0.06	0.04	0.85
CV %	19	35	48	60	70

Table 4.10 Factor loadings of the second version of the 7mWT conceptual model

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance, G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; PCI: Phase Coordination Index; Reg: Regularity; RMS: Root Mean Square; SD: Standard Deviation; V: Vertical

4.4.3. CST FACTOR MODEL

Thirty-three outliers were identified by the robust linear regression. The factor analysis grouped 26 out of 30 sensor-based measures into 6 factors, accounting for 70% of total variance (see Table 4.11). The resulting independent domains were labelled as: "Range of motion", "Lateral weight shift control", "Stand-to-Sit impairment", "Stand-to-Sit forward bending", "Sit-to-Stand impairment", and "Sit-to-Stand forward bending".

Table 4.11 Factor	loadings o	of the second	version of	of the	CST	conceptual	model
1 4010 4.111 1 40101	iouumgo o	i une second	version	or the		conceptuur	mouci

	Range of motion	Lateral Weight Shift Control	Stand-to-Sit impairment	Stand-to-Sit Forward Bending	Sit-to-Stand impairment	Sit-to-Stand forward bending
	CST1	CST2	CST3	CST4	CST5	CST6
Sts G RMS ML	0.89	0.13	0.12	0.03	-0.03	0.10
Sts A Range V	0.88	0.24	-0.05	0.07	0.19	0.03
Sts A RMS V	0.88	0.23	-0.10	-0.01	0.21	-0.05
stS A RMS V	0.87	0.13	-0.04	0.13	0.10	-0.03
stS G RMS ML	0.85	0.05	-0.01	0.19	0.01	0.02
Sts G Range ML	0.82	0.16	0.13	0.06	0.00	0.27
stS A Range V	0.74	0.09	0.07	0.38	0.07	0.10
stS G Range ML	0.67	0.03	0.01	0.41	0.07	0.15
Sts A RMS ML	-0.02	0.91	-0.01	0.08	0.05	0.10
Sts A Range ML	0.05	0.91	0.05	0.11	0.13	0.19
Sts G Range AP	0.30	0.68	0.02	-0.02	0.11	0.17
Sts G RMS AP	0.21	0.67	0.01	-0.03	0.08	0.16
stS A RMS ML	0.12	0.57	0.03	0.35	0.02	-0.05
stS JS V	0.34	-0.02	0.83	0.14	-0.06	0.03
stS JS ML	0.05	0.20	0.74	0.08	-0.05	-0.04
stS JS AP	0.07	0.06	0.73	0.53	0.01	-0.01
Duration stS	-0.11	-0.15	0.68	-0.25	-0.24	0.12
SD Duration stS	-0.21	-0.01	0.55	0.01	-0.20	0.03
stS A Range AP	0.21	0.16	0.10	0.90	0.10	0.14
stS A RMS AP	0.35	0.13	-0.02	0.82	0.01	0.26
Sts JS V	0.54	0.17	-0.16	0.05	0.74	-0.06
Sts JS AP	0.14	0.14	-0.06	0.07	0.79	0.42
Sts JS ML	0.08	0.59	-0.18	0.06	0.69	-0.12
Duration Sts	0.10	0.05	-0.37	0.03	0.72	-0.31
Sts A Range AP	0.08	0.17	0.09	0.12	0.02	0.92
Sts A RMS AP	0.19	0.15	0.00	0.12	-0.09	0.88
stS A Range ML	0.13	0.38	0.10	0.48	0.10	0.04
stS G Range AP	0.26	0.29	0.07	0.28	0.00	-0.06
SD Duration Sts	-0.17	-0.11	-0.26	0.27	0.31	-0.07
stS G RMS AP	0.16	0.38	0.04	0.24	-0.02	-0.08
CV %	22	35	45	54	63	70

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; RMS: Root Mean Square; SD: Standard Deviation; Sts: Sit to Stand; stS: Stand to Sit; V: Vertical

4.4.4. TUG FACTOR MODEL

Fifty outliers were identified by the robust linear regression. The factor analysis grouped 30 out of 37 sensor-based measures into 8 factors, accounting for 68% of the total variance (see Table 4.12). The resulting independent domains were labelled as: "Walking intensity", "Sit-to-Walk smoothness", "Turn-to-Sit smoothness", "180 Turn impairment", "Turn-to-Sit ability", "ML weight transfer ability", "AP weight transfer ability", and "Weight lift difficulties".

	Walki ng Intensi ty	Sit-to- Walk Smoothnes s	Turn-to-Sit Smoothnes s	180Turn impairment	Turn-to-Sit ability	ML weight transfer ability	AP weight transfer ability	Weight lift difficulties
	TUG1	TUG2	TUG3	TUG4	TUG5	TUG6	TUG7	TUG8
Range Walk A V	0.83	-0.01	0.00	-0.03	0.04	0.00	0.12	0.02
RMS Walk A V	0.83	-0.03	-0.02	0.02	0.12	-0.03	0.05	0.01
RMS Walk A ML	0.78	0.02	0.03	0.08	0.05	0.06	0.02	0.11
Range Walk A ML	0.70	0.02	0.01	0.04	-0.03	0.06	-0.01	0.09
RMS Walk A AP	0.68	0.04	0.09	-0.06	0.03	0.21	-0.03	0.05
Range Walk A AP	0.62	-0.05	0.06	-0.09	-0.08	0.15	-0.02	0.05
Peak Angular Velocity 180T	0.50	0.01	-0.05	-0.27	0.33	0.01	0.06	0.07
JS V StW	0.03	0.93	-0.05	-0.06	-0.04	0.05	0.10	0.04
JS AP StW	0.02	0.91	-0.05	-0.10	-0.02	-0.01	0.34	0.01
StW Duration	-0.07	0.89	-0.05	-0.10	-0.03	-0.10	0.11	0.01
JS ML StW	0.04	0.88	-0.02	-0.01	-0.02	0.37	0.03	-0.02
JS AP TtS	0.03	-0.03	0.98	-0.01	0.02	0.07	0.06	0.04
JS V TtS	0.05	-0.07	0.90	0.02	0.06	0.11	0.08	0.24
JS ML TtS	0.02	0.01	0.89	-0.03	-0.09	0.16	0.04	0.02
TtS Duration	0.00	-0.10	0.56	0.00	-0.24	0.08	-0.04	-0.26
NJS 180T	0.13	-0.02	0.10	0.87	-0.24	0.01	-0.03	-0.02
MV 180T	0.39	-0.07	-0.10	-0.62	0.42	-0.09	0.00	0.07
180T Duration	-0.05	-0.09	-0.03	0.86	-0.21	-0.04	-0.05	-0.01
Number of Steps 180T	-0.02	-0.13	-0.08	0.76	-0.14	-0.05	-0.11	0.03
MV TtS	0.23	-0.03	-0.07	-0.13	0.93	-0.07	0.01	0.03
TtS Duration	0.06	0.04	-0.03	0.19	-0.68	0.04	-0.05	0.01
Peak Angular Velocity TtS	0.26	-0.05	-0.08	-0.14	0.80	-0.05	0.03	0.11
NJS TtS	0.20	-0.03	0.05	0.25	-0.67	0.07	-0.04	0.08
Range A ML StW	0.10	0.11	0.06	0.04	-0.01	0.98	-0.02	0.00
RMS A ML StW	0.01	0.01	0.08	0.01	-0.06	0.92	-0.07	0.01
RMS A ML TtS	0.01	0.09	0.05	0.03	-0.16	0.55	-0.11	0.32
Range A AP StW	0.01	0.25	-0.05	-0.11	0.04	0.07	0.93	0.01
RMS A AP StW	-0.04	0.19	0.00	-0.12	-0.01	-0.05	0.93	0.06
Range A V TtS	0.18	-0.03	0.11	0.01	0.07	0.15	0.14	0.87
RMS A V TtS	0.12	0.00	-0.14	-0.02	0.03	0.16	0.16	0.89
Range A AP TtS	0.17	0.08	0.35	0.03	0.10	-0.06	0.49	0.33
Range A ML TtS	0.10	0.06	0.19	0.02	-0.16	0.43	-0.02	0.40
RMS A AP TtS	0.15	0.08	0.24	0.04	0.08	-0.06	0.48	0.34
Walk Duration	-0.10	-0.27	-0.31	0.48	0.04	-0.06	-0.07	0.24
Number of Steps	0.06	-0.18	-0.18	-0.28	0.21	0.08	-0.14	0.10
RMS A V StW	0.14	-0.15	0.13	-0.14	0.03	0.42	0.11	0.07
Range A V StW	0.26	0.14	0.03	-0.07	0.01	0.36	0.04	0.04
CV%	11	21	30	38	47	55	61	68

ACRONYMS: 180T: 180 Turn; A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; RMS: Root Mean Square; SD: Standard Deviation; StW: Sit to Walk; TtS: Turn to Sit; V: Vertical

4.4.5. CORRELATION ANALYSIS

Pearson's correlation analysis between domains and between domains and health-related measures are reported in Tables 4.13 and 4.14 respectively. Spearman correlation analysis between health-related measures is reported in Table 4.15.

		ADL	CES-D	V	ALLN	UND	WR	IMTA	SPPB	/mW tot luratio	rUG tot luratio
Ineffectiveness of the Balance Control	QS1	- .15	.08	02	.20	07	01	.10	15	.01	.09
Dynamics of the Postural Sway in AP Direction	QS2	.04	.00	.01	.09	.01	.01	.04	05	02	.00
Reactivity and Smoothness of the AP Balance Control	QS3	01	07	.01	01	02	.02	.16	.05	.01	.00
Reactivity and Smoothness of the ML Balance Control	QS4	.04	04	11	02	03	03	.04	06	.04	.05
Complexity of the Balance Control	QS5	.04	08	.08	.16	.02	06	06	.02	.00	.01
Global Performance	7MW1	02	12	.12	.04	.09	.12	11	.20	37	26
Gait Regularity	7MW2	.01	13	.12	02	.02	.04	01	.00	09	04
Gait Smoothness	7MW3	.00	.05	.04	.10	.07	.02	.08	02	.01	.00
ML Weight Shift Control	7MW4	.09	01	.03	.04	10	.05	.02	01	05	04
Gait Variability	7MW5	13	.02	04	.12	04	06	.00	01	02	.00
Range of motion	CST1	04	01	01	07	.06	.02	.00	.01	13	14
Lateral Weight Shift Control	CST2	.00	12	03	.04	.03	.07	.06	03	.01	04
Stand-to-Sit impairment	CST3	.01	.00	.00	.01	.03	01	.04	01	.02	.03
Stand-to-Sit Forward Bending	CST4	.07	.07	08	.13	03	.03	.08	.01	.08	.01
Sit-to-Stand impairment	CST5	02	.05	.00	.01	.00	.02	.10	13	.10	.10
Sit-to-Stand forward bending	CST6	.02	15	.11	07	.07	.09	.03	.17	16	19
Walking Intensity	TUG1	.02	06	.14	05	.09	.11	05	.19	26	34
Sit-to-Walk Smoothness	TUG2	.01	.00	.01	04	.01	02	.01	01	.01	.02
Turn-to-Sit Smoothness	TUG3	.03	01	03	.06	01	02	.00	10	.02	.07
180Turn impairment	TUG4	02	.03	.07	02	.01	.09	.05	.01	01	.01
Turn-to-Sit ability	TUG5	.00	11	03	.10	.03	.04	09	.09	08	16
ML weight transfer ability	TUG6	.10	04	.01	.02	07	.00	.04	03	.00	03
AP weight transfer ability	TUG7	.06	.04	04	.00	06	06	.05	15	01	.06
Weight lift difficulties	TUG8	.02	.15	.04	.04	06	09	.00	08	.04	01

Table 4.13 Correlation analysis between domains of the second version of the conceptual model and health-related measures

Correlation coefficients with a p-value < .05 are bolded

ACRONYMS: AP: Anteroposterior; CESD: Epidemiologic Studies Depression Scale; FALLN: declared number of falls; HAND. Hand-Grip strength test; IADL: Instrumental Activities of Daily Living; ML: Medio-Lateral; MMSE: Mini-Mental State Examination; PA: Physical Activity; PR. Power Rig; SPPB: Short Physical Performance Battery; TMTA: Trail Making Test A.
	Ineffectiveness of the Balance Control	Dynamics of the Postural Sway in AP Direction	Reactivity and Smoothness of the AP Balance Control	Reactivity and Smoothness of the ML Balance Control	Complexity of the Balance Control	Global Performance	Gait Regularity	Gait Smoothness	ML Weight Shift Control	Gait Variability	Range of motion	Lateral Weight Shift Control	Stand-to-Sit impairment	Stand-to-Sit Forward Bending	Sit-to-Stand impairment	Sit-to-Stand forward bending	Walking Intensity	Sit-to-Walk Smoothness	Turn-to-Sit Smoothness	180Turn impairment	Turn-to-Sit ability	ML weight transfer ability	AP weight transfer ability	Weight lift difficulties
	JS1	QS2	QS3	QS4	JS5	7MW1	7MW2	7MW3	7MW4	7MW5	CST1	CST2	CST3	CST4	CST5	CST6	rug1	rug2	rug3	rug4	rug5	rug6	rug7	rug8
QS1	U	.00	.24	.00	.00	.82	.93	.34	.01	.21	.64	.02	.07	.00	.37	.63	.52	.53	.00	.87	.77	.51	.45	.00
QS2	.40		.73	.04	.00	.34	.43	.40	.03	.58	.90	.33	.19	.03	.10	.50	.04	.22	.03	.57	.07	.48	.50	.11
QS3	.07	.02		.43	.69	.19	.08	.65	.89	.67	.18	.90	.80	.40	.57	.66	.71	.92	.17	.40	.44	.27	.54	.13
QS4	.29	.12	.05		.33	.58	.78	.97	.18	.70	.68	.61	.66	.36	.11	.83	.51	.70	.07	.89	.52	.62	.74	.02
QS5	.46	.49	02	.06		.51	.32	.05	.20	.59	.83	.66	.38	.05	.93	.25	.83	.84	.13	.78	.68	.91	.92	.13
7MW1	01	05	10	04	06		.86	.81	.04	.06	.05	.58	.67	.29	.16	.41	.95	.88	.11	.45	.98	.37	.57	.92
7MW2	03	07	.13	.00	.04	28		.81	.59	.54	.70	.02	.76	.24	.70	.55	.44	.77	.28	.92	.79	.89	.59	.71
7MW3	.10	.09	.02	02	.16	.05	.01		.61	.00	.03	.01	.18	.27	.32	.89	.56	.66	.33	.98	.85	.86	.93	.36
7MW4	.16	.13	.01	08	.09	.13	11	.04		.82	.33	.31	.20	.47	.37	.06	.81	.64	.28	.55	.89	.46	.92	.51
7MW5	.08	.03	05	.03	.04	.16	.06	.14	02		.06	.92	.95	.42	.33	.00	.58	.03	.30	.11	.00	.04	.52	.06
CST1	.06	.01	.10	.02	.02	.14	.04	.14	.09	15		.17	.82	.83	.84	.66	.91	.50	.90	.01	.55	.10	.05	.60
CST2	08	10	05	.05	.01	12	14	07	.08	.00	13		.13	.09	.01	.04	.34	.54	.14	.02	.42	.00	.25	.24
CST3	.12	.09	.01	.09	.11	.06	13	.14	02	.10	.09	.15		.01	.30	.79	.00	.35	.00	.59	.06	.60	.85	.01
CST4	.14	.15	.03	10	.06	16	.00	.14	.05	.03	.05	51	.08		.98	.64	.06	.24	.00	.00	.41	.43	.06	.00
CST5	.15	.05	01	.01	.00	.09	14	.20	.05	06	.03	.10	.19	06		.16	.16	.40	.97	.60	.44	.67	.62	.31
CST6	07	06	.03	.01	.05	.11	.04	07	.15	23	.02	.24	05	.00	.05		.03	.16	.84	.14	.05	.70	.26	.52
TUG1	04	.13	02	.04	01	.00	.05	04	02	.04	01	07	20	.13	.10	16		.10	.71	.07	.08	.29	.09	.23
TUG2	.04	.08	01	.02	01	01	02	03	.03	14	05	.04	07	.08	.06	.10	10		.00	.00	.00	.00	.00	.00
TUG3	.26	.13	09	.11	.09	10	07	.06	.07	07	.01	.10	24	.25	.00	.01	02	.19		.02	.00	.01	.01	.00
TUG4	.01	.04	05	01	.02	.05	01	.00	.04	10	.18	.17	04	.32	04	.11	11	.93	.15		.00	.00	.00	.00
TUG5	.02	.11	.05	.04	03	.00	.02	.01	.01	.28	04	06	.13	06	.06	14	.11	55	19	54		.00	.00	.00
TUG6	04	.04	07	03	01	.06	01	.01	.05	.13	12	.36	04	06	03	.03	.07	65	16	65	.40		.00	.00
TUG7	05	04	.04	.02	01	.04	.03	01	.01	.04	.14	08	01	13	04	.08	.11	89	15	94	.51	.63		.00
TUG8	.25	.10	09	.14	.10	.01	02	06	.04	12	04	.08	19	.24	07	.05	08	.40	.78	.38	29	31	36	
p-values	are repo	orted al	oove th	ne mair	n diago	onal ar	nd corre	elation	coeffi	cients a	are rep	orted u	nder th	ie maii	n diago	nal. C	orrelat	ion coe	efficien	nts with	a p-va	alue <	.05 are	
bolded	ALC.	A.D. A				M- 1	- T - (
ACKON	INS: :	AP: A	nterop	usterno	T: IVIL.	iviedi	o-Late	rall																

Table 4.14 Correlation Analysis between domains of the second version of the conceptual model

Table 4.15 Correlation analysis between health-related measures

		•		7	•				n of	a t
	ADL	ES-I	PA	ALLI	INN	WR	MTA	PPB	IW t ratio	JG to ratio
	Ι	C		\mathbf{F}_{i}	H	Ι	T	0 1	VL du	L np
IADL		.00	.00	.00	.00	.00	.00	.00	.00	.00
CES-D	.32		.00	.00	.00	.00	.00	.00	.00	.00
РА	73	36		.00	.00	.00	.00	.00	.00	.00
FALLN	.14	.26	14		.00	.00	.00	.00	.00	.00
HG	51	47	.55	26		.00	.00	.00	.00	.00
PR	45	40	.45	18	.76		.00	.00	.00	.00
TMTA	.51	.37	36	.21	40	38		.00	.00	.00
SPPB	68	36	.65	34	.61	.58	50		.00	.00
7MW tot duration	.52	.28	48	.25	49	53	.48	81		.00
TUG tot duration	.57	.34	57	.25	54	59	.56	79	.85	

p-values are reported above the main diagonal and correlation coefficients are reported under the main diagonal. Correlation coefficients with a p-value < .05 are shaded and bolded

ACRONYMS: IADL: Instrumental Activities of Daily Living; MMSE: Mini-Mental State Examination; CESD: Epidemiologic Studies Depression Scale; PA: Physical Activity; FALLN: declared number of falls; Battery; HAND: Hand-Grip strength test; PWR: Power Rig; TMTA: Trail Making Test A, SPPB: Short Physical Performance

4.5. DISCUSSION

One EFA was performed on the residuals of the 7MW, CST and TUG tests obtained after removing the effect of age, gender, height, weight, MMSE and total duration of each test. Slight differences were found between the conceptual models obtained both removing or not the effect of overall performance. In general, the order of the domains changed and some domains were split or mixed. For example, in the CST model the domain "Sit-to-stand impairment" was the fourth domain in the conceptual model developed without adjusting for the overall performance and the fifth domain in the latest version of the conceptual model. The name of the domain labelled as "Effectiveness of the motor control during Stand-to-Sit" (CST3), was changed in "Stand-to-Sit forward bending" because only the AP range and RMS contributed to it in the latest version of the model. The domain labelled "Turning impairment" (TUG1) was split into two domains "180 Turn impairment" (TUG4) and "Turn-to-Sit ability" (TUG5) after adjusting for the overall performance. As described in Chapter 2, the total duration of the PP test is strongly correlated with most of all the other sensor-based measures. Since sensor-based measures in the EFA are grouped based on the correlation among them, we expected some differences in the first and second version of the conceptual model after removing the overall performance. However, we have not found big differences between the two versions and this confirms the validity of the conceptual model. Correlation analyses showed fewer significant correlations between domains and health-related measures. One aspect to consider is that in the latest version of the conceptual model the effect of confounders was not removed from the health-related measures. Some associations remained significant in the two versions of the conceptual model, as the correlations between conventional measures of performance (SPPB score, total 7MW and TUG stopwatch-based time) and the "Global performance" (7MW1), "Sit-to-Stand forward bending" (CST6) and "Walking intensity" (TUG1). These findings confirm the coherence of the conceptual model. More detailed description of the results follows.

4.5.1. CONVENTIONAL OUTCOME

Compared to the first version of the conceptual model, the domains related to the older adults' fitness and ability to walk ("Global performance", 7MW1, "Sit-to-Stand forward bending", CST6, "Walking intensity", TUG1) were still significantly associated with both the stopwatch-based total 7MW and TUG durations. The total TUG duration was also associated with domains that require good cognitive capacities along with lower limbs muscle strength ("Range of motion", CST1 and "Turn-to-Sit ability", TUG5).

4.5.2. IADL

The number of instrumental activities in which the older adults required help (IADL) was significantly associated with the "Ineffectiveness of the balance control" (QS1) and the "Gait variability" (7MW5).

4.5.3. CES-D

Participants with depressive symptoms (CES-D score > 16) showed lower "Gait regularity" (7MW2), lower "Sit-to-Stand forward bending" (CST6) and higher "Weight lift impairments" (TUG8). These results confirm the findings of the first version of the model, in which older adults with higher CES-D score appeared to be less confident and strong.

4.5.4. PA

Compared to the first version of the conceptual model, only the "Gait regularity" (7MW2) and the "Walking intensity" (TUG1) were significantly associated with the declared PA. This result suggests that after deducting age, gender, body composition, cognition and overall performance, the locomotion is the only physical domain related to the daily living physical activity.

4.5.5. FALLN

The reported number of falls in the year preceding the assessment was related to the "Ineffectiveness of the balance control" (QS1) and to the "Complexity of the balance control" (QS5). This result confirms that a poor postural sway control is related to a higher fall risk.

4.5.6. HAND AND PWR

No associations between measures of strength (HAND and PWR) and domains of the conceptual model were found. Then, the high number of associations found significant in the first version of the model was probably due to the overall performance.

4.5.7. TMTA

The TMTA is a measure of time, after removing the effect of the overall performance from the sensor-based measures only the association with the "Reactivity and smoothness of the balance control" (QS3) was significant.

4.5.8. SPPB

Despite the deduction of the overall performance, a number of domains were significantly related to the SPPB score. In particular, those domains, also related to the 7MW and TUG duration, that involve strength, balance and locomotion ("Ineffectiveness of the balance control", QS1, "Global performance", 7MW1, "Sit-to-Stand forward bending", CST6, "Walking intensity", TUG1, "AP weight transfer ability", TUG7).

In conclusion, these results confirmed the validity and the coherence of the domains constituting the conceptual model. However, the residuals computed by the robust linear regression analysis, use to obtain factor scores, are unitless and difficult to interpret. This increased the complexity of the model, making difficult its understanding and use. Sometimes it was not easy to understand if a higher score corresponded to a better or worse functioning. Furthermore, it was not clear whether, the residuals obtained after removing the effect of age, gender, height, weight, MMSE and overall performance brought useful information or only noise. All these considerations led to the development of the third version of the conceptual model, which was developed starting from the sensor-based measures instead of the residuals. First, one EFA was hence performed on each set of sensor-based measures from each PP test. Second, the coherence between the various domains that make up the model has been examined both adjusting and not adjusting for age, gender, height, weight, MMSE and Number of Medications (NM). Then, the concurrent validity between the domains of the model and a set of health-related measures was investigated. Finally, we show how the model could be used to illustrate relevant case studies.

4.6. REFINEMENT OF THE CONCEPTUAL MODEL: FINAL VERSION

4.6.1. POPULATION AND METHODS

The subsample of the InCHIANTI cohort study (ClinicalTrials.gov NCT01331512) [2] included 304 community-dwelling older adults (163 females, 80.9 ± 6.4 years old, range 65-98) assessed within the framework of the EU FARSEEING project [71]. Ethical approval was obtained by the Local Ethical Committee (approval number: 584/2012).

Not all the participants were able to complete the whole battery of tests: Table 4.16 reports the demographic and functional profiles of each subgroup undertaking the tests.

	Total Population	QS	7MW	CST	TUG
Sample size	304	204	210	173	204
Gender (females)	163 (54%)	97 (48%)	95 (47%)	80 (46%)	97 (48%)
Age, years	80.90 (6.37)	79.46 (6.43)	79.39 (6.44)	79.35 (6.25)	79.47 (6.44)
Weight, kg	69.60 (13.30)	70.52 (13.13)	70.35 (13.18)	70.90 (13)	70.54 (13.21)
Height, cm	159.72 (9.53)	160.51 (9.21)	160.50 (9.20)	160.79 (8.88)	160.53 (9.21)
MMSE, (range 0-30)	27.25 (1.77)	27.41 (1.76)	27.41 (1.77)	27.53 (1.72)	27.40 (1.75)
Medications >=4	169 (56%)	98 (48%)	95 (47%)	83 (48%)	97 (48%)
IADL ≥ 1 , (range 0-8)	114 (38%)	49 (24%)	47 (23%)	39 (23%)	47 (23%)
FALL >=2	16 (5%)	5 (2%)	5 (2%)	3 (2%)	11 (5%)
FALL history >=2	19 (6%)	11 (5%)	10 (5%)	7 (4%)	5 (2%)
CES-D >= 16, (range 0-60)	106 (35%)	58 (28%)	57 (28%)	49 (28%)	57 (28%)
PA, categories, (range 1-7)	2.91 (1.01)	3.16 (0.98)	3.15 (0.99)	3.24 (1.01)	3.15 (0.98)
SPPB, (range 0-12)	8.72 (3.18)	9.80 (1.98)	9.82 (1.98)	9.92 (1.87)	9.79 (1.99)
HAND, kg	26.98 (9.26)	28.85 (8.98)	28.81 (9.00)	29.09 (8.97)	28.78 (8.96)
PWR, watt	88.69 (51.28)	94.71 (51.28)	95.21 (51.62)	94.96 (48.54)	94.87 (51.54)
TMTA, s	78.37 (43.94)	70.51 (36.50)	70.69 (36.59)	69.48 (35.19)	70.47 (36.37)
Gait speed, m/s	1.11 (0.26)	1.15 (0.25)	1.15 (0.25)	1.15 (0.24)	1.14 (0.25)
Values are presented as mean	± sd or number (%), unless otherv	vise indicated.		

Table 4.16 Demographic and functional profiles of each subgroup undertaking the four functional tests

Acronyms: MMSE: mini-mental state examination; IADL: instrumental activities of daily living; FALL: prospective falls; FALL history: the number of falls in the last year declared during the assessment; CES-D: center for epidemiologic studies depression scale; PA: physical activity; SPPB: short physical performance battery;

HAND: the hand-grip strength test; PWR: lower extremity muscle power; TMTA: trail making test A

Gait speed, obtained from the distance covered (7 meters) and the total time taken to complete the test [m/s], Number of Medication (NM) and prospective falls (FALL) were assessed in addition to the health-related measures collected and already described in section 3.1.2. Linear regression analysis was used to investigate the association between domains in the conceptual model and the associations between each domain and the health-related measures. First, the linear regression was computed without adjusting for any covariate and then adjusting for age, gender, height, weight,

MMSE and NM. All statistical analyses were performed using R for Windows, version 3.4.3 [63]. Figure 4.2 shows the flowchart of the conceptual model development process.

4.6.2. RESULTS

Sensor-based measures contributing to each factor obtained from the exploratory factor analysis performed on each test of the battery and corresponding domains are shown in Table 4.17.



Figure 4.2 flowchart of the third version of the conceptual model development process

Domains	Original Features	Domains	Original Features	Domains	Original Features	Domains	Original Features
Quiet	Standing	7-Mete	ers Walk	Repeated Ch	air Standing		Timed Up and Go
Postural instability (QS1)	Range A ML RMS A ML SA DISPL SP ML DISPL MV ML DISPL EA DISPL SP Planar DISPL Range A AP RMS A AP	Walking impairment (7MW1)	Range A V RMS A V Range A AP RMS A AP Range A ML RMS A ML Cadence Total duration	Dynamic postural impairment (CST1)	Sts G RMS ML Sts G Range ML stS A RMS V stS G RMS ML Sts A Range V Sts A RMS V stS A Range V stS G Range ML	Shakiness (TUG1)	RMS Walk A ML RMS Walk A V Range Walk A V Range Walk A ML Range Walk A AP Range A ML TtS Peak Angular Velocity 180T Peak Angular Velocity TtS RMS Walk A AP MV TtS
AP postural reaction time and jerkiness (QS2)	CF AP F95 AP NJS AP F50 AP	Gait irregularity (7MW2)	Stride Reg V Stride Reg AP Step Reg V Step Reg AP Stride Reg ML	Sit-to-Stand jerkiness (CST2)	Sts JS V Sts JS AP Sts JS ML Duration Sts SD Duration Sts Total Duration	Turning impairment (TUG2)	NJS 180T 180T Duration Number of Steps 180T NJS TtS MV 180T TtS turning duration
ML postural reaction time and jerkiness (QS3)	CF ML F95 ML NJS ML F50 ML	Gait jerkiness (7MW3)	NJS V NJS AP	ML dynamic postural Instability (CST3)	Sts A RMS ML Sts A Range ML Sts G RMS AP stS A RMS ML Sts G Range AP stS A Range ML	Turn-to-Sit jerkiness (TUG3)	JS AP TtS JS ML TtS JS V TtS TtS Duration
AP postural control impairment (QS4)	MV AP DISPL SP AP DISPL	ML Gait instability (7MW4)	NJS ML Step Reg ML	Stand-to-Sit jerkiness (CST4)	stS JS AP stS JS ML stS JS V Duration stS SD Duration stS	Sit-to-Walk jerkiness (TUG4)	JS V StW JS AP StW JS ML StW StW Duration
NI	SE ML SE AP FD ML FD AP	Gait variability (7MW5)	PCI SD Cadence	AP Stand-to-Sit weakness (CST5)	stS A Range AP stS A RMS AP	AP postural transitions weakness (TUG5)	RMS A AP StW Range A AP StW RMS A AP TtS Range A AP TtS
				AP Sit-to-Stand weakness (CST6)	Sts A Range AP Sts A RMS AP	Walking impairment (TUG6)	Walk Duration Number of Steps Total Duration
				NI	stS G Range AP stS G RMS AP	ML Sit-to- Walk weakness (TUG7)	Range A ML StW
						V Turn-to- Sit weakness (TUG8)	RMS A V TtS Range A V TtS
						NI	RMS A ML TtS RMS A V StW Range A V StW

Table 4.17 Sensor-based measures contributing to each factor of the third version of the conceptual model, for each instrumented test

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CF: Centroidal Frequency; DISPL: displacement; EA: Ellipse Area; FD: Frequency Dispersion; F50: median frequency, F95: frequency bandwidth; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; MV: Mean Velocity; NI: Not Included in the model; NJS: Normalized Jerk Score; PCI: Phase Coordination Index; Reg: Regularity; RMS: Root Mean Square; SA: Sway Area; SD: Standard Deviation; SE: Spectral Entropy; SP: Sway Path; Sts: Sit to Stand; stS: Stand to Sit; V: Vertical

4.6.2.1. **QS** FACTOR MODEL

The factor analysis grouped 19 out of 23 sensor-based measures into 4 factors, accounting for 70% of total variance (see Table 4.18). The resulting independent domains were labelled as: "Postural impairment", "AP postural reaction time and jerkiness", "ML postural reaction time and jerkiness", "AP postural control impairment".

Domain	Postural Instability	AP Postural Reaction	ML Postural Reaction	AP Postural Control
Domani	i osturar mstaonity	Time and Jerkiness	Time and Jerkiness	Impairment
Factor	QS1	QS2	QS3	QS4
Range A ML	0.95	-0.11	-0.15	0.07
RMS A ML	0.93	-0.01	-0.25	0.02
SA DISPL	0.93	0.01	-0.07	0.13
SP ML DISPL	0.87	-0.14	-0.10	0.18
MV ML DISPL	0.80	-0.12	-0.11	0.20
EA DISPL	0.77	0.06	-0.12	-0.03
SP Planar DISPL	0.76	-0.06	-0.08	0.63
Range A AP	0.71	0.19	-0.11	0.43
RMS A AP	0.68	0.29	-0.14	0.30
CF AP	-0.13	-0.98	0.11	0.00
F95 AP	-0.10	-0.92	0.14	-0.07
NJS AP	0.12	-0.79	0.11	-0.13
F50 AP	-0.13	-0.77	0.10	0.17
CF ML	-0.20	-0.20	0.96	-0.02
F95 ML	-0.26	-0.15	0.87	-0.05
NJS ML	-0.05	-0.17	0.85	-0.11
F50 ML	-0.09	-0.21	0.79	-0.01
MV AP DISPL	0.53	-0.01	-0.10	0.80
SP AP DISPL	0.63	0.00	-0.08	0.77
SE ML	-0.17	0.03	0.23	-0.04
SE AP	0.12	-0.31	0.09	-0.07
FD ML	-0.07	0.18	-0.16	-0.11
FD AP	0.02	-0.28	0.03	-0.30
CV %	31	46	61	70

Table 4.18 Factor loadings of the third version of the QS conceptual model

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CF: Centroidal Frequency; CV: Cumulative Variance; EA: Ellipse Area; F50: Median Frequency; F95: Frequency below 95% of total signal power; FD: Frequency Dispersion; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; MV: Mean Velocity; NJS: Normalized Jerk Score; RMS: Root Mean Square; SA: Sway Area; SD: Standard Deviation; SE: Spectral Entropy; SP: Sway Path; V: Vertical.

4.6.2.2. 7MW FACTOR MODEL

The factor analysis grouped all 19 sensor-based measures into 5 factors, accounting for 77% of total variance (see Table 4.19). The resulting independent domains were labelled as: "Walking impairment", "Gait irregularity", "Gait jerkiness", "ML Gait instability", "Gait variability".

Domains	Walking	Gait Irregularity	Gait Jerkiness	ML Gait Instability	Gait Variability
	Impairment		=> 6110		
Factors	7MW1	7MW2	7MW3	7MW4	7MW5
Range A V	-0.92	-0.03	-0.12	0.04	-0.05
RMS A V	-0.91	-0.28	-0.11	0.05	-0.11
Range A AP	-0.88	-0.05	-0.16	0.11	-0.10
RMS A AP	-0.87	-0.18	-0.12	0.18	-0.14
Range A ML	-0.74	0.23	-0.11	0.52	-0.01
RMS A ML	-0.73	0.07	0.04	0.68	-0.01
Cadence	0.71	0.25	-0.65	0.01	0.05
Total duration	0.66	0.39	0.02	0.01	0.24
Stride Reg V	-0.16	-0.84	-0.01	-0.12	-0.16
Stride Reg AP	0.09	-0.82	-0.01	0.13	-0.17
Step Reg V	-0.28	-0.74	0.00	-0.15	-0.22
Step Reg AP	-0.15	-0.66	-0.06	0.07	-0.22
Stride Reg ML	-0.03	-0.63	0.18	0.45	0.01
NJS V	-0.13	0.05	-0.83	-0.01	0.15
NJS AP	-0.40	-0.18	-0.66	0.08	-0.12
NJS ML	-0.18	0.06	-0.39	0.67	-0.01
Step Reg ML	-0.07	-0.39	0.20	0.56	0.00
PCI	0.12	0.27	-0.01	0.00	0.89
SD Cadence	0.23	0.39	-0.12	-0.02	0.84
CV %	30	48	58	68	77

Table 4.19 Factor loadings of the third version of the 7mWT conceptual model

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance. G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; PCI: Phase Coordination Index; Reg: Regularity; RMS: Root Mean Square; SD: Standard Deviation; V: Vertical.

4.6.2.3. CST FACTOR MODEL

The factor analysis grouped 29 out of 31 instrumented measures into 6 factors, accounting for 80% of total variance (see Table 4.20). The resulting independent domains were labelled as: "Dynamic postural impairment", "Sit-to-Stand jerkiness", "ML dynamic postural instability", "Stand-to-Sit jerkiness", "AP Stand-to-Sit weakness", "AP Sit-to-Stand weakness".

Domains	Dynamic Postural Impairment	Sit-to-Stand Jerkiness	ML Dynamic Postural Instability	Stand-to-Sit Jerkiness	AP Stand-to-Sit Weakness	AP Sit-to-Stand Weakness
Factors	CST1	CST2	CST3	CST4	CST5	CST6
Sts G RMS ML	-0.90	-0.01	-0.12	-0.14	0.00	-0.06
Sts G Range ML	-0.85	0.03	-0.16	-0.05	-0.03	-0.29
stS A RMS V	-0.84	0.12	-0.20	0.26	-0.10	0.10
stS G RMS ML	-0.83	-0.20	-0.14	-0.15	-0.25	-0.04
Sts A Range V	-0.83	0.13	-0.21	0.39	0.00	0.07
Sts A RMS V	-0.81	0.13	-0.18	0.39	0.09	0.15
stS A Range V	-0.70	0.09	-0.23	0.11	-0.40	-0.09
stS G Range ML	-0.66	-0.13	-0.17	-0.09	-0.45	-0.15
Sts JS V	-0.21	0.91	0.08	0.21	0.12	0.08
Sts JS AP	-0.05	0.91	0.07	0.24	-0.10	0.13
Sts JS ML	-0.05	0.90	-0.03	0.21	0.15	0.13
Duration Sts	0.03	0.85	0.18	0.29	0.33	0.15
SD Duration Sts	0.15	0.72	0.02	-0.11	0.03	-0.08
Total Duration	-0.04	0.71	0.17	0.53	0.28	0.24
Sts A RMS ML	-0.06	0.02	-0.94	-0.05	-0.13	-0.16
Sts A Range ML	-0.12	0.01	-0.92	0.01	-0.13	-0.25
Sts G RMS AP	-0.26	-0.09	-0.65	-0.01	-0.05	-0.10
stS A RMS ML	-0.13	-0.14	-0.64	-0.11	-0.40	-0.05
Sts G Range AP	-0.39	-0.09	-0.64	0.08	-0.04	-0.11
stS A Range ML	-0.12	-0.06	-0.51	-0.08	-0.50	-0.11
stS JS AP	-0.16	0.23	0.04	0.91	0.10	-0.12
stS JS ML	-0.11	0.29	-0.23	0.86	0.12	0.22
stS JS V	-0.35	0.30	0.06	0.84	0.14	0.17
Duration stS	-0.10	0.40	0.16	0.78	0.20	0.34
SD Duration stS	0.21	-0.08	0.15	0.60	-0.13	0.09
stS A Range AP	-0.14	-0.16	-0.29	-0.07	-0.86	-0.19
stS A RMS AP	-0.21	-0.30	-0.30	-0.14	-0.76	-0.28
Sts A Range AP	-0.08	-0.22	-0.30	-0.24	-0.23	-0.84
Sts A RMS AP	-0.14	-0.22	-0.32	-0.28	-0.22	-0.79
stS G Range AP	-0.32	-0.06	-0.40	-0.06	-0.34	0.07
stS G RMS AP	-0.22	-0.13	-0.45	-0.11	-0.32	0.11
CV %	19	35	50	64	73	80

Table 4.20 Factor loadings of the third version of the CST conceptual model

ACRONYMS: A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; RMS: Root Mean Square; SD: Standard Deviation; Sts: Sit to Stand; stS: Stand to Sit; V: Vertical.

4.6.2.4. TUG FACTOR MODEL

The factor analysis grouped 35 out of 38 instrumented measures into 8 factors, accounting for the 77% of the total variance (see Table 4.21). The resulting independent domains were labelled as "Shakiness", "Turning impairment", "Turn-to-Sit jerkiness", "Sit-to-Walk jerkiness", "AP postural transitions weakness", "Walking impairment", "ML Sit-to-Walk weakness", "V Turn-to-Sit weakness".

Table 4.21 Factor loadings of the third	l version of the TUG conceptual model
-----------------------------------------	---------------------------------------

Domain	Walking impairment	Turning impairment	Turn-to-Sit Jerkiness	Sit-to-Walk Jerkiness	AP postural transitions weakness	Shakiness	ML Sit-to-Walk weakness	V Turn-to-Sit weakness
Factor	TUG1	TUG2	TUG3	TUG4	TUG5	TUG6	TUG7	TUG8
RMS Walk A ML	-0.81	-0.10	-0.06	0.01	0.02	-0.05	-0.21	-0.14
RMS Walk A V	-0.77	-0.24	-0.17	-0.17	-0.01	-0.29	-0.09	-0.11
Range Walk A V	-0.73	-0.20	-0.16	-0.16	-0.07	-0.18	-0.08	-0.13
Range Walk A ML	-0.73	-0.09	-0.04	-0.02	0.01	-0.07	-0.19	-0.16
Range Walk A AP	-0.71	-0.25	-0.09	-0.11	-0.08	-0.10	-0.06	-0.05
Range A ML TtS	-0.62	-0.02	-0.06	-0.11	-0.05	-0.18	-0.10	-0.34
Peak Angular Velocity 180T	-0.66	-0.52	-0.20	-0.14	-0.06	-0.17	-0.03	0.06
Peak Angular Velocity TtS	-0.56	-0.48	-0.39	-0.19	0.00	-0.10	-0.03	0.00
RMS Walk A AP	-0.58	-0.26	-0.22	-0.02	-0.20	-0.15	-0.04	-0.04
MV TtS	-0.56	-0.53	-0.40	-0.13	0.02	-0.07	-0.05	0.07
NJS 180T	0.12	0.87	0.26	0.11	-0.03	0.03	0.01	-0.01
180T Duration	0.27	0.83	0.28	0.15	-0.03	0.28	0.02	0.18
Number of Steps 180T	0.19	0.79	0.19	0.12	0.02	0.10	0.03	0.13
NJS TtS	0.17	0.61	0.37	-0.02	-0.02	-0.01	-0.02	-0.18
MV 180T	-0.57	-0.66	-0.26	-0.18	0.00	-0.17	-0.02	0.04
TtS turning duration	0.37	0.58	0.38	0.06	0.00	0.21	0.00	0.00
JS AP TtS	0.18	0.34	0.87	0.09	-0.13	0.13	0.04	0.02
JS ML TtS	0.18	0.39	0.84	0.08	-0.06	0.11	0.02	0.03
JS V TtS	0.18	0.39	0.84	0.11	-0.13	0.13	-0.02	-0.08
TtS Duration	0.27	0.37	0.78	0.16	-0.02	0.28	0.06	0.24
JS V StW	0.07	0.06	0.05	0.94	-0.09	-0.01	-0.08	-0.01
JS AP StW	0.11	0.11	0.09	0.94	-0.22	0.06	0.02	0.03
JS ML StW	0.08	0.11	0.09	0.90	-0.02	0.07	-0.30	-0.06
StW Duration	0.20	0.19	0.15	0.90	0.04	0.21	0.14	0.02
RMS A AP StW	0.06	-0.01	0.06	0.03	-0.91	0.02	0.03	-0.02
Range A AP StW	-0.08	0.02	-0.04	0.17	-0.91	-0.08	-0.04	0.05
RMS A AP TtS	-0.05	0.00	0.08	0.08	-0.61	-0.02	0.03	-0.31
Range A AP TtS	-0.18	0.10	0.26	0.03	-0.56	0.03	-0.03	-0.31
Walk Duration	0.42	0.23	0.21	0.14	0.03	0.83	0.07	0.08
Number of Steps	0.42	0.13	0.20	0.11	0.09	0.79	0.04	0.06
Total Duration	0.39	0.41	0.40	0.28	0.01	0.63	0.08	0.15
Range A ML StW	-0.31	-0.04	-0.02	0.20	0.04	-0.10	-0.87	-0.10
RMS A ML StW	-0.23	0.03	-0.02	0.02	-0.05	0.00	-0.79	-0.08
RMS A V TtS	-0.39	-0.08	-0.18	0.01	-0.40	-0.10	-0.11	-0.60
Range A V TtS	-0.37	0.01	0.06	0.07	-0.28	-0.05	-0.11	-0.59
RMS A ML TtS	-0.46	-0.07	-0.26	-0.08	-0.15	-0.12	-0.15	-0.37
RMS A V StW	-0.35	-0.29	-0.03	-0.15	-0.38	-0.15	-0.30	0.05
Range A V StW	-0.46	-0.25	-0.08	0.08	-0.11	-0.27	-0.26	0.07
CV%	18	32	43	54	62	68	73	77

ACRONYMS: 180T: 180 Turn; A: Accelerometer; AP: Antero-Posterior; CV: Cumulative Variance; G: Gyroscope; JS: Jerk Score; JS: Time-Normalized Jerk Score; M: Mean; ML: Medio-Lateral; NJS: Normalized Jerk Score; RMS: Root Mean Square; SD: Standard Deviation; StW: Sit to Walk; TtS: Turn to Sit; V: Vertical

4.6.2.5. LINEAR REGRESSION ANALYSIS

The results of the linear regression analysis between the domains of the conceptual model are reported in Table 4.22. The linear regression analysis between the domains of the conceptual model and the health-related measures provided results reported in Table 4.23. Beta coefficients with a p-value \leq 0.05 are shaded and bolded. The results of the linear regression analysis between health-related measures are reported in Table 4.24.

Table 4.22 Linear regression analysis between domains

	QS1	QS2	QS3	QS4	7MW1	7MW2	7MW3	7MW4	7MW5	CST1	CST2	CST3	CST4	CST5	CST6	TUG1	TUG2	TUG3	TUG4	TUG5	TUG6	TUG7	TUG8
OS1		.00	01	.02	.16	.12	11	.13	.10	03	.26	10	.38	21	.17	.09	.16	.18	.16	06	.03	08	05
QS2	.00		.00	.00	03	.11	.04	.05	03	.08	.08	.06	.02	03	.06	02	.04	08	.08	.14	.10	05	06
QS3	01	.00		.00	.06	.03	00	12	.02	.02	02	06	12	04	.01	.05	.01	05	.06	06	.03	03	.16
QS4	.02	.00	.00		.15	.12	01	.03	01	06	.07	.00	.30	.02	.15	.04	.27	.13	.15	05	10	08	.08
7MW1	.17	03	.06	.16		.02	02	03	.00	.15	.28	.17	.32	.15	.32	.62	.25	.16	.13	.08	.27	.06	.07
7MW2	.13	.12	.04	.14	.02		02	.03	.05	02	.25	18	.17	14	.14	.04	.20	.21	.18	07	.24	09	07
7MW3	12	.04	00	01	02	02		02	.01	.05	11	.30	11	.08	.17	.12	16	09	01	.16	.05	05	.16
7MW4	.14	.05	13	.03	03	.03	02	0.1	.00	10	.05	02	.11	03	12	32	.05	.07	.11	.05	.19	15	07
/MW5	.11	03	.02	02	.00	.04	.01	01	10	.13	.15	02	.08	.00	.18	.11	.23	.10	02	.02	.10	10	11
CST1 CST2	02	.09	.02	05	.13	02	.05	11	.12	00	.00	.01	01	.01	.00	.15	.05	.10	.01	.54	04	07	.11
CST2	.41	.09	02	.05	.25	- 15	11	- 02	- 02	.00	00	.00	.01	.01	.00	.17	• 21	- 03	- 02	14	.08	.00	14
CST4	30	.00	- 12	24	27	15	- 11	02	02	- 01	.00	00	.00	.02	.02	.23	13	2.1	23	- 24	- 03	- 02	02
CST5	17	03	04	.01	.13	12	.09	03	.00	.01	.01	.02	.01	.01	.01	.22	.00	02	15	07	03	.02	.13
CST6	.14	.07	.01	.12	.27	.12	.17	12	.17	.00	.00	.02	.01	.01		.36	.10	07	.09	04	.14	.09	01
TUG1	.10	02	.05	.04	.66	.04	.13	34	.11	.17	.21	.29	.23	.25	.41		.03	.00	.01	.01	.03	.03	.01
TUG2	.17	.04	.01	.29	.25	.19	16	.05	.22	.08	.30	05	.18	.00	.14	.02		.02	.00	.00	.00	01	.01
TUG3	.19	08	06	.13	.16	.20	09	.07	.09	.12	.32	04	.24	03	08	.00	.02		.00	01	.00	.00	.01
TUG4	.16	.08	.06	.16	.13	.17	01	.10	01	.02	.01	02	.24	15	.09	.01	.00	.00		01	.00	01	.00
TUG5	07	.15	06	05	.09	07	.17	.05	.02	.58	16	.06	26	07	05	.01	.00	01	01		.00	01	.02
TUG6	.03	.10	.04	10	.27	.22	.05	.19	.10	08	.16	.01	05	06	.26	.03	.00.	.00	.00.	.00	0.1	01	.01
TUG/	09	06	04	09	.07	09	06	16	10	07	.00	.23	02	.08	.09	.03	01	.00	01	01	01	0.2	.02
TUG8	06	06	.18	.10	.09	0/	.18	08	12	.17 E and	22	03	05	.19	01	.01	.01	.02	.00	.02	.01	.02	
CS1	iajusi	04	or Age	e, Gen	1000000000000000000000000000000000000	-neign	<u>t, we</u>	<u>1gnt, 1</u>	VINS.	E and	16	11	27	24	16	01	00	10	1.4	02	02	07	01
082	04	.04	01	04	.05	.05	07	.17	- 01	02	.10	11	.41	24	.10	01	.08	.10	.14	05 14	.05	07	01
053	01	.00	.00	01	.01	.04	00	08	01	.02	01	05	12	02	.00	.01	.02	05	.06	05	.05	04	.15
OS4	04	.01	01		.05	.05	03	.04	06	02	.02	10	.13	.00	.04	07	.18	.06	.13	.00	14	07	.14
7MW	.06	.01	.07	.06		09	12	.05	07	.24	.26	.06	.21	.13	.17	.47	.19	.09	.11	.17	.24	.09	.21
1 7MW	06	.18	05	06	- 08		05	01	- 01	00	.18	- 16	05	- 15	15	- 01	08	11	.16	- 02	.28	- 05	- 02
2 7MW	10	00	01	04	12	06	100	00	10	.05	05	26	16	07	0.0	07	.00	02	05	00	1.4	10	11
3	10	00	.01	04	13	.00		09	.10	.05	.05	.20	10	.07	00	.07	09	.02	00	.09	14	10	.11
7MW 4	.19	.05	10	.04	.04	.01	07		.04	08	.10	.00	.11	.00	08	23	.05	.10	.13	.04	.20	13	10
7MW	.06	01	.01	06	05	01	.08	.04		.14	.08	.02	.01	.01	.21	.06	.16	.03	03	.05	.13	08	07
CST1	- 02	10	02	- 02	16	00	03	- 08	14		- 01	03	08	01	- 01	14	05	13	03	50	- 04	- 07	11
CST2	13	13	- 01	01	.18	.16	.05	11	.14	- 01	-,01	.03	- 06	.01	02	.12	.05	.18	- 02	- 12	.14	04	- 07
CST2	09	.06	06	08	.04	14	.19	.00	.02	.03	.04	.01	06	01	12	.16	04	.01	03	.09	05	.22	02
CST4	.25	.05	16	.12	.16	.05	14	.13	.01	.10	08	07		.00	08	.12	.04	.13	.23	15	03	.03	.03
CST5	18	03	05	.00	.08	12	.05	.00	.01	.01	.01	01	.00		04	.16	.00	01	16	08	04	.07	.13
CST6	.14	.10	.00	.04	.13	.14	06	09	.24	02	.02	13	08	05		.18	.11	05	.10	09	.10	.10	03
TUG1	02	.01	.05	10	.54	01	.08	31	.08	.23	.20	.25	.16	.26	.25		11	09	06	.05	10	.01	.13
TUG2	.09	.09	.02	.22	.17	.08	08	.05	.18	.08	.17	06	.05	.00	.15	09		17	05	.07	.02	.06	.14
TUG3	11	.05	.06	07	07	11	02	09	03	16	22	01	13	.02	.05	.07	.15		.03	06	04	05	11
TUG4	.13	.08	.06	.12	.08	.14	03	.11	03	.03	02	03	.18	16	.08	04	04	03		.00	01	.01	.01
TUG5	03	.17	06	.00.	.14	02	.07	.04	.05	.58	14	.10	14	09	08	.04	.07	.06	.00	0.5	05	.01	04
TUG6	.03	.10	.05	14	.18	.25	11	.19	.13	09	.26	09	04	09	.16	07	.02	.04	02	05	0.1	01	01
TUG9	07	08	05	U/ 16	.07 19	05	U8	12	08	07	.04	.21	.03	.07	.08	.01	.05	.05	.01	.01	01	02	.01
Only Bo	oeffi	cients	with	a n-v	alue «	< 0.04	5 are 1	older	1	.10	-,11	.05	.04	.44	.04	.11	.13	.12	.02	.05	01	.02	

Table 4.23 Linear regression analysis between domains and health-related measures

QS1 0.091 0.069 0.054 -0.088 -0.721 -0.966 -4.357 8.835 -0.059 QS2 0.099 0.002 -0.109 0.004 0.127 -0.035 1.732 4.713 4.013 -0.000 QS4 0.033 -0.005 0.018 -0.077 -1.373 -7.576 9.340 -0.039 7MW1 -0.133 -0.066 -0.0103 0.283 0.730 0.734 -10.439 -8.028 0.092 7MW2 -0.066 -0.013 -0.283 0.730 -0.577 -1.373 -1.575 -0.011 -0.3851 -16.295 -0.270 -0.011 7MW3 0.023 -0.070 0.076 -0.175 -0.071 -0.3851 -14.293 0.021 -0.011 -0.495 -0.391 -3.496 3.815 -0.024 -0.025 -0.271 -0.031 -0.022 -1.550 -0.270 -0.014 0.035 -0.079 -0.014 0.036 -0.272 -1.550 -0.270		IADL	FALL history	CES-D	PA	SPPB	HAND	PWR	TMTA	Gait speed
QS2 0.009 0.002 0.019 0.014 0.172 -0.035 1.732 4.713 -0.066 QS3 0.034 -0.021 -0.031 0.005 -0.134 -1.0402 1.932 4.713 -0.066 QS4 0.033 -0.050 0.057 -0.137 1.317 3.038 19.142 -14.173 0.009 7MW1 -0.033 -0.070 0.076 -0.175 -0.071 -3.851 -16.295 -0.270 -0.011 7MW2 0.008 -0.070 0.0176 -0.0175 -0.071 -3.851 -16.295 -0.270 -0.011 7MW3 0.000 0.0100 0.079 0.004 -0.054 -0.334 2.786 1.346 0.084 CST1 -0.014 0.022 -1.550 -4.761 10.786 -0.070 CST3 0.021 0.031 -0.107 0.102 -0.021 0.026 -1.550 -4.761 10.786 -0.070 CST3 0.024 <	051	0.091	0.069	0.054	-0.088	-0.721	-0.966	-4 337	8.835	-0.059
QS3 0.034 -0.027 -0.031 -0.095 -0.134 -0.402 -1.994 1.431 -0.010 QS4 0.033 -0.005 0.083 -0.097 -1.373 7.756 9.340 -0.039 7MW1 -0.103 0.004 -0.1127 0.071 -3.851 -16.295 -0.270 -0.011 7MW2 -0.086 -0.070 0.076 -0.175 -0.071 -3.851 -16.295 -0.270 -0.011 7MW4 0.005 -0.017 -0.071 -3.851 -16.295 -0.270 -0.011 7MW5 0.016 0.017 -0.024 -0.086 -0.391 -3.496 3.815 -0.024 CST1 -0.042 0.016 -0.122 -1.250 -1.711 0.338 -2.908 -0.131 -0.021 -0.034 0.089 -1.914 0.089 -1.914 0.089 -1.915 0.338 -0.250 -1.761 -0.038 -0.250 -1.761 0.038 -0.071 -0.131 <	OS2	0.009	0.002	-0.109	0.004	0.127	-0.035	1.732	4.713	-0.006
Q84 0.033 -0.005 0.058 -0.077 -1.373 -7.576 9.340 -0.039 7MW1 -0.036 -0.050 -0.103 0.2383 0.730 0.754 7.039 8.028 0.070 7MW2 -0.036 -0.050 -0.113 -0.037 -0.568 4.473 -1.953 0.021 7MW3 0.018 -0.037 -0.037 -0.568 4.473 -1.953 0.051 7MW5 0.010 -0.0495 -0.037 -0.568 4.473 -1.953 0.051 CST1 -0.047 0.010 -0.0495 -0.374 2.786 1.448 0.038 CST2 0.074 0.020 -0.024 0.036 0.290 1.036 9.480 1.448 0.038 CST5 0.074 0.022 -0.140 -0.922 -1.150 -1.471 10.025 CST5 0.014 0.025 CST5 0.014 0.026 9.480 1.641 0.016 CST5 -0.051 -0.0	083	0.034	-0.027	-0.031	-0.095	-0.134	-0.402	-1.994	1.431	-0.010
ST MW1 -0.133 -0.004 -0.127 0.377 1.317 3.088 19.142 -14.173 0.206 TMW2 -0.086 0.050 -0.103 0.283 0.730 0.754 7.039 -8.028 0.092 TMW3 0.023 -0.070 -0.077 -3.851 1-16.295 0.070 -0.011 TMW4 0.005 0.018 -0.037 -0.508 4.473 -1.051 0.021 TMW5 0.010 0.079 0.092 -0.024 0.055 0.514 2.786 1.448 0.038 CST1 -0.012 0.016 0.022 -1.051 0.4495 6.339 -0.088 CST5 0.001 0.023 -0.014 0.003 0.290 1.1636 9.480 1.641 0.0102 CST6 0.063 0.015 0.046 -0.140 -0.922 -1.550 4.761 10.736 -0.094 TUG2 0.067 0.033 0.031 0.012 0.775	QS4	0.033	-0.005	0.058	-0.097	-0.577	-1.373	-7.576	9.340	-0.039
7MW2 -0.086 -0.050 -0.103 0.283 0.730 0.754 7.039 -8.028 0.092 7MW3 0.023 -0.070 0.076 -0.071 -3.881 -16.295 -0.270 -0.011 7MW4 0.005 -0.037 -0.088 4.473 -1.955 0.021 7MW5 0.016 0.079 0.009 -0.104 0.036 0.334 2.786 1.448 0.038 CST1 -0.074 0.025 -0.097 -0.914 0.086 -4.985 6.339 -0.038 CST3 -0.021 0.031 -0.107 0.080 -2.92 1.150 4.761 10.736 -0.070 CST3 -0.021 0.031 -0.107 0.020 1.055 4.761 0.016 -0.070 CST4 0.067 0.033 0.031 -0.122 -0.775 0.038 -2.290 1.3.299 -0.087 TUG1 -0.077 -0.023 0.074 -0.077 -0.435 0.2	7MW1	-0.133	-0.004	-0.127	0.377	1.317	3.038	19.142	-14.173	0.206
7MW3 0.023 0.070 0.076 -0.175 -0.071 -3.851 -16.295 -0.270 -0.011 7MW4 0.005 0.018 -0.037 0.058 +0.037 0.508 4.473 -1.933 0.0211 7MW5 0.010 -0.042 -0.066 0.037 -0.039 -3.496 1.448 0.038 CST1 -0.042 -0.016 0.027 -0.024 0.086 -0.334 2.786 1.448 0.038 CST2 0.074 0.020 0.035 0.097 -0.914 0.080 -4.985 6.339 -0.088 CST3 0.001 0.038 -0.107 0.1080 -0.322 -1.550 -1.761 10.736 -0.070 CST5 0.001 0.022 -0.115 0.413 1.010 2.966 19.887 -8.665 0.150 TUG3 0.079 0.024 -0.075 0.384 -2.99 5.047 -0.066 TUG3 0.067 0.034 -0.024	7MW2	-0.086	-0.050	-0.103	0.283	0.730	0.754	7.039	-8.028	0.092
7MW4 0.005 0.018 -0.037 0.038 4.473 -1.953 0.021 7MW5 0.010 0.079 0.009 -0.030 -0.308 4.473 -1.953 0.021 7MW5 0.014 0.027 -0.024 0.056 -0.314 2.786 1.448 0.038 CST2 0.074 0.020 0.055 -0.097 -0.914 0.080 4.985 6.339 -0.088 CST3 0.021 0.031 -0.107 0.032 2.518 12.943 1.101 0.025 CST5 0.001 0.028 -0.012 0.032 0.290 1.016 2.946 0.9487 0.094 TUG1 -0.077 -0.013 0.013 0.012 0.078 3.859 2.2155 -4.530 0.094 TUG2 0.067 0.033 0.031 -0.122 -0.775 0.038 -2.909 3.047 -0.066 TUG3 0.079 0.065 0.081 -0.222 -0.256	7MW3	0.023	-0.070	0.076	-0.175	-0.071	-3.851	-16.295	-0.270	-0.011
TMW5 0.010 0.079 0.009 0.100 -0.495 0.331 -3.496 3.815 -0.054 CST1 0.042 0.016 0.027 -0.024 0.086 -4.985 6.339 -0.088 CST2 0.074 0.020 0.055 -0.914 0.086 -4.985 6.339 -0.088 CST3 -0.021 0.031 -0.107 0.108 0.232 2.518 12.943 1.101 0.025 CST4 0.063 0.012 -0.012 0.029 1.036 9.480 1.641 0.016 CST5 0.001 -0.022 -0.115 0.413 1.010 2.966 19.887 8.665 0.051 TUG2 0.067 0.033 0.051 -0.172 -0.783 0.326 -2.399 5.047 -0.066 TUG3 0.079 0.006 -0.009 0.019 -0.783 0.326 -2.797 6.498 -0.044 TUG4 0.058 0.027 -0.014	7MW4	0.005	0.018	-0.037	0.095	-0.037	-0.508	4.473	-1.953	0.021
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	7MW5	0.010	0.079	0.009	-0.100	-0.495	-0.391	-3.496	3.815	-0.054
CST2 0.074 0.020 0.055 -0.097 -0.914 0.080 -4.985 6.339 -0.088 CST3 -0.021 0.031 -0.107 0.108 0.232 2.518 12.943 1.101 0.025 CST4 0.063 0.015 0.046 -0.140 -0.922 -1.550 -4.761 10.736 -0.070 CST5 0.001 0.028 -0.012 0.003 0.290 1.036 9.480 1.641 0.016 CST6 -0.051 -0.042 -0.198 0.312 0.728 3.859 2.2155 -4.530 0.094 TUG1 -0.077 0.033 0.051 -0.122 -0.775 0.068 -2.290 5.047 -0.066 TUG3 0.079 0.006 -0.009 -0.019 -0.783 0.326 -2.199 5.047 -0.066 TUG5 0.017 0.023 0.024 -0.026 -2.722 -14.765 4.801 -0.108 TUG5 0.017<	CST1	-0.042	-0.016	0.027	-0.024	0.056	0.334	2.786	1.448	0.038
CST3 -0.021 0.031 -0.107 0.108 0.232 2.518 12.943 1.101 0.025 CST4 0.063 0.015 0.046 -0.140 -0.922 -1.550 -4.761 10.736 -0.070 CST6 0.001 0.022 -0.012 0.013 0.290 1.036 9.480 1.641 0.016 CST6 -0.007 -0.022 -0.115 0.413 1.010 2.966 19.887 -8.665 0.150 TUG3 0.077 -0.022 -0.115 0.413 1.010 2.966 19.887 -8.665 0.015 TUG3 0.077 -0.021 -0.415 -0.775 0.038 -2.290 13.299 -0.067 TUG3 0.017 0.023 0.024 -0.054 -0.326 0.411 2.990 2.906 0.018 TUG6 0.087 0.068 -0.173 0.51 0.897 -2.547 -0.007 TUG6 0.088 0.002 -0.018	CST2	0.074	0.020	0.055	-0.097	-0.914	0.080	-4.985	6.339	-0.088
CST4 0.063 0.015 0.046 -0.140 -0.922 -1.550 -4.761 10.736 -0.070 CST5 0.001 0.028 -0.012 0.003 0.290 1.036 9.480 1.641 0.016 CST6 -0.051 -0.022 -0.115 0.413 1.010 2.966 19.887 -8.665 0.150 TUG2 0.067 0.033 0.051 -0.122 -0.775 0.038 -2.200 13.299 -0.087 TUG3 0.079 0.006 -0.009 0.019 -0.783 0.326 -2.399 5.047 -0.066 TUG4 0.087 0.065 0.081 -0.222 -0.926 -2.722 -14.765 4.801 -0.108 TUG6 0.087 0.065 0.081 -0.222 -0.926 -2.722 -14.765 4.801 -0.108 TUG7 0.018 0.086 -0.077 -0.101 -0.021 0.897 -2.547 -0.051 Results adjusted for Age	CST3	-0.021	0.031	-0.107	0.108	0.232	2.518	12.943	1.101	0.025
CST5 0.001 0.028 -0.012 0.003 0.290 1.036 9.480 1.641 0.016 CST6 -0.051 -0.042 -0.198 0.312 0.728 3.859 22.155 -4.1530 0.094 TUG1 -0.077 -0.022 -0.115 0.413 1.010 2.366 19.887 -8.665 0.150 TUG2 0.067 -0.022 -0.077 -0.375 -0.686 -2.290 5.047 -0.066 TUG5 0.017 -0.0475 -0.685 -2.399 5.047 -0.066 TUG5 0.018 0.002 0.021 -0.077 -0.475 -0.686 -2.797 6.498 -0.0044 TUG5 0.018 0.008 -0.077 -0.012 0.411 0.016 1.785 0.007 TUG8 0.023 0.008 -0.071 -0.022 0.641 0.036 1.78 0.007 TUG8 0.023 0.038 0.065 0.017 0.013 0.587 <th>CST4</th> <th>0.063</th> <th>0.015</th> <th>0.046</th> <th>-0.140</th> <th>-0.922</th> <th>-1.550</th> <th>-4.761</th> <th>10.736</th> <th>-0.070</th>	CST4	0.063	0.015	0.046	-0.140	-0.922	-1.550	-4.761	10.736	-0.070
CST6 -0.051 -0.042 -0.198 0.312 0.728 3.859 22.155 -4.530 0.094 TUG1 -0.077 -0.022 -0.115 0.413 1.010 2.966 19.887 -8.665 0.150 TUG3 0.067 0.033 0.51 -0.122 -0.775 0.038 -2.290 13.299 -0.087 TUG3 0.079 0.006 -0.009 0.019 -0.775 0.038 -2.290 5.047 -0.066 TUG4 0.050 -0.020 0.045 -0.077 -0.475 -0.686 -2.797 6.498 -0.044 TUG5 0.017 0.023 0.081 -0.222 -0.926 -2.722 -14.765 4.801 -0.007 TUG7 0.018 -0.023 0.082 -0.008 -0.173 0.551 0.897 -2.547 -0.005 Results adjusted for Age, Genetr, Height, Weight, MMKE and NM - - -0.232 -2.988 2.615 0.006 0.023 -0.034	CST5	0.001	0.028	-0.012	0.003	0.290	1.036	9.480	1.641	0.016
TUG1 -0.077 -0.022 -0.115 0.413 1.010 2.966 19.887 -8.665 0.150 TUG2 0.067 0.033 0.051 -0.122 -0.775 0.038 -2.290 13.299 -0.087 TUG3 0.079 0.006 -0.009 0.017 -0.755 0.686 -2.797 6.498 -0.064 TUG5 0.017 0.023 0.024 -0.054 -0.326 0.410 2.990 2.906 0.019 TUG6 0.087 0.065 0.081 -0.222 -0.926 -2.722 -14.765 4.801 -0.108 TUG7 0.018 0.008 -0.077 -0.173 0.551 0.877 -0.021 Results adjusted for Age, Gender, Height, Weight, MMSE and NM V V -0.003 -0.003 -0.004 -0.013 0.221 -0.232 2.298 2.615 0.004 QS2 -0.003 -0.023 -0.047 -0.0121 -0.213 -0.025 -2.679 4.533	CST6	-0.051	-0.042	-0.198	0.312	0.728	3.859	22.155	-4.530	0.094
TUG2 0.067 0.033 0.051 -0.122 -0.775 0.038 -2.290 13.299 -0.087 TUG3 0.079 0.006 -0.009 0.019 -0.783 0.326 -2.399 5.047 -0.066 TUG4 0.050 -0.023 0.024 -0.054 -0.326 0.410 2.990 2.006 0.019 TUG6 0.087 0.065 0.081 -0.222 -0.926 -2.722 -14.765 4.801 -0.108 TUG7 0.018 0.008 -0.077 -0.101 -0.002 0.641 0.076 1.785 0.007 TUG8 0.023 0.039 0.082 -0.008 -0.17 0.511 0.855 3.654 -0.024 QS1 0.058 0.056 0.022 -0.005 -0.430 -0.764 -0.855 3.654 -0.024 QS2 -0.003 -0.017 0.019 -0.212 -2.679 4.533 -0.033 QS4 -0.004 -0.016 <th>TUG1</th> <th>-0.077</th> <th>-0.022</th> <th>-0.115</th> <th>0.413</th> <th>1.010</th> <th>2.966</th> <th>19.887</th> <th>-8.665</th> <th>0.150</th>	TUG1	-0.077	-0.022	-0.115	0.413	1.010	2.966	19.887	-8.665	0.150
TUG3 0.079 0.006 -0.009 0.019 -0.783 0.326 -2.399 5.047 -0.066 TUG4 0.050 -0.020 0.045 -0.077 -0.475 -0.686 -2.797 6.498 -0.044 TUG5 0.017 0.023 0.024 -0.326 -0.222 -14.765 4.801 -0.108 TUG6 0.087 0.065 0.081 -0.222 -0.926 -2.722 -14.765 4.801 -0.005 Results adjusted for Age, Gender, Height, Weight, MMSE and NM -0.023 0.897 -2.547 -0.005 QS1 0.058 0.056 0.022 -0.031 -0.764 -0.855 3.654 -0.026 QS2 -0.003 -0.009 -0.117 0.019 -0.211 -0.213 -0.065 0.893 -0.013 QS4 -0.004 -0.014 0.009 0.017 -0.205 -0.452 -2.679 4.533 -0.003 QS4 -0.004 -0.013 0.263 0.484	TUG2	0.067	0.033	0.051	-0.122	-0.775	0.038	-2.290	13.299	-0.087
TUG4 0.050 -0.020 0.045 -0.077 -0.475 -0.686 -2.797 6.498 -0.044 TUG5 0.017 0.023 0.024 -0.054 -0.326 0.410 2.990 2.906 0.019 TUG6 0.087 0.065 0.081 -0.222 -0.926 -2.722 -14.765 4.801 -0.087 TUG6 0.083 0.003 0.082 -0.008 -0.173 0.551 0.076 1.785 0.005 Results adjusted for Age, Gender, Height, Weight, MMSE and NM - - -0.035 -0.630 -0.764 -0.855 3.654 -0.024 QS2 -0.003 -0.009 -0.117 0.019 0.221 -0.232 2.298 2.615 0.006 QS4 -0.004 -0.014 0.009 0.017 -0.213 -0.065 0.893 -0.013 QS4 -0.064 -0.036 -0.103 0.263 0.484 1.142 7.652 -2.755 0.071	TUG3	0.079	0.006	-0.009	0.019	-0.783	0.326	-2.399	5.047	-0.066
TUG50.0170.0230.024-0.054-0.3260.4102.9902.9060.019TUG60.0870.0650.081-0.222-0.926-2.722-14.7654.801-0.108TUG70.0180.008-0.077-0.101-0.0020.6410.0761.7850.007TUG80.0230.0390.082-0.008-0.1730.5510.897-2.547-0.005Results adjusterGenere, Height, WMSE and NMVVVVVVVQS10.0580.0560.022-0.005-0.430-0.764-0.8553.654-0.024QS2-0.003-0.009-0.1170.0190.211-0.212-0.2322.2982.6150.006QS30.038-0.023-0.047-0.087-0.121-0.013-0.0650.893-0.013QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.013QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.013TMW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.161TMW2-0.064-0.036-0.0130.0260.045-0.141-0.07-2.7550.071TMW3-0.0100.0780.006-0.82-0.349-0.637-3.0010.17-0.039CST1-0.038-0.0170.017<	TUG4	0.050	-0.020	0.045	-0.077	-0.475	-0.686	-2.797	6.498	-0.044
TUG60.0870.0650.081-0.222-0.926-2.722-14.7654.801-0.108TUG70.0180.008-0.077-0.101-0.0020.6410.0761.7850.007TUG80.0230.0390.082-0.008-0.1730.510.876-2.547-0.005Results adjusted for Age, Gender, Height, Weight, MMSE and NM0.754-0.8553.654-0.024QS10.0580.0560.022-0.005-0.430-0.764-0.8553.654-0.024QS2-0.003-0.0090.1170.0190.221-0.2322.2982.6150.006QS30.038-0.024-0.047-0.087-0.121-0.213-0.0650.893-0.013QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.0037MW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.1617MW2-0.064-0.036-0.1030.2630.4841.1427.652-2.7550.0717MW3-0.004-0.084-0.011-0.0460.107-0.477-3.497-0.8920.0237MW40.0250.013-0.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.0170.016-0.818-0.8101.341-0.072CST30.0120.017-0.0540.210 </th <th>TUG5</th> <th>0.017</th> <th>0.023</th> <th>0.024</th> <th>-0.054</th> <th>-0.326</th> <th>0.410</th> <th>2.990</th> <th>2.906</th> <th>0.019</th>	TUG5	0.017	0.023	0.024	-0.054	-0.326	0.410	2.990	2.906	0.019
TUG7 0.018 0.008 -0.077 -0.101 -0.002 0.641 0.076 1.785 0.007 TUG8 0.023 0.039 0.082 -0.008 -0.173 0.551 0.897 -2.547 -0.005 Results adjusted for Age, Gender, Height, Wispert, MMSE and NM	TUG6	0.087	0.065	0.081	-0.222	-0.926	-2.722	-14.765	4.801	-0.108
TUG80.0230.0390.082-0.008-0.1730.5510.897-2.547-0.005Results adjusted for Age, Gender, Height, Weight, MMSE and NMVQS10.0580.0560.022-0.005-0.430-0.764-0.8553.654-0.024QS2-0.003-0.009-0.1170.0190.221-0.2322.2982.6150.006QS30.038-0.023-0.047-0.087-0.121-0.213-0.6650.893-0.013QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.0037MW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.1617MW2-0.064-0.036-0.1030.2630.4841.1427.652-2.7550.0717MW3-0.004-0.084-0.011-0.0460.107-0.407-3.497-0.8920.0237MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.818-0.801-6.6301.341-0.0727CS120.0520.0170.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST6<	TUG7	0.018	0.008	-0.077	-0.101	-0.002	0.641	0.076	1.785	0.007
Results adjusted for Age, Gender, Height, WMSE and NMQS10.0580.0560.022-0.005-0.430-0.764-0.8553.654-0.024QS2-0.003-0.009-0.1170.0190.211-0.2322.2982.6150.006QS30.038-0.023-0.047-0.087-0.121-0.213-0.0650.893-0.013QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.003TMW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.161TMW2-0.064-0.036-0.1030.2630.4841.1427.652-2.7550.0717MW3-0.046-0.038-0.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.828-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0170.0100.1400.1960.9912.4280.040CST20.0520.018-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0240.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.02	TUG8	0.023	0.039	0.082	-0.008	-0.173	0.551	0.897	-2.547	-0.005
QS10.0580.0560.022-0.005-0.430-0.764-0.8553.654-0.024QS2-0.003-0.009-0.1170.0190.221-0.2322.2982.6150.006QS30.038-0.023-0.047-0.087-0.121-0.213-0.0650.893-0.013QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.0037MW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.1617MW2-0.064-0.036-0.1030.2630.4841.1427.652-2.7550.0717MW3-0.004-0.084-0.011-0.0460.107-0.407-3.497-0.8920.0237MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.822-0.349-1.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.016-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST60.000-0.053-0.026-0.625-0.8900.8455.898-0.037CST60.001-0.053-0.072-0.444	Results adjust	sted for Age	e, Gender, Heig	ght, Weight, M	MSE and NM	Ν				
QS2-0.003-0.009-0.1170.0190.221-0.2322.2982.6150.006QS30.038-0.023-0.047-0.087-0.121-0.213-0.0650.893-0.013QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.0037MW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.1617MW2-0.064-0.036-0.1030.2630.4841.1427.652-2.7550.0717MW3-0.004-0.084-0.011-0.0460.107-0.407-3.497-0.8920.0237MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.082-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0540.2100.3015.2553.0840.002CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.115 <td< th=""><th>QS1</th><th>0.058</th><th>0.056</th><th>0.022</th><th>-0.005</th><th>-0.430</th><th>-0.764</th><th>-0.855</th><th>3.654</th><th>-0.024</th></td<>	QS1	0.058	0.056	0.022	-0.005	-0.430	-0.764	-0.855	3.654	-0.024
QS30.038-0.023-0.047-0.087-0.121-0.213-0.0650.893-0.013QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.0037MW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.1617MW2-0.064-0.036-0.0130.2630.4841.1427.652-2.7550.0717MW3-0.044-0.036-0.011-0.0460.107-0.407-3.497-0.8920.0237MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.082-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG30.054-0.014-0.077<	QS2	-0.003	-0.009	-0.117	0.019	0.221	-0.232	2.298	2.615	0.006
QS4-0.004-0.0140.0090.017-0.205-0.452-2.6794.533-0.0037MW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.1617MW2-0.064-0.036-0.1030.2630.4841.1427.652-2.7550.0717MW3-0.004-0.084-0.011-0.0460.107-0.407-3.497-0.8920.0237MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.082-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG30.054-0.014-0.0070.	QS3	0.038	-0.023	-0.047	-0.087	-0.121	-0.213	-0.065	0.893	-0.013
7MW1-0.0580.027-0.0160.1570.8360.6366.004-6.1100.1617MW2-0.064-0.036-0.1030.2630.4841.1427.652-2.7550.0717MW3-0.004-0.084-0.011-0.0460.107-0.407-3.497-0.8920.0237MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.082-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.023-0.057-0.568-0.589-4.784-0.731-0.043TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.032-0.367<	QS4	-0.004	-0.014	0.009	0.017	-0.205	-0.452	-2.679	4.533	-0.003
7MW2-0.064-0.036-0.1030.2630.4841.1427.652-2.7550.0717MW3-0.004-0.084-0.011-0.0460.107-0.407-3.497-0.8920.0237MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.082-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.053-0.072-0.444-0.434-2.9667.162-0.056TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.032 <t< th=""><th>7MW1</th><th>-0.058</th><th>0.027</th><th>-0.016</th><th>0.157</th><th>0.836</th><th>0.636</th><th>6.004</th><th>-6.110</th><th>0.161</th></t<>	7MW1	-0.058	0.027	-0.016	0.157	0.836	0.636	6.004	-6.110	0.161
7MW3-0.004-0.084-0.011-0.0460.107-0.407-3.497-0.8920.0237MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.082-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.053-0.072-0.444-0.434-2.9667.162-0.056TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.032-0.321-0.2060.0133.916-0.028TUG50.0260.0200.015-0.025 <t< th=""><th>7MW2</th><th>-0.064</th><th>-0.036</th><th>-0.103</th><th>0.263</th><th>0.484</th><th>1.142</th><th>7.652</th><th>-2.755</th><th>0.071</th></t<>	7MW2	-0.064	-0.036	-0.103	0.263	0.484	1.142	7.652	-2.755	0.071
7MW40.0250.013-0.0050.045-0.180-1.121-0.9080.6450.0067MW5-0.0100.0780.006-0.082-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.053-0.072-0.444-0.434-2.9667.162-0.056TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.032-0.321-0.2060.0133.916-0.028TUG50.0260.0200.015-0.025-0.191-0.3670.1232.9650.025	7MW3	-0.004	-0.084	-0.011	-0.046	0.107	-0.407	-3.497	-0.892	0.023
7MW5-0.0100.0780.006-0.082-0.349-0.673-3.0010.017-0.039CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.053-0.072-0.444-0.434-2.9667.162-0.056TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.032-0.321-0.2060.0133.916-0.028TUG50.0260.0200.015-0.025-0.191-0.3670.1232.9650.025	7MW4	0.025	0.013	-0.005	0.045	-0.180	-1.121	-0.908	0.645	0.006
CST1-0.038-0.0150.0170.0100.1400.1960.9912.4280.040CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.0210.053-0.072-0.444-0.434-2.9667.162-0.056TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.032-0.321-0.2060.0133.916-0.028TUG50.0260.0200.015-0.025-0.191-0.3670.1232.9650.025	7MW5	-0.010	0.078	0.006	-0.082	-0.349	-0.673	-3.001	0.017	-0.039
CST20.0520.0170.071-0.106-0.818-0.801-6.6301.341-0.072CST30.0020.018-0.049-0.0430.0170.7745.9342.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.053-0.072-0.444-0.434-2.9667.162-0.056TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.032-0.321-0.2060.0133.916-0.028TUG50.0260.0200.015-0.025-0.191-0.3670.1232.9650.025	CST1	-0.038	-0.015	0.017	0.010	0.140	0.196	0.991	2.428	0.040
CST30.0020.018-0.049-0.0430.0170.774 5.934 2.237-0.003CST40.0350.017-0.0220.026-0.625-0.8900.845 5.898 -0.037CST50.0130.0280.021-0.0540.2100.301 5.255 3.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.0210.053-0.072-0.444-0.434-2.966 7.162-0.056 TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.025-0.191-0.3670.1232.9650.025	CST2	0.052	0.017	0.071	-0.106	-0.818	-0.801	-6.630	1.341	-0.072
CST40.0350.017-0.0220.026-0.625-0.8900.8455.898-0.037CST50.0130.0280.021-0.0540.2100.3015.2553.0840.002CST60.000-0.053-0.1080.1150.4600.7376.3171.5960.047TUG10.022-0.0090.0110.2190.4690.1124.2091.1850.089TUG20.0210.0210.053-0.072-0.444-0.434-2.9667.162-0.056TUG30.054-0.014-0.0070.057-0.568-0.589-4.784-0.731-0.043TUG40.033-0.0240.023-0.032-0.321-0.2060.0133.916-0.028TUG50.0260.0200.015-0.025-0.191-0.3670.1232.9650.025	CST3	0.002	0.018	-0.049	-0.043	0.017	0.774	5.934	2.237	-0.003
CST5 0.013 0.028 0.021 -0.054 0.210 0.301 5.255 3.084 0.002 CST6 0.000 -0.053 -0.108 0.115 0.460 0.737 6.317 1.596 0.047 TUG1 0.022 -0.009 0.011 0.219 0.469 0.112 4.209 1.185 0.089 TUG2 0.021 0.053 -0.072 -0.444 -0.434 -2.966 7.162 -0.056 TUG3 0.054 -0.014 -0.007 0.057 -0.568 -0.589 -4.784 -0.731 -0.043 TUG4 0.033 -0.024 0.023 -0.032 -0.321 -0.206 0.013 3.916 -0.028 TUG5 0.026 0.020 0.015 -0.025 -0.191 -0.367 0.123 2.965 0.025	CST4	0.035	0.017	-0.022	0.026	-0.625	-0.890	0.845	5.898	-0.037
CST6 0.000 -0.053 -0.108 0.115 0.460 0.737 6.317 1.596 0.047 TUG1 0.022 -0.009 0.011 0.219 0.469 0.112 4.209 1.185 0.089 TUG2 0.021 0.021 0.053 -0.072 -0.444 -0.434 -2.966 7.162 -0.056 TUG3 0.054 -0.014 -0.007 0.057 -0.568 -0.589 -4.784 -0.731 -0.043 TUG4 0.033 -0.024 0.023 -0.032 -0.321 -0.206 0.013 3.916 -0.028 TUG5 0.026 0.020 0.015 -0.025 -0.191 -0.367 0.123 2.965 0.025	CST5	0.013	0.028	0.021	-0.054	0.210	0.301	5.255	3.084	0.002
TUG1 0.022 -0.009 0.011 0.219 0.469 0.112 4.209 1.185 0.089 TUG2 0.021 0.021 0.053 -0.072 -0.444 -0.434 -2.966 7.162 -0.056 TUG3 0.054 -0.014 -0.007 0.057 -0.568 -0.589 -4.784 -0.731 -0.043 TUG4 0.033 -0.024 0.023 -0.032 -0.321 -0.206 0.013 3.916 -0.028 TUG5 0.026 0.020 0.015 -0.025 -0.191 -0.367 0.123 2.965 0.025	CST6	0.000	-0.053	-0.108	0.115	0.460	0.737	6.317	1.596	0.047
TUG2 0.021 0.021 0.053 -0.072 -0.444 -0.434 -2.966 7.162 -0.056 TUG3 0.054 -0.014 -0.007 0.057 -0.568 -0.589 -4.784 -0.731 -0.043 TUG4 0.033 -0.024 0.023 -0.032 -0.321 -0.206 0.013 3.916 -0.028 TUG5 0.026 0.020 0.015 -0.025 -0.191 -0.367 0.123 2.965 0.025	TUG1	0.022	-0.009	0.011	0.219	0.469	0.112	4.209	1.185	0.089
TUG3 0.054 -0.014 -0.007 0.057 -0.568 -0.589 -4.784 -0.731 -0.043 TUG4 0.033 -0.024 0.023 -0.032 -0.321 -0.206 0.013 3.916 -0.028 TUG5 0.026 0.020 0.015 -0.025 -0.191 -0.367 0.123 2.965 0.025	TUG2	0.021	0.021	0.053	-0.072	-0.444	-0.434	-2.966	7.162	-0.056
TUG4 0.033 -0.024 0.023 -0.032 -0.321 -0.206 0.013 3.916 -0.028 TUG5 0.026 0.020 0.015 -0.025 -0.191 -0.367 0.123 2.965 0.025	TUG3	0.054	-0.014	-0.007	0.057	-0.568	-0.589	-4.784	-0.731	-0.043
TUGS 0.026 0.020 0.015 -0.025 -0.191 -0.367 0.123 2.965 0.025	TUG4	0.033	-0.024	0.023	-0.032	-0.321	-0.206	0.013	3.916	-0.028
	TUG5	0.026	0.020	0.015	-0.025	-0.191	-0.367	0.123	2.965	0.025
IUG6 0.059 0.066 0.024 -0.116 -0.788 -0.729 -6.500 3.237 -0.082 TUG7 0.000 0.001 0.005 0.126 0.0027 0.0260 1.510 0.051 0.012	TUG6	0.059	0.066	0.024	-0.116	-0.788	-0.729	-6.500	3.237	-0.082
IUG7 U.009 U.001 -U.005 -U.126 U.037 U.262 -1.518 -U.354 0.012 THCR 0.004 0.022 0.026 0.024 0.021 0.025 0.024		0.009	0.001	-0.065	-0.126	0.037	0.262	-1.518	-0.354	0.012
1000 -0.004 0.052 0.058 0.050 0.064 0.071 -0.357 -6.164 0.022 Only Configurate with a n value < 0.05 are holded -6.164 0.022 -6.164 0.022		-0.004	0.032	0.088	0.030	0.064	0.0/1	-0.337	-0.104	0.022

	IADL	FALL history	CES-D	PA	SPPB	HAND	PWR	TMTA	Gait speed
IADL		-0.038	0.714	-0.295	-0.902	-1.900	-11.782	11.805	-0.104
FALL history	-0.014		0.432	-0.050	-0.217	-0.618	-2.363	0.222	-0.022
CES-D	0.016	0.024		-0.035	-0.049	-0.421	-2.091	1.004	-0.009
PA	-0.377	-0.167	-2.039		0.955	3.654	19.125	-9.962	0.126
SPPB	-0.256	-0.160	-0.638	0.212		1.736	10.669	-7.883	0.091
HAND	-0.029	-0.024	-0.295	0.043	0.093		3.764	-1.311	0.012
PWR	-0.006	-0.003	-0.046	0.007	0.018	0.118		-0.187	0.002
TMTA	0.010	0.000	0.039	-0.006	-0.023	-0.072	-0.328		-0.003
Gait speed	-2.013	-1.083	-7.897	1.905	6.198	15.703	98.927	-76.769	
Results adjusted fo	r Age, Gen	der, Height, Weigł	nt, MMSE ar	nd NM					
IADL	1	-0.212	-0.313	-0.133	-0.462	0.056	-1.681	2.992	-0.039
FALL history	-0.064		0.269	-0.027	-0.170	-0.149	0.115	-1.307	-0.010
CES-D	-0.006	0.017		-0.010	0.002	-0.044	-0.321	0.323	-0.003
PA	-0.177	-0.121	-0.668		0.421	0.398	3.257	-0.577	0.061
SPPB	-0.165	-0.202	0.043	0.113		0.768	6.378	-2.539	0.070
HAND	0.002	-0.018	-0.085	0.011	0.080		2.059	-0.815	0.007
PWR	-0.001	0.000	-0.012	0.002	0.013	0.039		0.050	0.001
TMTA	0.003	-0.004	0.017	0.000	-0.007	-0.022	0.072		-0.001
Gait speed	-1.049	-0.904	-3.734	1.222	5.199	5.239	52.521	-35.582	1

 β coefficients with a p-value < .05 are bolded

ACRONYMS: CES-D: Center for Epidemiologic Studies Depression Scale; FALL history: declared number of falls; HAND. Hand-Grip strength test; IADL: Instrumental Activities of Daily Living; MMSE: Mini-Mental State Examination; NM: Number of Medications; PA: Physical Activity; PWR. lower extremity muscle power; SPPB: Short Physical Performance Battery; TMTA: Trail Making Test A

4.6.3. DISCUSSION

As we discussed in the previous sections, working with residuals of the linear regression analysis increases the complexity of the conceptual model and the difficulties in understanding the meaning of the domains that make up the model. In the third version of the conceptual model, one EFA was conducted on each set of PP sensor-based measures without removing the effect of confounders and under the assumption that the factors are independent. As expected, no association between the factor scores of each functional test was found (see Table 4.23). The linear regression analysis was then computed to examine the association between domains and between domains and health-related measures, either adjusting or not adjusting for age, gender, body composition (height and weight), cognition (MMSE) and the number of medications. The overall performance was not added as covariate in the linear regression analysis because i) this cannot be applied to the QS test since the test duration is fixed and the clinical outcome is limited to "is able/not able to perform the test"; ii) instrumenting the PP tests with wearable inertial sensors allow to assess specific sub-components of PP tests and the test duration is part of the model, since it is possible to compute it from the inertial signals; iii) one of our aims was to explain how the specific domains contributed to the overall performance (PP tests duration).

Table 4.24 shows that we found several significant associations between domains and conventional health-related measures. Some of these were not explained by the covariates, confirming the functional meaning of the domains.

Overall, higher-functioning (both physical, SPPB, and cognitive, TMTA) older adults who were more active (PA) and stronger (HAND, PWR) performed better on the instrumented functional tests. The "Walking impairment" (7MW1) and "Gait irregularity" (7MW2) domains obtained from the 7-meter Walk test were significantly associated with measures of leg muscle power, usual gait speed, and overall lower extremity function. Many of the domains were significantly associated with the SPPB, which includes tests of balance, gait speed, and chair stands. Furthermore, gait speed serves as the conventional clinical outcome measure of an older adult's PC assessment. The associations between gait speed and domains of the 7MW and CST were significant both in the unadjusted and adjusted model. Conversely, the association between this measure and the capacities to maintain the static balance were explained by the covariates.

After adjusting for the covariates, two domains were not associated with any health-related measures (see Table 4.24): the "ML postural reaction time and jerkiness" of the QS factor model (QS3), and the "Gait jerkiness" of the 7MW factor model (7MW3). This could be due either to non-linear associations between domains and measures or to their association with other health-related measures that were not included in this study. For example, it has been proposed that the capacities in ML

direction may be associated with the risk of falling [95] which may not be adequately described by the history of falls.

4.6.3.1. CONVENTIONAL OUTCOME

Gait speed served as a conventional clinical outcome measure of older adults' PC. The association between this measure and the capacities to maintain the static balance were explained by age, gender, height, weight, MMSE and NM. This result suggests that after deduction the covariates, the QS test does not give information related to locomotion and dynamic balance. The associations between gait speed and domains of 7MW, CST and TUG ("Walking impairment", 7MW1, "Gait irregularity", 7MW2, "Gait variability", 7MW5, "Dynamic postural impairment", CST1, "Sit-to-Stand jerkiness", CST2, "Stand-to-Sit jerkiness", CST4, "AP Sit-to-Stand weakness", CST6, "Shakiness", TUG1, "Turning impairment", TUG2, "Turn-to-Sit jerkiness", TUG3, "Sit-to-Walk jerkiness", TUG4, "Walking impairment", TUG6) were not explained by the covariates, meaning that these domains of the conceptual model bring information about the older adults' ability to walk, turn and perform postural transitions. This is in agreement with other studies in which gait speed was shown to be a good health indicator for older adults [96].

4.6.3.2. IADL

The associations that were still significant after adjusting for the covariates showed that older adults who had a higher number of IADL were also less active and fit, and they had more difficulties while walking (PA, SPPB, gait speed, "Walking Impairment",7MW1, "Gait irregularity", 7MW2, and "Walking impairment", TUG6).

4.6.3.3. FALL-HISTORY

The associations between the number of falls experienced during the last 12 months (FALL-history) and SPPB, "Gait irregularity" (7MW2), "Sit-to-Stand jerkiness" (CST2) and "Walking impairment" (TUG6) were not explained by the covariates. This implies that older adults who experienced a higher number of falls in the previous year, were less smooth while standing from a chair. Gait speed was not related to the history of falls, but older adults who fell more showed a more impaired and irregular gait. These results are in agreement with a recent study, in which the relationships between the history of falling and gait, single leg stance and CST was investigated [97].

4.6.3.4. CES-D

CES-D is a screening test for assessing depressive disorder. After adjusting for the covariates, older adults who reported depressive symptoms were less reactive and smooth during the QS test ("AP postural reaction time and jerkiness", QS2), they showed lower limbs weakness ("AP Sit-to-Stand

weakness", CST6, and "V Turn-to-Sit weakness", TUG8) and their locomotion was less regular ("Gait Irregularity", 7MW2). These results are in agreement with the study by Penninx et al. [90] in which depressive symptoms were predictive of the decline in physical performance.

4.6.3.5. PA

After adjusting for the covariates, older adults who were less active, showed a higher number of IADL, they were less fit (SPPB), and less strong and with a more impaired gait (gait speed, "Walking impairment", 7MW1, "Gait irregularity", 7MW2), "Shakiness", TUG1, and "ML Sit-to-Walk weakness", TUG7).

4.6.3.6. SPPB

The associations between the Short Physical Performance Battery (SPPB) score and the CES-D, TMTA, "AP Postural Control Impairment" (QS4) and "AP Stand-to-Sit Weakness" (CST5) were explained by the covariates. The SPPB score is a measure of the older adults' functional capacity and includes tests of balance, gait speed, and repeated chair stands. The higher the SPPB score, the better the adults' performances. As we expected, older adults with high SPPB score, showed less IADL, less number of falls in the previous 12 months (FALL-History), they were more active (PA) and more strong (HG and PR). Furthermore, they had less "Postural control impairment" (QS1), they showed better walking ability (gait speed, "Walking impairment", 7MW1, "Gait irregularity", 7MW2, "Gait variability", 7MW5, "Walking impairment", TUG6) and better capacities to perform postural transitions and turns ("Sit-to-Stand jerkiness", CST2, "Stand-to-Sit jerkiness", CST4, "AP Sit-to-Stand weakness", CST6, "Shakiness", TUG1, "Turning impairment", TUG2, "Turn-to-Sit jerkiness", TUG3, "Sit-to-Walk jerkiness", TUG4).

4.6.3.7. HAND

The association between Hand-Grip strength test (HAND) and IADL, CES-D, PA, TMTA, "AP Postural Instability" (QS4) and some domains of the 7MW ("Walking Impairment", 7MW1, "Gait Jerkiness", 7MW3) and CST ("ML Dynamic Postural Instability", CST3, "Stand-to-Sit Jerkiness", CST4, "AP Sit-to-Stand Weakness", CST6) factor models were explained by the covariates. The performances in performing the CST test reflect the strength of the lower limbs. Surprisingly, after adjusting for the covariates, no significant associations between upper limbs strength (HAND) and CST factor model were found. However, older adults with higher HAND were more fit (SPPB) and showed stronger lower limbs (PWR), they showed better abilities while performing the QS ("Postural instability", QS1), 7MW (gait speed, "Gait irregularity", 7MW2, and "ML gait instability", 7MW4)

and TUG ("Shakiness", TUG). These results are consistent with the findings of a previous study that highlights the association between grip-strength and future outcome in ageing adults [92].

4.6.3.8. PWR

After adjusting for the covariates, only the SPPB score, the HAND and the gait speed were significantly associated with the lower limbs strength (PWR). No significant associations between PWR and domains of the QS factor model were found, confirming the results of the two previous versions of the conceptual model. In our findings, the association between strength (both HAND and PWR) and the ability to maintain the static balance ("AP postural control impairment", QS4) was explained by the covariates. Older adults who had higher lower limbs strength, were also more able during the locomotion (gait speed, "Walking impairment", 7MW1, "Gait irregularity", 7MW2, "Shakiness", TUG6) and, as expected, performed better during the CST test ("Sit-to-Stand jerkiness", CST2, "ML dynamic postural instability", CST3, "AP Stand-to-Sit weakness", CST5, "AP Sit-to-Stand weakness", CST6).

4.6.3.9. TMTA

The Trail Making Test part A (TMTA) assesses psychomotor speed. Attention and executive function are related to the cognitive control of gait, posture, and balance (6,7). Performance on the TMTA is a strong, independent predictor of mobility impairment, accelerated decline in lower extremity function, and mortality in older community-living adults (8). After adjusting for the covariates, it was significantly related to those domains that require good cognition, motor-control and motor-planning ("AP postural control impairment", QS4, gait speed, "Walking impairment", 7MW1, "Stand-to-Sit jerkiness", CST4, "Turning impairment", TUG2 and "Turn-to-Sit weakness", TUG8).

In conclusion, these results suggest that the sensor-based model is coherent with the conventional clinical measures of PC. The coherence and concurrent validity analyses confirmed that inertial sensors embedded in smartphones can detect and assess the status of different functional domains, adding useful information to the conventional clinical assessment. In the next section, a graphical representation of the conceptual model and a possible scenario in which a clinician could benefit from the additional information provided by the sensor-based conceptual model are presented.

4.6.3.10. CASE STUDIES

Figure 4.4 shows three radar plots, for three different case studies. Favourable values of the scores, represented below the 75th percentile, reflected good performances in the domain.



Figure 4.3 Radar plots of three case studies. The black lines represent the median, 25th and 75th percentile of the older adults' factor scores. The dark grey area represents extreme values (very high values above the 75th percentile and very low values under the 25th percentile). Favourable values of the scores, below the 75th percentile, reflected good performances in the domains.

Case 1: based on the clinical assessment, the subject (male, 69 years old) was not at risk of a fall, but 2 prospective falls occurred. As you can see in Figure 3, he showed high instability in ML direction during the QS, 7MW and postural transitions ("ML postural reaction time and jerkiness", QS3, "ML gait instability", 7MW4, and "ML dynamic postural instability", CST3) were above the 75th percentile), poor walking abilities ("Gait Irregularity", 7MW2, "Gait jerkiness", 7MW3), and high "AP postural transitions weakness" (TUG5). This may corroborate the idea that the ML stability is crucial to prevent falls in community-dwelling older adults [98–100].

Case 2: the older adult (female, 81 years old) had all the health-related measures within their reference values, but she had poor strength (low HAND and PWR). Her weakness is reflected in poor ability to maintain the static balance ("ML postural reaction time and jerkiness", QS3, and "AP postural control impairment", QS4), to perform postural transitions and walk ("Dynamic postural impairment", CST1, "AP Stand-to-Sit weakness", CST5, "Sit-to-Walk jerkiness", TUG4 and "Walking impairment", TUG6), confirming the findings reported elsewhere [101].

Case 3: the older adult (male, 86 years old) had all the health-related measures within their reference values, except for the gait speed, which was below 1 m/s. This cut-off point has been related to the risk of adverse health outcomes and disabilities [78,102]. Indeed, the Radar Plots show that his capacities to maintain static balance are not compromised, but he had difficulties while walking ("Walking impairment", 7MW1, "ML gait instability", 7MW4, "Gait variability", 7MW5 and "Walking impairment", TUG6) and while performing postural transitions ("Dynamic postural impairment", CST1, "Stand-to-Sit jerkiness", CST4, "Shakiness", TUG1, "AP postural transitions weakness", TUG5).

4.7. CONCLUSIONS

A battery of functional tests, instrumented by means of a smartphone, could be used for outlining a sensor-based conceptual model suitable for the assessment of older adults' PC. EFA allowed us to reduce the number of sensor-based measures computed from the PP tests and find domains with clear functional meaning. Regression analysis suggests that such domains confirm and expand information obtained with clinical testing and provide quantitative information about several mobility skills that are usually not captured by conventional outcomes. Instrumented functional testing hence has the potential to i) advance the quality of current mobility assessments; ii) enhances our understanding of an individual's true PC; and iii) disclose subtle changes in PC that would otherwise remain undetected. Increasing our understanding and the sensitivity of mobility assessment is of the utmost importance since it may enable earlier detection of functional decline and identify therapeutic targets for rehabilitation. Further work is needed to evaluate whether this more detailed information adds to our ability to predict adverse outcomes, over and above clinical testing like gait and SPPB.

5. THE PRE.C.I.S.A STUDY: APPLICATION OF THE SENSOR-BASED CONCEPTUAL MODEL

5.1. OUTLINE OF THE STUDY AND DESCRIPTION OF THE POPULATION

The PRE.C.I.S.A Study (PREvenzione Cadute per un Invecchiamento Sano e Attivo, preventing falls and promoting active and healthy ageing [3]) is a randomised controlled trial which involved the units of Rehabilitation Medicine, Geriatric and Neurologic in Modena and Reggio Emilia AUO, two health authorities of Emilia-Romagna (Italy). One million people aged 65 years and older are living in Emilia-Romagna. Of these, one out of three is a risk of falling. The fall risk increases in people aged 80 years and older and it is even higher when the older adult is affected by neurological diseases like stroke or Parkinson's disease. When a fall occurs, the consequences could be severe and sometimes lead to hospitalisation and loss of independence. The aim of this randomized controlled trial was the evaluation of a multiple, personalised, treatment based on a multidisciplinary assessment for the prevention of falls and the promotion of an active and healthy lifestyle in community-dwelling older adults. For the first time, it was also possible to expand the intervention to older adults with neurological diseases like stroke or Parkinson's disease. The aim of this study was to evaluate whether the conceptual model developed on a healthy population of community-dwelling older adults (section 4.3) can be applied on a population of people at risk of falling to obtain information about their physical functional status. Three relevant case studies have been illustrated.

5.2. Methods

Sixty-five participants (75.8 ±5.9 years old, range [65-89] years, 26 females) including 13 people affected by neurological diseases (7 Parkinson's and 16 Stroke) underwent a battery of PP tests wearing an inertial sensor at the lower back. A set of health-related measures, including TUG total time, gait speed, the number of falls in the previous year (FALLN pre-randomization), were collected during the assessment. Participants received phone calls during the following 12 months to collect the number of falls occurred (FALLN post-randomization). The sensor-based PP tests included the TUG, 5-times CST (5CST) and 10-meters Walking Test (10MWT). The algorithms used for the signal analysis and measures computation are part of the system developed within the FARSEEING project [71] and are more detailed described in section 3.3.2. Data collected during the study were used to validate the sensor-based conceptual model presented in section 4.3. The conceptual model was applied to the set of sensor-based measures to compute the participants' scores for each domain of the conceptual model.

Table 5.1 Description of the PRE.C.I.S.A. population

	Total population	Parkinson	Stroke	65+					
N	65	7	12	46					
Age, years	75.8 ± 5.8	76.6 ± 5.5	76.7 ± 6.8	75.4 ± 5.6					
Gender, Females	40 (61.5 %)	2 (28.6 %)	6 (50 %)	32 (69.6 %)					
FALLN pre-randomization, ≥ 2	33 (50.8 %)	5 (71.4%)	5 (41.6 %)	23 (50 %)					
FALLN post-randomization, ≥ 2	14 (21.5 %)	5 (71.4 %)	2 (16.6 %)	7 (15.2 %)					
TUG, s	14.7 ± 6.3	13.9 ± 3.9	18.6 ± 8	13.7 ± 5.8					
Gait speed, m/s	0.98 ± 0.3	0.95 ± 0.2	0.77 ± 0.3	1.03 ± 0.3					
Values are presented as mean + SD or number (%) unless otherwise indicated.									

5.3. RESULTS

Based on the TUG total time, participants were, in average, all at risk of falling (cut-off 13.5s [103]); more than 50% of participants fell two or more time in the past year, and the 21.5% fell two or more time in the following year. In total, 88 sensor-based measures were computed from the 10MW, CST and TUG tests (19, 31 and 38 for the 10MW, CST and TUG tests, respectively). In order to externally validate the conceptual model described in section 4.3, the scores related to each domain of each participant were computed applying the factor model on each set of sensor-based measures. Figure 5.1 shows the graphic representation of the results. The vertices represent the domains of the conceptual model. The black lines represent the median, 25th and 75th percentile of the InCHIANTI population, took as a reference. The coloured lines represent the scores' mean value of the participants, grouped into three categories: Parkinson (pink), Stroke (green) and 65+ (blue). External dark green area indicates the extreme values of the scores, which reflect the poor functional ability in the domains. The participants who were grouped in the 65+ category, were scored similarly with respect to the reference population (InCHIANTI). Indeed, the blue line is near the region of normality (median values of the reference population). Conversely, Parkinson and Stroke showed high Gait variability and turning and postural transitions impairment, indicating a lower physical function and consequently a higher risk of falling.



Figure 5.1 Graphical representation of the scores of the PRE.C.I.S.A study participants. The black lines represent the median, 25th and 75th percentile of the InCHIANTI population, used as a reference. The coloured lines represent the scores of the three groups of the PRE.C.I.S.A. study (Parkinson, Stroke and 65+). The dark grey area represents extreme values (very high values above the 75th percentile and very low values under the 25th percentile). Favourable values of the scores, below the 75th percentile, reflected good performances in the domains.

5.4. DISCUSSION

In section 4.3 A sensor-based conceptual model was developed instrumenting a battery of PP tests by means of inertial sensors. The model was demonstrated to be suitable for the assessment of older adults' PC. The domains of the conceptual model provide additional quantitative information about several mobility skills that are traditionally not observed using the conventional total duration of the PP tests. To evaluate whether the detailed, objective information gained from the conceptual model can be useful in assessing the individuals' mobility skills, we applied the conceptual model to a population of older adults at risk of falling. The PRE.C.I.S.A population include also people with neurological diseases, like Stroke and Parkinson's disease, giving the possibility to assess the abilities of the conceptual model to explore the relationships with specific impairments and diseases. Participants underwent a battery of PP tests wearing one inertial sensor at L5. A number of sensor-based measures were computed applying the factor model on each set of sensor-based measures.

Figure 5.1 shows that the performances of people in the 65+ category (blue line) were similar to the reference population. Conversely, people with Parkinson's disease showed a higher "Gait variability", "ML postural instability" and jerkiness during sitting and standing transitions. However, people with Stroke showed high "Gait variability" and jerkiness during sitting, turning and walking impairments, which might be related to the risk of falling [42,95,104].

5.4.1. Case studies



Figure 5.2 shows three case studies. The black lines represent the median, 25th and 75th percentile of the InCHIANTI population, used as a reference. The coloured lines represent the scores of the three groups of PRE.C.I.S.A. study (Parkinson, Stroke and 65+). The dark grey area represents extreme values (very high values above the 75th percentile and very low values under the 25th percentile). Favourable values of the scores, below the 75th percentile, reflected good performances in the domains.

Case 1: female, 79 years old. Based on the total TUG duration she was at risk of falling (cut-off 13.5 s [103]) but she did not experience any falls in the previous year. During the assessment, she showed a gait speed faster than 1 m/s and the radar plots confirmed that her gait was not impaired (low "Walking Impairment" of the TUG model and all the domains of the Gait inside of the region of normality). As we can see in Figure 5.2, the high duration of the TUG was probably a consequence of her impairments during the postural transitions that reflect a low muscle strength (high "Shakiness" of the TUG model).

Case 2: female, 69 years old, affected by Parkinson's disease. She reported 3 falls in the previous year and 5 falls in the following year. Both the gait speed and the TUG duration were under the cutoff. In Figure 5.2, we can see that she showed an impaired gait and a high instability in the ML direction that might be related to the fall risk [98–100].

Case 3: male, 81 years old, affected by Stroke. He reported 3 falls in the previous year, 6 falls in the following year and he was slow in completing the TUG test. As we can see in Figure 5.2, he shows high impairments while performing postural transitions and turns. Despite the gait speed was under the limits of normality, he showed also high values of the Gait variability, which has been related to the fall risk [42].

5.5. CONCLUSIONS

In conclusion, the conceptual model developed on a healthy population of community-dwelling older adults (section 4.3) can be applied on a population of people at risk of falling to obtain more detailed quantitative information about different functional domains. The domains of the conceptual model confirm and expand information obtained by conventional clinical testing (Figure 5.1). The three relevant case studies (Figure 5.2) confirmed the conceptual model could help clinicians in assessing individuals' PC and prescribing rehabilitation programs. Domains of the conceptual model allowed to explore the relationships with specific neurological conditions, like Stroke and Parkinson's disease, increasing our knowledge of the older adult's functional status.

6. SENSOR-BASED PA MEASURES FOR THE ASSESSMENT OF USUAL PERFORMANCE

Some contents of this chapter are taken from: Coni Alice, et al. "Association between smartphone-based activity monitoring and traditional clinical assessment tools in community-dwelling older people." [105].

6.1. BACKGROUND AND AIM

One characteristic of the PP tests is that individuals' performances are assessed in a standard and supervised environment, in which people are asked to show their best capacities (e.g. "Please, do this as fast as you can"), which reflect what people can do and might differ from their usual performance. A recent study showed that laboratory gait measurements do relate to the daily-life walking, but are more indicative of an individual's best performance [106]. Furthermore, in another study, the associations between objective PP and PA measures in older adults were investigated and the results showed that PP and PA represent associated but also separate domains of the mobility domain of physical function [107]. The objective assessment of daily PA can be useful for independent living of older adults, although there is still need for consolidation on the use of wearables [108]. The use of inertial sensors to continuously monitor the activities of daily living, such as walking and turning, is beneficial with respect to the questionnaires. Continuous monitoring allows obtaining information about the quality, frequency and variability of these daily activities. In a recent study, the relationships between natural turns and fall history/risk in community-dwelling older adults were assessed using the signals recorded by SP to measure a broad angular range of turns for about one week. In this study, the authors demonstrated that characterizing natural turning during daily activities via continuous monitoring methods has great potential and may enable early detection of increased fall risk [104]. Other studies recorded the daily-life walking of older people using inertial sensors, and their findings confirmed that daily-life walking can be used to improve the assessment of fall risk in older people [109,110]. Previous studies used the mean or median of gait characteristics under the hypothesis that this would be the most representative estimate of a person's capacity [111]. However, extreme values of gait characteristics may better reflect the capacity of adapting the gait pattern to the variety of daily life conditions. Situations where people show "high gait quality" might be informative about the best possible performance they can achieve, which may be closely related to their performance in a laboratory setting [112]. SPs were used in the framework of the FARSEEING-InCHIANTI study to gain information on activities of daily living, like gait and turnings and define objective physical activity profiles [2].

The first aim of this study was to investigate the association between mean and extreme values of PA and gait characteristics derived from daily living activities and well-established clinical tools for

quantifying motor and cognitive impairments in a cohort of community-dwelling older adults. Secondly, datasets of mean or extreme values have been used as an input for a factor analysis in order to define conceptual models of daily living activities.

6.2. Methods

6.2.1. POPULATION

One hundred seventy-one older adults (79.72 ± 6.55 years old. 87 females) wore a SP at home for at least 5 days (up to 9). Several measures representative of the participants' health status were collected during the assessment, including MMSE, IADL, CES-D, PA, HAND, TMTA, PWR, and SPPB. The SPs were equipped with a custom Android application designed for long-term monitoring of PA [71]. Ethical approval was obtained by the Local Ethical Committee (approval number: 584/2012).

6.2.2. INSTRUMENTED MEASURES

The signals recorded by the 3D accelerometer and gyroscope embedded in the SPs were analysed to compute the sensor-based PA measures, including the percentage of sedentary, active, and walking time, the duration and intensity (METs) of the activities, as well as the gait and turning characteristics. Mean or extreme (5th or 95th percentile) values of each variable were computed in order to define two sets of features: the first set represents the mean performance and the second set represents the best performance observed among the daily activities.

6.2.3. STATISTICAL ANALYSIS

Robust linear regression was performed to remove the effect of age, gender, height, weight, and MMSE. Spearman's correlation analysis was used to investigate the association between the sensor-based measures of PA and the health-related measures.

Factor analysis was performed to extract the underlying structure of PA and gait features. Outliers were identified by the linear robust regression analysis and excluded from the factor analysis. The scores obtained from the fitted model were computed for all participants. Statistical analysis were performed using R for Windows, version 3.4.3 [63].

6.3. RESULTS

Fifteen measures were obtained from the SP-based activity monitoring dataset for both mean and extreme values. Table 6.1 reports the associations between the mean and extreme measures values and health-related measures.

Table 6.1 Spearman's correlation coefficient between features and health-related variables

Health-related measures	IADL	CES-D	PA	FALLN	HG	PR	TMTA	SPPB	
PHYSICAL ACTIVITY VARIABLES									
Sedentary time %			-0.23					-0.18	
Active time %		-0.16	0.29			0.19		0.26	
Walking time %			0.32					0.21	
Total N. Steps									
	Mea	AN VALUES O	F THE FEA	TURES					
Step Duration									
SD Step Duration									
C.V. Step Duration									
Coordination Index									
Mean Turning Duration					-0.19	-0.18	0.21	-0.38	
METs			0.33			0.23		0.32	
Cadence					-0.17				
AP Harmonic Ratio								0.17	
ML Harmonic Ratio									
V Harmonic Ratio					0.18			0.17	
AP Step Regularity					0.18				
V Step Regularity					0.20		-0.16	0.20	
Mean Turning Velocity			0.20		0.16		-0.20	0.44	
Peak Turning Velocity			0.27				-0.17	0.41	
Jerkiness of the Tuning Velocity				0.17	-0.17				
	Extri	EME VALUES	OF THE FE	ATURES					
Step Duration (5)								-0.19	
SD Step Duration (5)									
C.V. Step Duration (5)									
Coordination Index (5)									
Mean Turning Duration (5)									
METs (95)			0.32			0.26		0.31	
Cadence (95)									
Harmonic Ratio AP (95)								0.25	
Harmonic Ratio ML (95)	-0.15								
Harmonic Ratio V (95)	-0.18				0.25			0.27	
Step Regularity AP (95)					0.17			0.16	
Step Regularity V (95)	-0.21				0.28	0.21	-0.18	0.37	
Mean Turning Velocity (95)			0.26		0.18	0.18	-0.22	0.49	
Peak Turning Velocity (95)			0.30		0.16	0.20	-0.18	0.46	
Jerkiness of the Tuning Velocity (5)							0.21	-0.20	
ACRONYMS: ML = Medio-Lateral; AP = Antero-Posterior; V = Vertical; E.V = Proportion of Explained Variance; SD= Standard									
Deviation; CV = Coefficient of Variation; METs = Metabolic Equivalents.									

Only significant correlations (p<0.05) are displayed. As expected, the information derived from activity monitoring is related to the participants' health status. Subjects who were less sedentary had better IADL, CES-D, PA and SPPB scores. Also, turning abilities (duration of turning and mean and peak turning velocities) and gait regularity (Harmonic Ratios and Step Regularities) measures were associated with measures of fitness (HG, PR and SPPB) and cognitive capacities (TMTA). Tables 6.2 and 6.3 report the factor loadings and explained variance for mean and extreme values.

	FACTOR LOADINGS FOR THE MEAN VALUES								
features	E.V.	Gait Variability and Regularity	Activity Level	Turning Ability	Cadence	Coordination			
SD step duration		-0.80							
CV step duration		-0.68							
Coordination Index		0.86							
AP Harmonic Ratio	0.24	0.51							
ML Harmonic Ratio		0.89							
V Harmonic Ratio		0.68							
AP step regularity		0.86							
V step regularity		-0.80							
Sedentary time %			-0.78						
Active time %	0.18		0.97						
Walking time %			0.88						
Mean sedentary time			-0.81						
Mean turning duration				-0.66					
Mean turning velocity	0.14			0.92					
Peak turning velocity				0.90					
Cadence	0.07				0.83				
Coordination Index	0.07					0.76			
ACRONYMS: E.V = Explained Variance; ML = Medio-Lateral; AP = Antero-Posterior; V = Vertical; E.V = Proportion of									

Table 6.2 Loadings of the Factor Analysis of the mean values dataset

ACRONYMS: E.V = Explained Variance; ML = Medio-Lateral; AP = Antero-Posterior; V = Vertical; E.V = Proportion of Explained Variance; SD = Standard Deviation; CV = Coefficient of Variation; METs = Metabolic Equivalents.

Table 6.3 Loadings of the Factor Analysis of the extreme values dataset

FACTOR LOADINGS FOR THE EXTREME VALUES									
features	ΕV	Activity	Turning	Gait	Gait Variability	Agility	Cadence		
	L.v.	Level	Ability	Regularity	Gait Variability				
Sedentary time %		-0.79							
Active time %	0.14	0.97							
Walking time %		0.94							
METs (95)			0.60						
Mean turning velocity			0.81						
(95)	0.13		0.81						
Peak turning velocity (95)			0.89						
AP Harmonic Ratio (95)				0.84					
V Harmonic Ratio (95)	0.13			0.57					
AP step regularity (95)				0.73					
V step regularity (95)				0.63					
SD step duration (5)	0.12				0.90				
CV step duration (5)					0.84				
Step duration (5)	0.07					-0.53			
Coordination Index (5)						0.63			
Cadence (95)	0.05						0.80		

ACRONYMS: E.V = Explained Variance; ML = Medio-Lateral; AP = Antero-Posterior; V = Vertical; E.V = Proportion of Explained Variance; SD= Standard Deviation; CV = Coefficient of Variation; METs = Metabolic Equivalents.

From the mean values dataset were obtained five factors, explaining 70% of the Total Variance (E.V.). The factors were labelled as "Gait variability and regularity" (24% E.V.), "Activity level" (18% E.V). "Turning ability" (14% E.V.), "Gait cadence" (7% E.V.), and "Gait coordination" (7% E.V.). Six factors were obtained from the extreme values dataset, explaining 64% of the Total Variance. The factors were labelled as "Activity level" (14% E.V.), "Turning ability" (13% E.V.), "Gait regularity" (13% E.V.), "Gait variability" (12% E.V.), "Agility" (7% E.V.), and "Gait cadence" (5% E.V.).

6.4. DISCUSSION

We aimed to investigate the association between well-established clinical measures of motor and cognitive capacities and mean and extreme values of measures derived from daily living activities in a cohort of community-dwelling older adults. The datasets of mean or extreme values have been also used as an input for an exploratory factor analysis to discover the structure of monitored ADL. The measures associated with the activity level were related to the self-reported PA, suggesting that participants accurately perceived and reported their personal level of activity. Older adults who were less sedentary during activity monitoring performed better the activities of daily living (IADL) and were less prone to depression (CES-D). They also had higher lower limbs strength (PWR) and scored higher in the functional assessment (SPPB). These findings agree with the results reported elsewhere [113–117] in which was shown that daily physical activity is associated with incident mobility disability, premature death, depression and quality of life. Mean and extreme values of METs were positively related to PA, PWR and SPPB, meaning that the energy consumption is higher in adults who are more fit. Indeed, it was proven that older adults tend to slow down to minimize the increase of energy expenditure caused by the age-related inefficiencies [118]. The features associated with turning ability were related to activity level, fitness and psychomotor speed. As already described in literature, natural turning during daily activity is related to mobility disability that may enable early detection of increased fall risk [104]. In our study, both the mean and extreme values of mean and peak turn velocity were positively associated with the self-reported PA, the SPPB, and negatively associated with TMTA. Extreme values of mean and peak velocity were also positively associated with PWR. Mean values of turning duration were negatively associated with measures of fitness (PWR, HAND and SPPB) and positively associated with psychomotor speed (TMTA). The association of turning ability with TMTA may reflect the motor planning component that is also associated with this motor task. The extreme values of turn duration were not associated with fitness level or cognition, suggesting that best turning performance seems to be a function of context rather than fitness level. Mean values of the turning velocity jerkiness were negatively associated with the hand-grip strength (HAND) and with information about falls (number of falls, FALLN). The extreme

values of this feature are negatively associated with functional status (SPPB) and positively associated with TMTA. It was shown elsewhere that sedentariness influence negatively the cognitive function [119,120]. In our study, older adults who were more fit had fewer difficulties in turning, both for planning and execution of this task. Mean values of the cadence feature were negatively associated with the hand-grip strength (HAND). The features associated with gait regularity were related to strength, functional status, and disability. Both the mean and extreme values of the harmonic ratio and step regularity were positively associated with hand-grip strength (HAND) and functional status (SPPB). Extremes values of the harmonic ratio and step regularity were also negatively associated with disability (IADL). Subjects with high gait regularity seem to be stronger and healthier. Mean and extremes values of the features associated with gait variability and agility (coordination and step duration) were not related to any of the clinical variables. Only extreme values of the step duration were negatively associated with the functional status (SPPB). This could be due to the high number of confounders that can affect variability values as environmental factors (e.g. how large is the home environment) and dual tasking (e.g. walking while talking). Activity level, turning ability, and cadence serve as factors in both conceptual models. The remaining factors that differ between the two models relate to gait characteristics. In the factor analysis based on mean values, features relating to gait variability and regularity are grouped together in one factor and gait coordination is identified as an independent factor. In the factor analysis based on extreme values, gait variability, gait regularity, and agility (coordination plus speed) are identified as three independent factors. In the model based on extreme values, the gait regularity factor groups together the features associated with disability, strength, and the functional level. Agility is also associated with the functional level. On the contrary, in the model based on the mean values, gait characteristics are fused together into one factor and are not associated with any of the clinical variables. This finding suggests that distinguishing between gait variability and regularity could be important, especially when assessing features that likely represent extreme values (i.e. in a supervised clinical setting). In the factor analysis based on the mean values, the coordination factor is composed of the coordination index feature. In the model based on extreme values coordination index and step duration are grouped together. This represents the association between high speed (low step duration) and coordination for high performance. In conclusion, these findings suggest that the accuracy of adaptive walking (which involves gait regularity and variability) is better in physically active, higher functioning older adults, as also shown in previous studies [121–123].

6.5. CONCLUSIONS

In conclusion, outcomes of the SP-based activity monitoring are consistent with the clinical assessment, suggesting that SP-based technology has great potential in the clinical realm. SPs may effectively enable the ecological, quantitative behavioural analysis of community-dwelling older adults. As predicted, extreme values of the physical activity features seem to be more indicative of functional status and are more closely related with motor performance assessed in a supervised clinical setting.

7. FINAL REMARKS AND FUTURE DIRECTIONS

The central aim of this thesis was the design of a general model for providing an objective and comprehensive functional assessment tool, being able to also explore the relationships among instrumented scores, clinical scores and specific impairments and diseases.

First, the discriminative ability of standard clinical and instrumented measures of PP in distinguishing between different levels of functional status (as measured with Late-Life Function and Disability Instrument, LLFDI [55]) was evaluated in a very healthy and fit group of adults living in the community. The first limitation of this study was the homogeneous population, characterized by a very skewed distribution of the LLFDI scores. The second limitation was that the ratio between the sample size and the number of instrumented measures required the performance of a feature selection and this might have led to a loss of information. Lastly, there was a lack in the literature for validated cut-off for discriminating between different LLFDI levels. Despite these limitations, instrumented 30CST and TUG measures proofed to be comparable to the standard clinical measures, with moderate discriminative ability, in detecting slight differences of LLFDI even in this homogeneous, healthy and fit population. Further investigations are needed to define validated cut-off scores to distinguish between different levels of LLFDI and therefore confirm the hypothesis that slight differences in functional status can be detected, also in an older cohort of community dwellers. Second, age and gender effect on a set of sensor-based measures were investigated in a large group of communitydwelling adults. The findings showed that many sensor-based PP measures exhibited a significant association with age. As expected, speed/time related features clearly worsen with aging, but also features computed from the locomotion, static and dynamic balance control, as well as features which can be related to the global fitness of the persons. Third, an EFA was performed on a set of sensorbased measures extracted from the instrumented TUG test in a group of community-dwelling elderly people. The aim was to classify domains of an instrumented TUG and investigate the functional decline with age of these domains. Gender-related differences were also investigated. This study showed that the sensor-based TUG measures were grouped in domains with clear clinical meaning. Statistical analysis provided evidence about the feasibility of a sensor-based assessment in assessing the functional decline in the general population. TUG domains computed by the EFA allowed to objectively measure several mobility skills well beyond the conventional clinical outcome (total TUG duration). Starting from these results, the EFA was applied on a battery of PP tests, to define a conceptual model, supporting the design of a sensor-based tool for assessing older adults' PC. The conceptual model development process included three stages. In the first stage, EFA was performed on the residuals obtained from a robust linear regression analysis, to remove the effect of age, gender, body composition (height and weight) and cognition (MMSE) from the sensor-based PP measures.

In the second stage, the overall physical performance was removed from the sensor-based PP measures along with age, gender, body composition and cognition, before performing the EFA. At this stage, the scores used to evaluate the individuals' PC were obtained performing the EFA on the residuals, which made the model complex and difficult to understand and use. In the last stage of the conceptual model development process, EFA was performed on the sensor-based measures, and not on the residuals. This version of the conceptual model resulted in domains with a clear clinical meaning and coherent with the conventional clinical assessment of older adults' PC. Regression analysis suggested that such domains expand information obtained with clinical testing and provide quantitative information about several mobility skills that are usually not captured by conventional outcomes. Fifth, the conceptual model was applied on the sensor-based measures extracted from a population of older people at risk of falling, to obtain information about their physical functional status. Three relevant case studies have also been illustrated. The information gained from the conceptual model were coherent with the conventional assessment of PC and allowed to obtain detailed, quantitative, information about individuals' physical impairments. The limit of the EFA is that it is exploratory, meaning that it does not require a priori hypotheses and knowledge about the exact nature of the underlying structure. Further work is needed to test and confirm the hypothesized structure of the conceptual model. Furthermore, it would be valuable also to understand the causal relationships between domains and between domains and clinical outcomes to increase our knowledge and understanding of the factors that influence the individuals' PC. In addition, the domains of the conceptual model allowed to explore the relationships with specific neurological conditions, like Stroke and Parkinson's disease, however, further work is needed to evaluate whether this more detailed information adds to our ability to predict adverse outcomes, over and above clinical testing like gait and SPPB. A follow-up could be of interest to evaluate the performance of the proposed model in discriminating robust and pre-frail people compared to clinical assessment. The application of the model in different populations demonstrates its validity and clinical significance. Unfortunately, the three cohorts presented in this thesis have different outcome measures and it was possible to deeply investigate only the participants' physical function. A more specific and detailed cognitive assessment of the population would have been useful to better describe the potential of the model to detect also cognitive decline. We also provide interesting/representative use cases to show how such a model would be used in practice. The so defined conceptual model could be of value for clinicians in assessing individuals' PC and identify therapeutic targets for rehabilitation. The domains of the conceptual model have shown a clear clinical meaning and cold contribute to facilitate the adoption of the sensor-based assessment in everyday clinical practice; a significant step forward in the direction of an evidence based medicine.

At last, the individuals' usual performance, was objectively measured through daily PA monitoring. The association between mean and extreme values of PA and gait characteristics derived from daily living activities and well-established clinical tools were explored for quantifying motor and cognitive impairments in a cohort of community-dwelling older adults. The datasets of mean and extreme values have also been used as an input for an EFA to define conceptual models of daily living activities. As expected, extreme values of the PA features seem to be more indicative of functional status and are more closely related with motor performance assessed in a supervised clinical setting. Outcomes of both the sensor-based PP assessment and continuous PA monitoring are consistent with the conventional clinical assessment, suggesting that inertial sensing technology has great potential in the clinical realm, for the evaluation of individuals' PC. Inertial sensors are becoming widely deployed into objects of daily living like smartphones and stopwatches. Further work is needed to investigate whether the information collected from the PC's sensor-based measures could be integrated to go beyond the clinical outcome assessment, to support remote health and to empower people to self-manage their own health and function by adopting a healthy and active lifestyle.

In conclusion, the development and implementation of an easy to use, objective and comprehensive tool for the assessment of the individuals' PC has demonstrated to be feasible. This tool enriches the conventional clinical outcomes, allowing to objectively measure several mobility skills that would otherwise remain undetected. The sensor-based assessment tool could foster the achievement of the early detection of the age-related functional decline, facilitating the design of interventions and rehabilitation strategies.
8. APPENDIX A: SENSOR-BASED MEASURES COMPUTED FROM THE INSTRUMENTED PHYSICAL PERFORMANCE TESTS

Feature		Sensor	Description			
			Centroidal frequency; frequency at which spectral mass is concentrated. Spectral moments are needed for the			
CF		Accelerometer	estimate: $\sum_{k=1}^{N} p_{k} $			
AP ML [124,125]			$\mu_0 = \sum_{i=1}^{n} PSD_i = TP; \ \mu_2 = \sum_{i=1}^{n} f_i^2 PSD_i; \ CF = \sqrt{\frac{1-1}{\mu_0}}$			
			Where PSD is the Power Spectral Density of the signal, f is the frequency vector, and N is the total number of points of the PSD . Frequencies below 0.15Hz are usually ignored.			
EA DISPL [124,125]		Accelerometer, Displacement	The 95% confidence Ellipse Area is the area of the confidence ellipse enclosing 95% of the points on the sway trajectory. The accelerometer-based postural parameter can be defined by analogy with the parameter based on the displacement.			
		Accelerometer	Median frequency; frequency below which 50% of total signal power (<i>TP</i>) is present. Starting from the Power Spectral Density (<i>PSD</i>) of the signal:			
F50%			Spectral Density (15D) of the signal. $\sum_{n=1}^{n} p_{n} p$			
AP ML			$g_n = \sum_{i=1}^{N} PSD_i$; $F_{50\%} = f_n$, min $_n: g_n \ge 50\% TP$			
[124,125]			Where the second formula means that $F_{50\%}$ is the frequency, f , corresponding to the nth index which is the smallest index such that $g(n)$ is $\geq 50\%$ of the total power. The total power is equal to $g(N)$ where N is the total number of points of the <i>PSD</i> . Frequencies below 0.15Hz are usually ignored.			
			Frequency below which 95% of total signal power (<i>TP</i>) is present. Starting from the Power Spectral Density (<i>PSD</i>) of the signal:			
F95%			$\sum_{n=1}^{n}$			
AP ML		Accelerometer	$g_n = \sum_{i=1}^{n} PSD_i$; $F_{95\%} = f_n$, min $_n: g_n \ge 95\% TP$			
[124,125]			Where the second formula mean that $F_{95\%}$ is the frequency, f , corresponding to the nth index which is the smallest index such that $g(n)$ is $\geq 95\%$ of the total power. The total power is equal to $g(N)$ where N is the total number of points of the <i>PSD</i> . Frequencies below 0.15Hz are usually ignored.			
FD		Accelerometer	Frequency dispersion; unitless measure of the variability of the power spectral density frequency content (zero for pure sinusoid; increases with spectral bandwidth to one). Spectral moments are needed for the estimate:			
AP ML			$\mu_0 = \sum_{i=1}^N PSD_i = TP; \ \mu_1 = \sum_{i=1}^N f_i \ PSD_i \ ; \ \mu_2 = \sum_{i=1}^N f_i^2 \ PSD_i; \ FD = \sqrt{\frac{1-\mu_1^2}{\mu_0\mu_2}}$			
[124,125]			Where PSD is the Power Spectral Density of the signal, f is the frequency vector, and N is the total number of points of the PSD . Frequencies below 0.15Hz are usually ignored.			
	ML	Accelerometer, Displacement	Mean Velocity of the postural sway computed as the median of the absolute value of the time series obtained integrating the acceleration:			
N (X)			$MV = median\left(\int_{Tstart}^{Tend} a(t)dt\right)$			
MV DISPL AP [124,125]			Where a is the acceleration component m/s ² , <i>Tend/Tstart</i> are the end and the beginning of the observation time respectively.			
			An alternative definition can be based upon the Sway Path (SP) of the displacement:			
			$MV = \left(\frac{SP}{T_{end} - T_{start}}\right)$			
NJS		Accelerometer	Normalized Jerk Score of the acceleration:			
AP ML [49,126]		Accelerometer				

Table 8.1 Sensor-based features extracted from the QS test

Range
AP MLAccelerometerRange of the signalAP MLAccelerometerRange of the signalRMS
AP MLAccelerometerRoot Mean Square (RMS) of the signal, s (it is a measure of dispersion):
$$RMS = \sqrt{\frac{1}{N}} \sum_{l=1}^{N} (s_l - m)^2$$

where N is the total number of points of the signal s, and m is the mean value mean(s)SA
DISPL [124,125]DisplacementSway Area (SA) estimated as the sum of the triangles formed by two consecutive points on the sway trajectory
on the horizontal plane (sar and suc) and the mean point (mar and max) on the plane:
SA $= \frac{1}{2} \sum_{n=1}^{N-1} [(S_{n,l+1} - m_{n,l})(S_{ML,l} - m_{n,l})] (S_{ML,l+1} - m_{ML})]SADISPL [124,125]DisplacementSa $= \frac{1}{2} \sum_{n=1}^{N-1} [(S_{n,l+1} - m_{n,l})(S_{ML,l} - m_{n,l})(S_{ML,l+1} - m_{ML})]Where s is a generic signal, sup and sup are the two sway components on the horizontal plane. N is the totalnumber of points of the signal time series.The accelerometer - based postural parameter can be defined by analogy with the parameter based on thedisplacement.SPAP MLDISPL [124,125]Accelerometer,DisplacementSpectral Entropy Power spectrum entropy of acceleration (unitless). $P = \sum_{l=1}^{l} (s_{l+1} - s_l)$ SP
DISPL [124,125]When considering the sway path on the horizontal plane:
 $Sp = \sum_{l=1}^{l} (S_{n'l+1} - S_{n'l,l})^2 + (S_{NL,l+1} - S_{NL,l})^2$ Where s is a generic signal, sup and sup, are the two sway components on the horizontal plane. N is the total
meanue of points of the signal time series.
 $P = \sum_{l=1}^{l} (S_{n'l+1} - S_{n'l,l})^2 + (S_{NL,l+1} - S_{NL,l})^2$ SP
DISPL [124,125]Mere s is a generic signal, sup and sup, are the two sway components on the horizontal plane. N is the total
meanue$$

 $NJS = \sqrt{\frac{T^5}{2SP^2}} \int_{T_{start}}^{T_{end}} (\dot{a})^2 dt$

Frequency Dispersion; ML: Medio-Lateral; MV: Mean Velocity; NJS: Normalized Jerk Score; RMS: Root Mean Square; SA: Sway Area; SE: Spectral Entropy; SP: Sway Path; V: Vertical

Feature	Sensor	Description		
Duration	Accelerometer/			
[s]	Gyroscope	Total duration of the test		
Cadence [steps/min]	Accelerometer	Cadence in the phase of the gait		
SD Cadence	Accelerometer	Standard deviation of the Cadence		
NJS [49,126]				
AP ML V	P ML V Accelerometer The Normalized Jerk Score during gait is computed for each step (i.e., between two or then normalized to the step duration, and then averaged across all steps			
[m]				
		Phase Coordination Index (PCI). PCI measures gait coordination (i.e., the accuracy and consistency of the phase generation).		
		$PCI = PhaseCV + 100 \cdot \frac{\frac{1}{N} \sum_{i=1}^{N} \varphi_i - 180^{\circ} }{180^{\circ}}$		
PCI [30 49]		where <i>PhaseCV</i> is the Coefficient of Variation of the Phase.		
[-]	Accelerometer	φ_i is the ith phase, which measures the step time with respect to the stride time assigning 360° to each stride (gait cycle):		
		$\varphi_i = 360^\circ \frac{hs_{S,i} - hs_{L,i}}{hs_{L,i+1} - hs_{L,i}}$		
		where $h_{SL(i)}$ and $h_{SS(i)}$ denote the time of the ith heel strike of the legs with the long and short step times, respectively.		
Range				
AP ML V	Accelerometer	Range of the signal		
[m/s ²]				
DMG		Root Mean Square (<i>RMS</i>) of the signal, <i>s</i> (it is a measure of dispersion):		
	A 1 -	$RMS = \frac{1}{N}\sum_{(c_1, \dots, m)^2}^{N}$		
AP ML V	Accelerometer	$\sqrt{N}\sum_{i=1}^{N}(S_i - M)$		
$[m/s^2]$		where N is the total number of points of the signal s , and m is the mean value $mean(s)$		
		Step and Stride regularity measured by means of the unbiased estimate of the autocorrelation function of the signal <i>s</i> :		
Reg [31]		$A_{\text{unbloced}} = \frac{1}{\sum_{i=1}^{N- n } \sum_{i=1}^{N- n } s_i s_{i+1}}$		
AP ML V [31]	Accelerometer	$N - n \sum_{i=1}^{n-1} n^{n-1}$		
[-]		Where N is the total number of points of the signal and n is the phase shift in number of samples.		
		First dominant period (A_{dI}) of the autocorrelation coefficient is an expression of the step regularity.		
		Second dominant period (A_{d2}) of the autocorrelation coefficient is an expression of the stride regularity		

ACRONYMS: AP: Antero-Posterior; ML: Medio-Lateral; NJS: Normalized Jerk Score; PCI: Phase Coordination Index; Reg: Regularity; RMS: Root Mean Square; SD: Standard Deviation; V: Vertical

Feature	Sensor	Task	Description
Repetitions	Accelerometer/	Total	
[s]	Gyroscope		I otal number of repetitions.
SD Duration	Accelerometer/ Gyroscope	Sit-to-Stand, Stand- to-Sit	Standard deviation of the duration of each subtask of the test.
Duration	Accelerometer/	Total, Sit-to-Stand,	Duration of each subtask of the test.
[s]	Gyroscope	Stand-to-Sit	
		Sit-to-Stand, Stand- to-Sit	Normalized Jerk Score of the acceleration (it is related with the smoothness of the movement):
NJS	Accelerometer		T5 cTend
AP ML V			$NJS = \int \frac{1^3}{2} \int_{Tstart}^{Tstart} (\dot{a})^2 dt$
[m]			where <i>T</i> is the duration (<i>Tend-Tstart</i>) of the considered sub-task and <i>a</i> is the acceleration measured in m/s^2 .
Range			
AP ML V	Accelerometer,	Sit-to-Stand, Stand-	
[m/s ²],	Gyroscope	to-Sit	Range of the signal, during the considered sub-task of the test
[°/s]			
RMS			Root Mean Square (<i>RMS</i>) of the signal, <i>s</i> , during the considered sub-task of
AP, ML, V	Accelerometer,	Sit-to-Stand, Stand- to-Sit	the test (it is a measure of dispersion): $\sqrt{\frac{1}{1}}$
[m/s ²],	Gyroscope		$RMS = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(s_i - m)^2}$
[°/s]			where N is the total number of points of the signal <i>s</i> , and m is the mean value $mean(s)$

Feature	Sensor	Sub-Phases	Description			
Duration [s]	Accelerometer/ Gyroscope	Total, Sit-to-Walk, Walk, 180Turn, Turn- to-Sit	Total duration and duration of each sub-phase of the TUG			
Number of Steps	Accelerometer/ Gyroscope	180Turn, Walk	Number of steps during each sub-phase of the TUG			
		61	Root Mean Square of the signal, <i>s</i> , during the considered sub- phase (hence a measure of dispersion):			
RMS AP, ML, V [m/s ²]	Accelerometer	Sit-to-Walk, Walk, Turn-to-Sit	$RMS = \sqrt{\frac{1}{N} \sum_{i=1}^{N} (s_i - m)^2}$			
			where N is the total number of points of the signal s , and m is the mean value: $mean(s)$			
NJS AP, ML, V [m]	Accelerometer	Sit-to-Walk, Turn-to-Sit	Time-Normalized Jerk Score of the acceleration: $NJS = \sqrt{\frac{T^5}{2} \int_{Tstart}^{Tend} (\dot{a})^2 dt}$ where <i>T</i> is the duration of the (<i>Tend-Tstart</i>) of the considered sub-phase and <i>a</i> is the acceleration measured in m/s ² .			
NJS V [-]	Gyroscope	180Turn, Turn-to-Sit Turning	Normalized angular Jerk Score: $NJS = \sqrt{\frac{T^5}{2TA^2}} \int_{Tstart}^{Tend} (\ddot{\omega})^2 dt;$ where <i>T</i> is the turn duration (<i>Tend-Tstart</i>) of the considered component, ϖ is the angular velocity °/s, and <i>TA</i> is the Turning Angle in °. $TA = \int_{Tstart}^{Tend} \omega dt$			
Mean Velocity [°/s]	Gyroscope	180Turn, Turn-to-Sit Turning	Mean Velocity, as the mean value of the angular velocity along the vertical axis during the turn: $Mean \ Velocity = \frac{1}{NE-NS} \sum_{i=NS}^{NE} \omega(i)$ Where ω is the angular velocity in °/s; NE and NS are the index of the end and the index of the beginning of the turn, respectively.			
Maximum Velocity [°/s]	Gyroscope	180Turn, Turn-to-Sit Turning	Maximum Velocity as the maximum value of the angular velocity along the vertical axis during the turn: $Maximum Velocity = \max(\omega)_{NS}^{NE}$ Where ω is the angular velocity in °/s; <i>NE</i> and NS are the index of the end and the index of the beginning of the turn, respectively.			
ACRONYMS: AP: Antero-Posterior; ML: Medio-Lateral; V: Vertical						

Table 8.4 Sensor-based features extracted from the TUG test

9. **BIBLIOGRAPHY**

- 1. PreventIT project Available online: http://www.preventit.eu/ (accessed on Jan 21, 2019).
- 2. InCHIANTI Study Available online: http://inchiantistudy.net.
- 3. PRE.C.I.S.A. study.
- 4. Eurostat Population structure and ageing Statistics Explained Available online: https://ec.europa.eu/eurostat/statisticsexplained/index.php?title=Population_structure_and_ageing#The_share_of_elderly_people_ continues_to_increase.
- 5. World Health Organization Ageing and health Available online: http://www.who.int/news-room/fact-sheets/detail/ageing-and-health.
- 6. World Health Organization WHO | The Global strategy and action plan on ageing and health Available online: http://www.who.int/ageing/global-strategy/en/.
- 7. Vaupel, J. W. Biodemography of human ageing. **2010**, doi:10.1038/nature08984.
- Bauman, A.; Merom, D.; Bull, F. C.; Buchner, D. M.; Fiatarone Singh, M. A. Updating the Evidence for Physical Activity: Summative Reviews of the Epidemiological Evidence, Prevalence, and Interventions to Promote "Active Aging." *Gerontologist* 2016, 56, S268– S280, doi:10.1093/geront/gnw031.
- 9. Martin-Ruiz, C.; Von Zglinicki, T. Biomarkers of healthy ageing: expectations and validation. **2018**, doi:10.1017/S0029665114000147.
- Lara, J.; Cooper, R.; Nissan, J.; Ginty, A. T.; Khaw, K.-T.; Deary, I. J.; Lord, J. M.; Kuh, D.; Mathers, J. C. A proposed panel of biomarkers of healthy ageing. *BMC Med.* 2015, *13*, 222, doi:10.1186/s12916-015-0470-9.
- 11. Cooper, R.; Strand, B. H.; Hardy, R.; V Patel, K.; Kuh, D. Physical capability in mid-life and survival over 13 years of follow-up: British birth cohort study. *BMJ* **2014**, *348*, doi:10.1136/bmj.g2219.
- 12. Kuh Diana, Cooper Rachel, Hardy Rebecca, Richards Marcus, B.-S. Y. A Life Course Approach to Healthy Ageing; ISBN 0191008176.
- Guralnik, J. M.; Ferrucci, L.; Pieper, C. F.; Leveille, S. G.; Markides, K. S.; Ostir, G. V.; Studenski, S.; Berkman, L. F.; Wallace, R. B. Lower Extremity Function and Subsequent Disability. *Journals Gerontol. Ser. A Biol. Sci. Med. Sci.* 2000, 55, M221–M231, doi:10.1093/GERONA/55.4.M221.
- Buchman, A. S.; Wilson, R. S.; Boyle, P. A.; Bienias, J. L.; Bennett, D. A. Change in Motor Function and Risk of Mortality in Older Persons. J. Am. Geriatr. Soc. 2007, 55, 11–19, doi:10.1111/j.1532-5415.2006.01032.x.
- 15. Cooper, R.; Kuh, D.; Cooper, C.; Gale, C. R.; Lawlor, D. A.; Matthews, F.; Hardy, R. Objective measures of physical capability and subsequent health: A systematic review. *Age Ageing* **2011**, *40*, 14–23, doi:10.1093/ageing/afq117.
- 16. Keevil, V. L.; Luben, R.; Hayat, S.; Sayer, A. A.; Wareham, N. J.; Khaw, K.-T. Physical capability predicts mortality in late mid-life as well as in old age: Findings from a large British cohort study. **2017**, doi:10.1016/j.archger.2017.10.001.

- Sikkes, S. A. M.; de Lange-de Klerk, E. S. M.; Pijnenburg, Y. A. L.; Scheltens, P.; Uitdehaag, B. M. J. A systematic review of Instrumental Activities of Daily Living scales in dementia: room for improvement. *J. Neurol. Neurosurg. Psychiatry* 2009, *80*, 7–12, doi:10.1136/jnnp.2008.155838.
- Hobart, J. C.; Cano, S. J.; Zajicek, J. P.; Thompson, A. J. Rating scales as outcome measures for clinical trials in neurology: problems, solutions, and recommendations. *neurology.thelancet.com* 2007, *6*, doi:10.1016/S1474-4422(07)70290-9.
- 19. den Ouden, M. E. M.; Schuurmans, M. J.; Arts, I. E. M. A.; van der Schouw, Y. T. Physical performance characteristics related to disability in older persons: a systematic review. *Maturitas* **2011**, *69*, 208–19, doi:10.1016/j.maturitas.2011.04.008.
- 20. Freiberger, E.; de Vreede, P.; Schoene, D.; Rydwik, E.; Mueller, V.; Frändin, K.; Hopman-Rock, M. Performance-based physical function in older community-dwelling persons: a systematic review of instruments. *Age Ageing* **2012**, *41*, 712–721, doi:10.1093/ageing/afs099.
- Guralnik, J. M.; Simonsick, E. M.; Ferrucci, L.; Glynn, R. J.; Berkman, L. F.; Blazer, D. G.; Scherr, P. A.; Wallace, R. B. A Short Physical Performance Battery Assessing Lower Extremity Function: Association With Self-Reported Disability and Prediction of Mortality and Nursing Home Admission. J. Gerontol. 1994, 49, M85–M94, doi:10.1093/geronj/49.2.M85.
- Ferrucci, L.; Cooper, R.; Shardell, M.; Simonsick, E. M.; Schrack, J. A.; Kuh, D. Age-Related Change in Mobility: Perspectives From Life Course Epidemiology and Geroscience. *Journals Gerontol. Ser. A Biol. Sci. Med. Sci.* 2016, 71, 1184–1194, doi:10.1093/gerona/glw043.
- 23. Mathie, M. J.; Coster, A. C. F.; Lovell, N. H.; Celler, B. G. Accelerometry: providing an integrated, practical method for long-term, ambulatory monitoring of human movement. *Physiol. Meas* **2004**, *25*, 1–20, doi:10.1088/0967-3334/25/2/R01.
- 24. Henriksen, M.; Lund, H.; Moe-Nilssen, R.; Bliddal, H.; Danneskiod-Samsøe, B. Test–retest reliability of trunk accelerometric gait analysis. *Gait Posture* **2004**, *19*, 288–297, doi:10.1016/S0966-6362(03)00069-9.
- Mancini, M.; Salarian, A.; Carlson-Kuhta, P.; Zampieri, C.; King, L.; Chiari, L.; Horak, F. B. ISway: a sensitive, valid and reliable measure of postural control. *J. Neuroeng. Rehabil.* 2012, 9, 59, doi:10.1186/1743-0003-9-59.
- Van Lummel, R. C.; Ainsworth, E.; Lindemann, U.; Zijlstra, W.; Chiari, L.; Van Campen, P.; Hausdorff, J. M. Automated approach for quantifying the repeated sit-to-stand using one body fixed sensor in young and older adults. *Gait Posture* 2013, *38*, 153–156, doi:10.1016/J.GAITPOST.2012.10.008.
- Mellone, S.; Tacconi, C.; Schwickert, L.; Klenk, J.; Becker, C.; Chiari, L. Smartphone-based solutions for fall detection and prevention: the FARSEEING approach. *Z. Gerontol. Geriatr.* 2012, 45, 722–727, doi:10.1007/s00391-012-0404-5.
- 28. Zijlstra, W. Assessment of spatio-temporal parameters during unconstrained walking. *Eur. J. Appl. Physiol.* **2004**, *92*, 39–44, doi:10.1007/s00421-004-1041-5.
- 29. Hartmann, A.; Luzi, S.; Murer, K.; de Bie, R. A.; de Bruin, E. D. Concurrent validity of a trunk tri-axial accelerometer system for gait analysis in older adults. *Gait Posture* **2009**, *29*, 444–448, doi:10.1016/j.gaitpost.2008.11.003.

- 30. Plotnik, M.; Giladi, N.; Hausdorff, J. M. A new measure for quantifying the bilateral coordination of human gait: effects of aging and Parkinson's disease. *Exp. Brain Res.* **2007**, *181*, 561–570, doi:10.1007/s00221-007-0955-7.
- 31. Moe-Nilssen, R.; Helbostad, J. L. Estimation of gait cycle characteristics by trunk accelerometry. *J. Biomech.* **2004**, *37*, 121–126, doi:10.1016/S0021-9290(03)00233-1.
- Brach, J. S.; McGurl, D.; Wert, D.; Vanswearingen, J. M.; Perera, S.; Cham, R.; Studenski, S. Validation of a measure of smoothness of walking. *J. Gerontol. A. Biol. Sci. Med. Sci.* 2011, *66*, 136–41, doi:10.1093/gerona/glq170.
- 33. Weiss, A.; Herman, T.; Plotnik, M.; Brozgol, M.; Maidan, I.; Giladi, N.; Gurevich, T.; Hausdorff, J. M. Can an accelerometer enhance the utility of the Timed Up and Go Test when evaluating patients with Parkinson's disease? *Med. Eng. Phys.* **2010**, *32*, 119–125, doi:10.1016/j.medengphy.2009.10.015.
- 34. Zampieri, C.; Salarian, A.; Carlson-Kuhta, P.; Aminian, K.; Nutt, J. G.; Horak, F. B. The instrumented timed up and go test: potential outcome measure for disease modifying therapies in Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* **2010**, *81*, 171–6, doi:10.1136/jnnp.2009.173740.
- 35. Stijntjes, M.; Meskers, C. G. M. G. M.; De Craen, A. J. M. J. M.; Van Lummel, R. C. C.; Rispens, S. M. M.; Slagboom, P. E. E.; Maier, A. B. B. Effect of calendar age on physical performance: A comparison of standard clinical measures with instrumented measures in middle-aged to older adults. *Gait Posture* 2016, 45, 12–18, doi:10.1016/j.gaitpost.2015.12.018.
- 36. Park, J.-H.; Mancini, M.; Carlson-Kuhta, P.; Nutt, J. G.; Horak, F. B. Quantifying effects of age on balance and gait with inertial sensors in community-dwelling healthy adults. *Exp. Gerontol.* **2016**, *85*, 48–58, doi:10.1016/j.exger.2016.09.018.
- 37. Awais, M.; Chiari, L.; Ihlen, E. A. F.; Helbostad, J.; Palmerini, L. Physical Activity Classification for Elderly People in Free Living Conditions. *IEEE J. Biomed. Heal. Informatics* **2018**, 1–1, doi:10.1109/JBHI.2018.2820179.
- 38. Grimm, B.; Bolink, S. Evaluating physical function and activity in the elderly patient using wearable motion sensors. *EFORT open Rev.* **2016**, *1*, 112–120, doi:10.1302/2058-5241.1.160022.
- 39. Reio, T. G.; Shuck, B. Exploratory Factor Analysis: Implications for Theory, Research, and Practice. *Adv. Dev. Hum. Resour.* **2015**, *17*, 12–25, doi:10.1177/1523422314559804.
- 40. Verghese, J.; Wang, C.; Lipton, R. B.; Holtzer, R.; Xue, X. Quantitative gait dysfunction and risk of cognitive decline and dementia. *J. Neurol. Neurosurg. Psychiatry* **2007**, *78*, 929–35, doi:10.1136/jnnp.2006.106914.
- 41. Verghese, J.; Robbins, M.; Holtzer, R.; Zimmerman, M.; Wang, C.; Xue, X.; Lipton, R. B. Gait Dysfunction in Mild Cognitive Impairment Syndromes. *J. Am. Geriatr. Soc.* **2008**, *56*, 1244–1251, doi:10.1111/j.1532-5415.2008.01758.x.
- 42. Verghese, J.; Holtzer, R.; Lipton, R. B.; Wang, C. Quantitative Gait Markers and Incident Fall Risk in Older Adults. *Journals Gerontol. Ser. A Biol. Sci. Med. Sci.* **2009**, *64A*, 896–901, doi:10.1093/gerona/glp033.
- 43. Lord, S.; Galna, B.; Verghese, J.; Coleman, S.; Burn, D.; Rochester, L. Independent domains of gait in older adults and associated motor and nonmotor attributes: Validation of a factor

analysis approach. *Journals Gerontol. - Ser. A Biol. Sci. Med. Sci.* **2013**, 68, 820–827, doi:10.1093/gerona/gls255.

- 44. Mahoney, J. R.; Verghese, J. Visual-Somatosensory Integration and Quantitative Gait Performance in Aging. *Front. Aging Neurosci.* **2018**, *10*, 377, doi:10.3389/fnagi.2018.00377.
- 45. Hollman, J. H.; McDade, E. M.; Petersen, R. C. Normative spatiotemporal gait parameters in older adults. *Gait Posture* **2011**, *34*, 111–118, doi:10.1016/J.GAITPOST.2011.03.024.
- 46. Kirkwood, R. N.; Gomes, H. A.; Sampaio, R. F.; Furtado, S. R. C.; Moreira, B. S. Spatiotemporal and variability gait data in community-dwelling elderly women from Brazil. *Brazilian J. Phys. Ther.* **2016**, *20*, 258–266, doi:10.1590/bjpt-rbf.2014.0157.
- 47. Buckley, C.; Galna, B.; Rochester, L.; Mazzà, C. Upper body accelerations as a biomarker of gait impairment in the early stages of Parkinson's disease. *Gait Posture* **2018**, doi:10.1016/J.GAITPOST.2018.06.166.
- 48. Hubble, R. P.; Naughton, G. A.; Silburn, P. A.; Cole, M. H. Wearable sensor use for assessing standing balance and walking stability in people with Parkinson's disease: A systematic review. *PLoS One* **2015**, *10*, 1–22, doi:10.1371/journal.pone.0123705.
- 49. Palmerini, L.; Mellone, S.; Avanzolini, G.; Valzania, F.; Chiari, L. Quantification of Motor Impairment in Parkinson's Disease Using an Instrumented Timed Up and Go Test. *IEEE Trans. Neural Syst. Rehabil. Eng.* **2013**, *21*, 664–673, doi:10.1109/TNSRE.2012.2236577.
- Coni, A.; Ancum, J. M. Van; Bergquist, R.; Mikolaizak, A. S.; Mellone, S.; Chiari, L.; Maier, A. B.; Pijnappels, M. Comparison of Standard Clinical and Instrumented Physical Performance Tests in Discriminating Functional Status of High-Functioning People Aged 61–70 Years Old. *Sensors* 2019, 19, 449, doi:10.3390/s19030449.
- 51. Jette, Alan M and Haley, Stephen M and Kooyoomjian, J. T. Late-Life FDI Manual. *Boston, MA Bost. Univ.* **2002**, 73.
- 52. Helbostad, J. L.; Vereijken, B.; Becker, C.; Todd, C.; Taraldsen, K.; Pijnappels, M.; Aminian, K.; Mellone, S. Mobile Health Applications to Promote Active and Healthy Ageing. *Sensors* **2017**, *17*, 622, doi:10.3390/s17030622.
- Haley, S. M.; Jette, A. M.; Coster, W. J.; Kooyoomjian, J. T.; Levenson, S.; Heeren, T.; Ashba, J. Late Life Function and Disability Instrument: II. Development and evaluation of the function component. *Journals Gerontol. Ser. A Biol. Sci. Med. Sci.* 2002, *57*, M217--M222.
- Nasreddine, Z. S.; Phillips, N. A.; Bédirian, V.; Charbonneau, S.; Whitehead, V.; Collin, I.; Cummings, J. L.; Chertkow, H. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. *J. Am. Geriatr. Soc.* 2005, *53*, 695–699, doi:10.1111/j.1532-5415.2005.53221.x.
- 55. Jette, A. M.; Haley, S. M.; Kooyoomjian, J. T. Late-Life FDI Manual Roybal Center for the Enhancement of Late-Life Function; 2002;
- 56. Mellone, S.; Tacconi, C.; Chiari, L. Validity of a Smartphone-based instrumented Timed Up and Go. *Gait Posture* **2012**, *36*, 163–165, doi:10.1016/j.gaitpost.2012.02.006.
- 57. MATLAB and Statistics Toolbox Release 2017b.
- 58. Mellone, S. **2013** Movement Analysis by means of inertial sensors: from bench to bedside. PhD Thesis. Alma Mater Studiorum - Università di Bologna.

- 59. Zijlstra, A.; Mancini, M.; Lindemann, U.; Chiari, L.; Zijlstra, W. Sit-stand and stand-sit transitions in older adults and patients with Parkinson's disease: event detection based on motion sensors versus force plates. *J. Neuroeng. Rehabil.* **2012**, *9*, 75, doi:10.1186/1743-0003-9-75.
- 60. Weiss, A.; Mirelman, A.; Buchman, A. S.; Bennett, D. A.; Hausdorff, J. M.; Kado, D. Using a Body-Fixed Sensor to Identify Subclinical Gait Difficulties in Older Adults with IADL Disability: Maximizing the Output of the Timed Up and Go. **2013**, doi:10.1371/journal.pone.0068885.
- El-Gohary, M.; Pearson, S.; McNames, J.; Mancini, M.; Horak, F.; Mellone, S.; Chiari, L. Continuous monitoring of turning in patients with movement disability. *Sensors (Basel)*. 2013, *14*, 356–69, doi:10.3390/s140100356.
- 62. Salarian, A.; Horak, F. B.; Zampieri, C.; Carlson-Kuhta, P.; Nutt, J. G.; Aminian, K. iTUG, a sensitive and reliable measure of mobility. *IEEE Trans. Neural Syst. Rehabil. Eng.* **2010**, *18*, 303–10, doi:10.1109/TNSRE.2010.2047606.
- 63. R: A language and environment for statistical computing.
- 64. DeLong, E. R.; DeLong, D. M.; Clarke-Pearson, D. L. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* **1988**, *44*, 837–45.
- 65. Schroeder, M. A.; Lander, J.; Levine-Silverman, S. Diagnosing and Dealing with Multicollinearity. *West. J. Nurs. Res.* **1990**, *12*, 175–187, doi:10.1177/019394599001200204.
- van Lummel, R.; Evers, J.; Niessen, M.; Beek, P.; van Dieën, J. Older Adults with Weaker Muscle Strength Stand up from a Sitting Position with More Dynamic Trunk Use. *Sensors* 2018, 18, 1235, doi:10.3390/s18041235.
- 67. Mirelman, A.; Weiss, A.; Buchman, A. S.; Bennett, D. A.; Giladi, N.; Hausdorff, J. M. Association between performance on Timed Up and Go subtasks and mild cognitive impairment: further insights into the links between cognitive and motor function. *J. Am. Geriatr. Soc.* **2014**, *62*, 673–8, doi:10.1111/jgs.12734.
- 68. Coni, A.; Mellone, S.; Colpo, M.; Bandinelli, S.; Chiari, L. Influence of age and gender on sensor-based functional measures: A factor analysis approach. In *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*; 2015; Vol. 2015–Novem.
- 69. Ferrucci, L.; Bandinelli, S.; Benvenuti, E.; Di Iorio, A.; Macchi, C.; Harris, T. B.; Guralnik, J. M. Subsystems contributing to the decline in ability to walk: Bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. *J. Am. Geriatr. Soc.* **2000**, *48*, 1618–1625, doi:10.1111/j.1532-5415.2000.tb03873.x.
- Palmerini, L.; Rocchi, L.; Mellone, S.; Valzania, F.; Chiari, L. Feature Selection for Accelerometer-Based Posture Analysis in Parkinson's Disease. *IEEE Trans. Inf. Technol. Biomed.* 2011, 15, 481–490, doi:10.1109/TITB.2011.2107916.
- 71. FARSEEING Project Available online: http://farseeingresearch.eu.
- 72. Deshpande, N.; Metter, E. J.; Lauretani, F.; Bandinelli, S.; Guralnik, J.; Ferrucci, L. Activity restriction induced by fear of falling and objective and subjective measures of physical function: A prospective cohort study. *J. Am. Geriatr. Soc.* **2008**, *56*, 615–620, doi:10.1111/j.1532-5415.2007.01639.x.

- 73. Radloff, L. S. A Self-Report Depression Scale for Research in the General Population. *Appl. Psychol. Meas.* **1977**, *1*, 385–401, doi:10.1177/014662167700100306.
- 74. Patel, K. V; Coppin, A. K.; Manini, T. M.; Lauretani, F.; Bandinelli, S.; Ferrucci, L.; Guralnik, J. M. Midlife Physical Activity and Mobility in Older Age: The InCHIANTI Study. *Am. J. Prev. Med.* **2006**, *31*, 217–24, doi:10.1016/j.amepre.2006.05.005.
- 75. Cesari, M.; Leeuwenburgh, C.; Lauretani, F.; Onder, G.; Bandinelli, S.; Maraldi, C.; Guralnik, J. M.; Pahor, M.; Ferrucci, L. Frailty syndrome and skeletal muscle: Results from the Invecchiare in Chianti study. *Am. J. Clin. Nutr.* **2006**, *83*, 1142–1148.
- 76. Bassey, E. J.; Short, A. H. A new method for measuring power output in a single leg extension: feasibility, reliability and validity. *Eur. J. Appl. Physiol. Occup. Physiol.* **1990**, *60*, 385–390, doi:10.1007/BF00713504.
- 77. Vazzana, R.; Bandinelli, S.; Lauretani, F.; Volpato, S.; Lauretani, F.; Di Iorio, A.; Abate, M.; Corsi, A. M.; Milaneschi, Y.; Guralnik, J. M.; Ferrucci, L. Trail making test predicts physical impairment and mortality in older persons. *J. Am. Geriatr. Soc.* **2010**, *58*, 719–723, doi:10.1111/j.1532-5415.2010.02780.x.
- Cesari, M.; Kritchevsky, S. B.; Penninx, B. W. H. J.; Nicklas, B. J.; Simonsick, E. M.; Newman, A. B.; Tylavsky, F. A.; Brach, J. S.; Satterfield, S.; Bauer, D. C.; Visser, M.; Rubin, S. M.; Harris, T. B.; Pahor, M. Prognostic value of usual gait speed in wellfunctioning older people - Results from the health, aging and body composition study. *J. Am. Geriatr. Soc.* 2005, *53*, 1675–1680, doi:10.1111/j.1532-5415.2005.53501.x.
- 79. Zhang, F.; Ferrucci, L.; Culham, E.; Metter, E. J.; Guralnik, J.; Deshpande, N. Performance on Five Times Sit-to-Stand Task as a Predictor of Subsequent Falls and Disability in Older Persons. *J. Aging Health* **2013**, *25*, 478–492, doi:10.1177/0898264313475813.
- 80. Podsiadlo, D.; Richardson, S. The Timed "Up & Go": A Test of Basic Functional Mobility for Frail Elderly Persons. *J. Am. Geriatr. Soc.* **1991**, *39*, 142–148, doi:10.1111/j.1532-5415.1991.tb01616.x.
- Shumway-Cook, A.; Brauer, S.; Woollacott, M. Predicting the Probability for Falls in Community-Dwelling Older Adults Using the Timed Up & Go Test. *Phys. Ther.* 2000, *80*, 896–903, doi:10.1093/ptj/80.9.896.
- 82. Riva, D.; Mamo, C.; Fanì, M.; Saccavino, P.; Rocca, F.; Momenté, M.; Fratta, M. Single stance stability and proprioceptive control in older adults living at home: gender and age differences. *J. Aging Res.* **2013**, *2013*, 561695, doi:10.1155/2013/561695.
- 83. Daly, R. M.; Rosengren, B. E.; Alwis, G.; Ahlborg, H. G.; Sernbo, I.; Karlsson, M. K. Gender specific age-related changes in bone density, muscle strength and functional performance in the elderly: A-10 year prospective population-based study. *BMC Geriatr.* 2013, *13*, 71.
- 84. Iosa, M.; Fusco, A.; Morone, G.; Paolucci, S. Development and decline of upright gait stability. *Front. Aging Neurosci.* **2014**, *6*, 14, doi:10.3389/fnagi.2014.00014.
- 85. Corp., I. IBM SPSS Statistics for Windows, Version 20.0 Released 2011.
- 86. Zaffarana N, Colpo M, Baccini M, Mellone S, Chiari L, Tacconi C, B. S. Fallers In Community Can Be Identified By Timed Up and Go Test: Data From The InCHIANTI -FARSEEING. In 67th Annual Scientific Meeting of The Gerontological Society of America; 2014.

- 87. Coni, A.; Mellone, S.; Colpo, M.; Bandinelli, S.; Chiari, L. A Factor Analysis model of the instrumented Timed Up and Go test for physical capability assessment. *Gait Posture* **2018**, *66*, S11–S12, doi:https://doi.org/10.1016/j.gaitpost.2018.07.117.
- 88. Norman R. draper HS.; Norman R. draper, H. S.; HS, N. R. draper *Applied Regression Analysis*; Third.;
- 89. Costello, A. B.; Osborne, J. W. Best practices in exploratory factor analysis: four recommendations for getting the most from your analysis. Practical Assessment, Research & amp; Evaluation. **2005**, *10*.
- Penninx, B. W.; Guralnik, J. M.; Ferrucci, L.; Simonsick, E. M.; Deeg, D. J. H.; Wallace, R. B. Depressive Symptoms and Physical Decline in Community-Dwelling Older Persons FREE. *Jama* 1998, 279, 1720–1726, doi:10.1001/jama.279.21.1720.
- Deshpande, N.; Metter, E. J.; Bandinelli, S.; Lauretani, F.; Windham, B. G.; Ferrucci, L. Psychological, physical, and sensory correlates of fear of falling and consequent activity restriction in the elderly: the InCHIANTI study. *Am. J. Phys. Med. Rehabil.* 2008, 87, 354– 62, doi:10.1097/PHM.0b013e31815e6e9b.
- 92. Bohannon, R. W. Hand-Grip Dynamometry Predicts Future Outcomes in Aging Adults. J. Geriatr. Phys. Ther. 2008, 31, 3–10, doi:10.1519/00139143-200831010-00002.
- 93. Hausdorff, J. M.; Doniger, G. M.; Springer, S.; Yogev, G.; Simon, E. S.; Giladi, N. A Common Cognitive Profile in Elderly Fallers and in Patients with Parkinson's Disease: The Prominence of Impaired Executive Function and Attention.
- 94. Van Uem, J. M. T.; Walgaard, S.; Ainsworth, E.; Hasmann, S. E.; Heger, T.; Nussbaum, S.; Hobert, M. A.; Micó-Amigo, E. M.; Van Lummel, R. C.; Berg, D.; Maetzler, W. Quantitative Timed-Up-and-Go Parameters in Relation to Cognitive Parameters and Health-Related Quality of Life in Mild-to-Moderate Parkinson's Disease. *PLoS One* 2016, *11*, e0151997, doi:10.1371/journal.pone.0151997.
- 95. Palumbo P, Coni A, Mellone S, Palmerini L, Colpo M, Bandinelli S, C. L. Fall risk assessment via instrumented TUG. Preliminary results from the InCHIANTI study. In *Health—exploring Complexity: An Interdisciplinary Systems Approach HEC2016*; Munich, 2016; pp. S148–S149.
- 96. Studenski, S.; Perera, S.; Patel, K.; Rosano, C.; Faulkner, K.; Inzitari, M.; Brach, J.; Chandler, J.; Cawthon, P.; Connor, E. B.; Nevitt, M.; Visser, M.; Kritchevsky, S.; Badinelli, S.; Harris, T.; Newman, A. B.; Cauley, J.; Ferrucci, L.; Guralnik, J. Gait Speed and Survival in Older Adults. *JAMA* 2011, *305*, 50, doi:10.1001/jama.2010.1923.
- 97. Jordre, B.; Schweinle, W.; Oetjen, S.; Dybsetter, N.; Braun, M. Fall History and Associated Physical Performance Measures in Competitive Senior Athletes. *Top. Geriatr. Rehabil.* **2016**, *32*, 1–16, doi:10.1097/TGR.0000000000086.
- Hilliard, M. J.; Martinez, K. M.; Janssen, I.; Edwards, B.; Mille, M.-L.; Zhang, Y.; Rogers, M. W. Lateral Balance Factors Predict Future Falls in Community-Living Older Adults. *Arch. Phys. Med. Rehabil.* 2008, 89, 1708–1713, doi:10.1016/j.apmr.2008.01.023.
- 99. Schrager, M. A.; Kelly, V. E.; Price, R.; Ferrucci, L.; Shumway-Cook, A. The effects of age on medio-lateral stability during normal and narrow base walking. *Gait Posture* **2008**, *28*, 466–471, doi:10.1016/J.GAITPOST.2008.02.009.
- 100. Rogers, M. W.; Mille, M.-L. Lateral Stability and Falls in Older People; 2003; Vol. 31, pp.

182–187;.

- Daubney, M. E.; Culham, E. G. Lower-Extremity Muscle Force and Balance Performance in Adults Aged 65 Years and Older. *Phys. Ther.* **1999**, *79*, 1177–1185, doi:10.1093/ptj/79.12.1177.
- Verghese, J.; Wang, C.; Holtzer, R. Relationship of clinic-based gait speed measurement to limitations in community-based activities in older adults. *Arch. Phys. Med. Rehabil.* 2011, 92, 844–6, doi:10.1016/j.apmr.2010.12.030.
- 103. Barry, E.; Galvin, R.; Keogh, C.; Horgan, F.; Fahey, T. Is the Timed Up and Go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. *BMC Geriatr.* **2014**, *14*, 14, doi:10.1186/1471-2318-14-14.
- 104. Leach, J. M.; Mellone, S.; Palumbo, P.; Bandinelli, S.; Chiari, L. Natural turn measures predict recurrent falls in community-dwelling older adults: a longitudinal cohort study. *Sci. Rep.* 2018, 8, 4316, doi:10.1038/s41598-018-22492-6.
- 105. Coni, A.; Mellone, S.; Leach, J. M.; Colpo, M.; Bandinelli, S.; Chiari, L. Association between smartphone-based activity monitoring and traditional clinical assessment tools in community-dwelling older people. In 2016 IEEE 2nd International Forum on Research and Technologies for Society and Industry Leveraging a Better Tomorrow, RTSI 2016; 2016.
- 106. Brodie, M. A. D.; Coppens, M. J. M.; Lord, S. R.; Lovell, N. H.; Gschwind, Y. J.; Redmond, S. J.; Del Rosario, M. B.; Wang, K.; Sturnieks, D. L.; Persiani, M.; Delbaere, K. Wearable pendant device monitoring using new wavelet-based methods shows daily life and laboratory gaits are different. *Med. Biol. Eng. Comput.* **2016**, *54*, 663–74, doi:10.1007/s11517-015-1357-9.
- 107. van Lummel, R. C.; Walgaard, S.; Pijnappels, M.; Elders, P. J. M.; Garcia-Aymerich, J.; van Dieën, J. H.; Beek, P. J. Physical Performance and Physical Activity in Older Adults: Associated but Separate Domains of Physical Function in Old Age. *PLoS One* 2015, *10*, e0144048, doi:10.1371/journal.pone.0144048.
- 108. Godfrey, A. Wearables for independent living in older adults: Gait and falls. *Maturitas* **2017**, *100*, 16–26, doi:10.1016/j.maturitas.2017.03.317.
- Ihlen, E. A. F.; Weiss, A.; Bourke, A.; Helbostad, J. L.; Hausdorff, J. M. The complexity of daily life walking in older adult community-dwelling fallers and non-fallers. *J. Biomech.* 2016, 49, 1420–1428, doi:10.1016/j.jbiomech.2016.02.055.
- van Schooten, K. S.; Pijnappels, M.; Rispens, S. M.; Elders, P. J. M.; Lips, P.; Daffertshofer, A.; Beek, P. J.; van Dieën, J. H. Daily-Life Gait Quality as Predictor of Falls in Older People: A 1-Year Prospective Cohort Study. *PLoS One* 2016, *11*, e0158623, doi:10.1371/journal.pone.0158623.
- 111. Rispens, S. M.; van Schooten, K. S.; Pijnappels, M.; Daffertshofer, A.; Beek, P. J.; van Dieën, J. H. Identification of fall risk predictors in daily life measurements: gait characteristics' reliability and association with self-reported fall history. *Neurorehabil. Neural Repair* 2015, 29, 54–61, doi:10.1177/1545968314532031.
- 112. Rispens, S. M.; van Schooten, K. S.; Pijnappels, M.; Daffertshofer, A.; Beek, P. J.; van Dieën, J. H.; Schooten, K. S. Van; Pijnappels, M.; Daffertshofer, A.; Beek, P. J.; Die, J. H. Van; van Schooten, K. S.; Pijnappels, M.; Daffertshofer, A.; Beek, P. J.; van Dieën, J. H. Do Extreme Values of Daily-Life Gait Characteristics Provide More Information About Fall Risk Than Median Values? *JMIR Res. Protoc.* 2015, *4*, e4, doi:10.2196/resprot.3931.

- 113. Stenholm, S.; Koster, A.; Valkeinen, H.; Patel, K. V.; Bandinelli, S.; Guralnik, J. M.; Ferrucci, L. Association of physical activity history with physical function and mortality in old age. *Journals Gerontol. - Ser. A Biol. Sci. Med. Sci.* 2016, 71, 496–501, doi:10.1093/gerona/glv111.
- 114. Strawbridge, W. J.; Deleger, S.; Roberts, R. E.; Kaplan, G. A. Physical Activity Reduces the Risk of Subsequent Depression for Older Adults. *Am. J. Epidemiol.* 2002, *156*, 328–334, doi:10.1093/aje/kwf047.
- Dunn, A. L.; Trivedi, M. H.; O'Neal, H. A. Physical activity dose-response effects on outcomes of depression and anxiety. *Med. Sci. Sports Exerc.* 2001, 33, S587-97; discussion 609–10.
- Halaweh, H.; Willen, C.; Grimby-Ekman, A.; Svantesson, U. Physical Activity and Health-Related Quality of Life Among Community Dwelling Elderly. J. Clin. Med. Res. 2015, 7, 845–852, doi:10.14740/jocmr2307w.
- 117. Haider, S.; Luger, E.; Kapan, A.; Titze, S.; Lackinger, C.; Schindler, K. E.; Dorner, T. E. Associations between daily physical activity, handgrip strength, muscle mass, physical performance and quality of life in prefrail and frail community-dwelling older adults. *Qual. Life Res.* 2016, 25, 3129–3138, doi:10.1007/s11136-016-1349-8.
- 118. Schrack, J. A.; Simonsick, E. M.; Chaves, P. H. M.; Ferrucci, L. The Role of Energetic Cost in the Age-Related Slowing of Gait Speed. J. Am. Geriatr. Soc. 2012, 60, 1811–1816, doi:10.1111/j.1532-5415.2012.04153.x.
- 119. Colcombe, S.; Kramer, A. F. Fitness Effects on the Cognitive Function of Older Adults. *Psychol. Sci.* **2003**, *14*, 125–130, doi:10.1111/1467-9280.t01-1-01430.
- 120. Rosano, C.; Venkatraman, V. K.; Guralnik, J.; Newman, A. B.; Glynn, N. W.; Launer, L.; Taylor, C. A.; Williamson, J.; Studenski, S.; Pahor, M.; Aizenstein, H. Psychomotor Speed and Functional Brain MRI 2 Years After Completing a Physical Activity Treatment. *Journals Gerontol. Ser. A* 2010, 65A, 639–647, doi:10.1093/gerona/glq038.
- 121. Shumway-Cook, A.; Guralnik, J. M.; Phillips, C. L.; Coppin, A. K.; Ciol, M. A.; Bandinelli, S.; Ferrucci, L. Age-Associated Declines in Complex Walking Task Performance: The Walking InCHIANTI Toolkit. *J. Am. Geriatr. Soc.* 2007, 55, 58–65, doi:10.1111/j.1532-5415.2006.00962.x.
- Cavanaugh, J. T.; Kochi, N.; Stergiou, N. Nonlinear Analysis of Ambulatory Activity Patterns in Community-Dwelling Older Adults. *Journals Gerontol. Ser. A Biol. Sci. Med. Sci.* 2010, 65A, 197–203, doi:10.1093/gerona/glp144.
- 123. Lindemann, U.; Klenk, J.; Becker, C.; Moe-Nilssen, R. Assessment of adaptive walking performance. *Med. Eng. Phys.* **2013**, *35*, 217–220, doi:10.1016/j.medengphy.2012.11.005.
- 124. Prieto, T. E.; Myklebust, J. B.; Hoffmann, R. G.; Lovett, E. G.; Myklebust, B. M. Measures of postural steadiness: differences between healthy young and elderly adults. *IEEE Trans. Biomed. Eng.* **1996**, *43*, 956–966, doi:10.1109/10.532130.
- Chiari, L.; Rocchi, L.; Cappello, A. Stabilometric parameters are affected by anthropometry and foot placement. *Clin. Biomech.* 2002, *17*, 666–677, doi:10.1016/S0268-0033(02)00107-9.
- 126. Balasubramanian, S.; Melendez-Calderon, A.; Roby-Brami, A.; Burdet, E. On the analysis of movement smoothness. *J. Neuroeng. Rehabil.* **2015**, *12*, doi:10.1186/10.1186/s12984-015-

0090-9.