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Clinical Guidelines Formalized (vers b)

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2.3.7	01.04.2018	Final	Materia	Final Version

EXECUTIVE SUMMARY

In the context of WP2, FrailSafe used information capture, analysis and modelling, in order to make an overall assessment of an individual's dietary, nutritional, mental and physical activity. In the scope of D2.2, the collected information was compared with current healthcare and European advices in order to identify whether the collected information was adequate or modifications on the requirements would need to be made. Therefore, FrailSafe data combined with existing recommendations, led to the development of FrailSafe's preliminary recommendations for the prevention, prediction and management frailty.

The scope of D2.3 is to assess the parameters measured in the FrailSafe system development phase, to identify those that predict or are highly correlated with frailty and consequently develop, based on those, a set of guidelines to be used for the prediction, prevention and/or management of frailty. The list of clinical guidelines, to be used in the Virtual Patient Model (VPM) of the FrailSafe system, will be drafted utilizing also the results of the review of the literature conducted in the first version of this deliverable (D2.2)

DOCUMENT INFORMATION

Contract Number:	H2020-PHC–690140	**Acronym:**	FRAILSAFE
Full title	Sensing and predictive treatment of frailty and associated co-morbidities using advanced personalized models and advanced interventions		
Project URL	http://frailsafe-project.eu		
EU Project officer	Mr. Jan Komarek		

Deliverable number:	2.3	**Title:**	Clinical Guidelines Formalized (vers b)
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Date of Contractual delivery	**31/03/2018 (M27)**	**Actual**	**31/03/2018**
Status	Draft ☐	Final ☒	
Nature	Report ☒ Demonstrator ☐ Other ☐		
Dissemination Level	Public ☒ Consortium ☐		
Abstract (for dissemination)	This deliverable focuses on the development of clinical guidelines to be used in the Virtual Patient Model of the FrailSafe system.		
Keywords	Clinical measurements, preliminary data, physiological parameters, guidelines, age, gender frailty, physical activity, diet, nutrition, cognitive, psychological, medical, social, activity/exercise		

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List of abbreviations and acronyms

(In alphabetical order)

FS	FrailSafe
IMUs	Inertial Measurement Units
MO	Medical Objectives
UCD	User Centred Design
VPM	Virtual Patient Model
WBAN	Wireless Body Area Network
WWBS	Wearable WBAN System
WWS	Wearable Wellness System

1 INTRODUCTION

The ageing of the population constitutes an undeniable fact caused from higher life expectancy on the one hand and lower birth rates on the other. According to the UN's World Population Prospects (2017), the population is ageing on a rate of about 3 per cent per year with Europe possessing the higher percentage (25%) of people aged 60 and over years old. Population ageing is expected to rise in the next decades, calling urgently for measures to be adapted for handling the various issues that might arise. One such issue is the fact that many of these people will manifest frailty phenotypes as they age. A common feature of frailty is a loss of muscle mass and strength, which makes those affected more vulnerable to falls, and places them at greater risk of becoming disabled. The frail are also more likely to be hospitalised or to require long-term care. Frailty therefore has a huge impact on older people's quality of life and represents a significant burden for health and social care systems. Santos-Eggimann et al (2009) noted that 17% of Europeans were found to be frail whereas 42% were found to be pre-frail on the population aged 65 and over, in a study using a sample deriving from 10 European countries. The frailty process may be delayed or even reversed, so early interventions are highly desirable. However, little is known about the determinants of frailty state changes (Bernabei et al, 2017)

1.1 Project objectives

FrailSafe is proposing a novel frailty management system based on a patient-specific approach that is part of a comprehensive plan to manage and support frailty in older people, as well as exploring different causes of frailty manifestation. The system focuses on monitoring older people's everyday life in order to capture frailty-related information, and through augmented reality combined with state-of-the–art data mining techniques, to build a self-adaptive personalized Virtual Patient Model (VPM), aiming to assist older people in delaying and/or preventing frailty and frailty level transitions. This will be achieved by measuring adherence to personalized guidelines that include medical treatment and lifestyle recommendations as well as evaluating the frailty level improvement as an intervention outcome. Specifically, a personalised guidance platform will transmit all the measurements to a prediction engine for giving appropriate feedback to the user on how to manage and reduce the risk for frailty.

WP2 and consequently D2.3 is related to the following project Medical Objectives (MO):

Table 1: FrailSafe MOs related to D2.3

M01	Better understand frailty and its relation to co-morbidities
M02	Develop quantitative and qualitative measures to define frailty
M03	Use these measures to predict short and long-term outcome
M04	Develop real life tools for the assessment of physiological reserve and external challenges
M05	Provide a model sensitive to change in order that pharmaceutical and non-pharmaceutical interventions which will be designed to delay, arrest or even reverse the transition to frailty can

	be tested.
M06	Create “prevent-frailty” evidence based recommendations for older people regarding activities of daily living, lifestyle, nutrition, etc. to strengthen the motor, cognitive, and other “anti-frailty” activities through the delivery of personalized treatment programs, monitoring alerts, guidance and education and estimate the influence of these interventions
M07	Achieve all with a safe and acceptable to older people system.

The FrailSafe system is being developed and improved as the study evolves with the incorporation of results and the feedback provided by the users given continuously to the technical partners of the project.

Using this large-scale data collection methodology, it is possible to make comparisons between the clinical expression of different frailty levels and also between the performance of various measurements and tools to identify and even predict frailty, as well as between people who use FrailSafe and those who don’t. A fully developed FrailSafe system will contribute to clinical work to prevent frailty and loss of autonomy both in individual and in population scale.

1.2 Scope of the deliverable D2.3

In the context of WP2, FrailSafe used information capture, analysis and modelling, in order to make an overall assessment of an individual’s dietary, nutritional, mental and physical activity. In the scope of D2.2, the collected information was compared with current healthcare and European advices in order to identify whether the collected information was adequate or modifications on the requirements would need to be made. Therefore, FrailSafe data combined with existing recommendations, led to the development of FrailSafe’s preliminary recommendations for the prevention, prediction and management frailty.

The scope of D2.3 is to assess the parameters measured in the FrailSafe system development phase, to identify those that predict or are highly correlated with frailty and consequently develop, based on those, a set of guidelines to be used for the prediction, prevention and/or management of frailty. The list of clinical guidelines, to be used in the Virtual Patient Model (VPM) of the FrailSafe system, will be drafted utilizing also the results of the review of the literature conducted in the first version of this deliverable (D2.2)

The developed recommendations or guidelines will be targeting older adults, clinicians, researchers, doctors as well as families and/or care-givers.

The goal of FrailSafe at the end of the clinical assessments and trials is to be able to distinguish the metrics which are significant in relation to predicting and preventing frailty, and to assign weights to each one so that a new metric is created, which will integrate all the significant variables found through the data analysis.

The deliverable provides recommendations for use in the Virtual Patient Model, but it has to be noted that the list is not exhaustive and modifications to it might be made as the development of the VPM progresses.

2 FRAILSAFE CLINICAL ASSESSMENT

The FrailSafe project will test the efficacy of a combination of tools so as to detect and quantify frailty. Decision making tools are essential to clinical practise and guide the clinicians on the way a person's healthcare needs to be managed. For the purposes of FrailSafe it is very important to detect non-frail and pre-frail participants in order to provide prevention recommendations while frail participants are important to detect in order to provide recommendations to delay the progression of frailty. It is necessary and vital to break the cycle of frailty. Therefore, the Fried's Phenotype Frailty Criteria were selected to identify the frailty level of the participants.

Other parameters are also important and were considered before conducting the analysis. After the preliminary data and the link with existing recommendations, parameters were found to adequately address the criterion of frailty and no modifications on the data collection were made.

Therefore, data gathered in the first phase of the study are being used to aid the creation of the quantification of models whereas in the second phase of the project the data will be used for the evaluation and validation of the FrailSafe system.

Table 2 presents the types of clinical assessments carried out with the participants, the parameters tested and the tools which were employed to gather those data. For the analysis of the data, univariate analysis was used to analyse frailty in relation to cognitive function, housing environment, individuals' functionality, unintentional weight loss, physical activity, blood pressure and co-morbidities, BMI, limb strength, psychological status, anxiety, social factor, and wellness. Univariate analysis identifies potential patterns between the variable which will help in indicating whether frailty changes correspondingly with the aforementioned variables. In addition, linear multiple regression was conducted to examine which of all the parameters are found to be predictors of frailty. The results of the analysis will contribute to the development of FrailSafe's Virtual Patient Model through as guidelines and recommendations will be drafted to be used for the prevention, delay, management or even reversal of frailty in individuals.

Table 2: FrailSafe frailty-related variables which relate to clinical guidelines

Clinical Assessment	Parameters	Tools
Generalities	demographics, leisure, social life / communication assessment	Questionnaires
Medication history	Medical history and prescription	Questions Medical records
	Co-morbidities	Medical records Self-report Clinician estimation
	Medication list	Drug prescriptions
	Autonomy, pain	Self-reporting
	Physical activity	Questions
	Alcohol use	Questions
Clinical exam / measurements	Blood pressure	B/P Monitor Values
	Arterial stiffness evaluation, waist, chest and BMI measurements	Mobilograph Measuring tape Electronic scale
Balance and gait	Lower limb strength,	Stopwatch,

Clinical Assessment	Parameters	Tools
evaluation		Measuring tape IMUs
	Balance	Stopwatch
Fried's criteria of frailty assessment: allocation into frailty categories	Weight loss, exhaustion / physical activity, strength, walking speed	Questions, Dynamometer Stopwatch
	Muscle strength	Dynamometer / Tablet games
Psychological Evaluation	Depression	GDS
Sensory system evaluation	Vision, hearing	Questions Clinician's estimation
Nutritional assessment	Weight loss	MNA short and extended form
Activities of Daily Living	Autonomy	Katz Index of Independence of ADL
		Lawton IADL scale
Adverse events	Functionality of daily activities	Phone follow-up Questionnaire
Housing conditions	Autonomy	Home visits User & clinician estimation
Movements and habits	Sleep and eating behaviour, indoor activity, bladder and bowel habits	Beacons
	Location, mobility, activity profile	Mobile devices (tablets and mobile phone) - Games
Cognitive evaluation	Cognitive function	MoCA test MMSE test

3 EXISTING GUIDELINES

In the context of Task 2.3 – Clinical guidelines for system development, a review of the literature was conducted in order to investigate the existing and most well-supported recommendations referring to the prevention, delay and slowing down of frailty related phenotypes. The guidelines or recommendations available in the literature are primarily targeting social and healthcare professionals, policy makers and the general public.

The British Geriatric Society (2017) developed a list of guidelines for the recognition and management of frailty in community and outpatient settings. One of their most important recommendations concerns the creation of a care plan, personalized on each person, detailing treatment goals, management plans and urgent care plans (BGS, 2017). Addressing healthcare professionals as well as policy makers they also recommend the development of systems for sharing health records among primary and secondary care as well as emergency and social services for people who have been identified as having frailty (BGS, 2017). This guideline might indeed become crucially important in urgent cases where sudden deterioration of a frail's person health occurs. The sharing of health records provides an example of the necessity for developing protocols for handling cases of people with frailty in circumstances such as falls, delirium or sudden immobility (Turner & Clegg, 2014).

For the management of an urgent situation, health and social care professionals should assess the person's clinical condition in addition to his/her current physical and cognitive

function (Turner & Clegg, 2014). Whenever needed, BGS (2017) indicates that healthcare professionals should apply clinical judgement and utilize agreed personalized goals for deciding whether the person suffering from frailty will need to follow clinical guidelines for other diseases as part of their management of frailty.

Healthcare professionals should furthermore undertake evidence-based reviewing of medication taken from people having frailty, such as enforcing the STOPP/START criteria (O'Mahony et al, 2015) to assess whether medication taken is really helping without causing or worsening the frailty syndrome (BGS, 2017). Recent research indicates that polypharmacy can cause instability and falls to an individual (Wilson et al, 2011), thus assessments in cases of polypharmacy are of utmost importance. Moreover, literature in the field of sarcopenia indicated that various drug interventions can increase muscle mass and function as well as muscle strength, which are vital components for the reversal and prevention of frailty (Sayer et al, 2013).

Current literature suggests that cognitive function is directly related with frailty where frail individuals seem to get lower scores on cognitive function tests than non-frail or pre-frail individuals (Chen et al, 2016; Brigola et al, 2015).It is therefore suggested, that clinicians assess the cognitive function of a person when they are undertaking an examination for frailty. Parallel to that, the British Geriatric Society recommends the referral of older people suffering from frailty alongside other psychiatric conditions including dementia, to specialized old age psychiatrists (BGS, 2017) as such co-morbidities might have a direct impact on a person's frailty status. Avoiding social isolation and maintaining an active social life enhances the person's ability to remain healthy and prevent frailty. Thus, guidelines should revolve around finding ways for older people to remain socially active.

It is recommended by several organizations that clinicians should screen for disability in self-care tasks (ADL) and tasks that permit an individual live independently in a community (IADL: Instrumental Activities of Daily Living) on an annual basis for people over the age of 70. Home-based interventions and groups-based interventions are suggested which can result in improvement in mobility and functional ability. Also, resistance exercise is beneficial both in terms of preventing and treating the physical performance component of frailty (BGS, 2017). There is a growing evidence in the literature, on the fact that a balanced and nutritional diet (Clegg et al, 2013) as well as regular exercise can stabilize (or even reverse) frailty (Aguirre & Villareal, 2015)

Last, policies and regulations as well as governmental programs should be developed focusing on encouraging healthy lifestyles for older people offering them options for quitting smoking, becoming more physically active, reducing their alcohol consumption, adapting a healthy and well-balanced diet (NICE, 2015)

FrailSafe identified the abovementioned guidelines for the prevention, management and reversal of frailty and has integrated them in its data collection and system development. The below table details on how FrailSafe addresses each one of the identified guidelines.

Table 3: Existing guidelines and how FrailSafe will address relevant parameters

European guidelines	1. A personalized shared care and support plan should be created by outlining the goals of the treatment, management and creating urgent care plans (BGS, 2017)
Target group	▪ Clinician

	▪ Researcher ▪ Family / caregiver
Guideline implementation examples	Support plans include: Health and social care summary: symptoms, medication, social status diagnoses A maintenance plan: goals, aspirations, actions to take, timescale, roles of people in his/her life and how/who can help. An escalation plan for each individual and carer in order to help them identify which service they should use (geriatrics service, falls service), who to call etc. An urgent care plan, for possible crisis, which include his/her wishes, person to contact, actions to be taken etc.
How FrailSafe addresses this parameter	FrailSafe aims to integrate knowledge, pair up of VPM and result in individual guidelines for each patient.
Background / Comments	Personalized patient models can form the basis of prediction and suggestion capabilities that may indicate a foreseen risk and offer solutions that can be used for the reduction or even better prevention of future situations that may jeopardise the health of the specific patient.
European guidelines	2. Electronic Health Records When an older person is identified as frail, establish systems to share health records between doctors, hospitals, nurses etc, in order to receive monitoring, support and recommendations based on a patient centred approach (BGS, 2017)
Target group	Healthcare Professionals
Guideline implementation examples	Creating electronic health records of patients, taking into account medical parameters used for monitoring by healthcare personnel and sharing across different health care settings.
How FrailSafe addresses this parameter	FrailSafe aims to integrate knowledge with the development of a Virtual Patient Model (VPM) and result in individual guidelines for each patient. The VPM is developed according to openEHR archetype, ensuring interoperability with other systems. Also, the VPM will be paired with a call centre which will monitor the patients and handle alerts from the VPM.
Background / Comments	The goal of user modelling may be to predict user behaviour, to gain knowledge of a particular user in order to tailor interactions to that user, or to create a database of users that can be accessed by others (BGS, 2017)

	In general, user modelling can be seen as a broad mixture of many disciplines including the interaction of the user with interfaces and devices as well as the analysis of user tasks and user characteristics (sensory, physical and cognitive abilities, psychological and behavioural). The notion of user profiling has been introduced in order to record the user context and personalize applications so as to be tailored to the user needs (BGS, 2017)
European guidelines	3. Urgent situations / adverse events interventions (BGS, 2017) ▪ Assess clinical condition ▪ Assess current physical function ▪ Assess current cognitive / mood function
Target group	▪ Clinician ▪ Researcher ▪ Family / caregiver ▪ User
Guideline implementation examples	Recommendations include transfer to a doctor/hospital or/and transfer to a care and nursing unit if unable to take care his/her self before or after the adverse event. Prevent adverse outcomes in frail individuals, such as infections, new medication, changes in physical and mental well being
How FrailSafe addresses parameter	Telephone follow up procedures every 3 months or/and during the clinical assessment of the participants.
European guidelines	4. Evidence-based medication review checklists (Turner & Clegg, 2014)
Target group	▪ Clinician ▪ Researcher
Guideline implementation examples	STOPP/START criteria (O'Mahony et al, 2015)
How FrailSafe addresses this parameter	FrailSafe will provide notification to clinicians to undertake medication reviews for patients that take too many drugs and their functional status seems to be affected
European guidelines	5. Recommend a referral for frail old age who have complex co-existing psychiatric problems as well as difficult behaviour in dementia (Turner & Clegg, 2014)
Target group	▪ Clinician ▪ Researcher
How FrailSafe	FrailSafe takes into account a combination of parameters regarding

addresses this parameter	frailty (Fried et al, 2001)
European guidelines	6. Use your clinical judgment and personalized goals to apply disease-based guidelines to individuals (Turner & Clegg, 2014)
Target group	▪ Clinician ▪ Researcher
How FrailSafe addresses this parameter	FrailSafe will provide recommendations for action to the users depending on the disease their profile contains, after it has been examined and approved by their clinician.
European guidelines	7. For frail individuals, take into account presence of delirium and sudden immobility (Turner & Clegg, 2014)
Target group	▪ Clinician ▪ Researcher ▪ User
Guideline implementation examples	No real time assessment on FrailSafe
How FrailSafe addresses this parameter	During the clinical assessment, telephone follow ups and clinical assessment follow ups FrailSafe is interested in sarcopenia (Rizzoli et al, 2013; Waters & Baumgartner, 2011) and two of Fried's criteria are walking speed and grip strength (Bernabei et al, 2017). These two criteria (along with 3 more) are used for grouping participants into frail, pre-frail and non-frail categories (Fried et al, 2001) FrailSafe uses already a dynamometer for evaluating grip strength as well as for training purposes by playing games on a tablet using the dynamometer.
Background / Comments	These parameters are linked with quality of life and frailty (Bernabei et al, 2017; Rizzoli et al, 2013; Waters & Baumgartner, 2011) The main 2 clinical expressions of sarcopenia are low gait speed and diminished strength (Bernabei et al, 2017)
European guidelines	8. Polypharmacy (McNeil et al, 2016; Coehlo et al, 2015; Turner & Clegg, 2014; Wilson et al, 2011)
Target group	Clinicians
Guideline implementation examples	Recommendations include a full re-evaluation of their medication.

How FrailSafe addresses this parameter	FrailSafe takes into account medical history and one of the parameters is polypharmacy. Clinicians ensure during the clinical assessment as well as throughout the project that indeed the medication list is adapted to the needs of the individual.
Background / Comments	Polypharmacy is linked with increase risk of falls and adverse side effects and hence frailty (McNeil et al, 2016; Coehlo et al, 2015; Mitchell, Lord & Harvey, 2015; Turner & Clegg, 2014 Wilson et al, 2011)
European guidelines	9. Nutrition / diet (Turner & Clegg, 2014)
Target group	▪ Clinicians ▪ Researcher
Guideline implementation examples	▪ Regular physical exercise/ activity, more than 2hrs per week. ▪ A healthy and balanced diet ▪ A healthy weight (according to BMI of each individual)
How FrailSafe addresses this parameter	Administers the Mini Nutritional Assessment and based on its result will provide nutritional advices to users
Background / Comments	Weight loss, values outside the normal standards of each individual and reduced exercise are linked with frailty (Reinders, Visser & Schaap, 2017; Mitchell, Lord & Harvey, 2015; Kelaiditi, Van Kan & Cesari, 2014; Fried et al, 2001; Newman et al, 2001 -)
European guidelines	10. Drug interventions (Sayer et al, 2013)
Target group	▪ Clinicians ▪ Researchers
Guideline implementation examples	Recommendations include always consulting their doctor for any changes/side effects of medication or new medication.
How FrailSafe addresses this parameter	Recommendations will be provided to clinicians for examining the fact to prescribe specific drugs that can increase muscle mass
European guidelines	11. Social life Recommendations are targeted to avoid social isolation and low mood (Turner & Clegg, 2014)
Target group	▪ Clinicians ▪ Researchers

Guideline implementation examples	▪ Encouragement of joining a society/club ▪ Encouragement of social life with family, friends etc
How FrailSafe addresses parameter	One of the parameters of FrailSafe regarding social life is membership to a club, social activity (social media, social contact, outgoing activity)
European guidelines	12. Drugs/Medicine should be considered using validated medication checklists such as the STOPP and START guidelines. (O'Mahony et al, 2015; Turner & Clegg, 2014)
Target group	Clinicians
Guideline implementation examples	A referral to his/her doctor if during the clinical assessment some of the mentioned drugs are taken by the individual.
How FrailSafe addresses parameter	Suggestion will be made to clinicians whenever polypharmacy is present
Background / Comments	Some drugs are found to be linked with adverse outcomes such as delirium and confusion (Wilson et al, 2011; Coehlo et al, 2015; Fried et al, 2001) Drug interventions are suggested to improve muscle mass and function. Testosterone improves muscle strength but is also linked with adverse effects especially on the cardiovascular system. Therefore, keeping always in mind a patient-centred approach. Also, growth hormone improves muscle mass (O'Mahony et al, 2015; Turner & Clegg, 2014)
European guidelines	13. Disability/physical It is recommended by several organizations that clinicians should screen for: ▪ disability in self-care tasks (ADL) ▪ tasks that permit an individual live independently in a community (IADL: Instrumental Activities of Daily Living) on an annual basis people over the age of 70
Target group	▪ Users
Guideline implementation examples	Recommendations include: optimising protein intake and correcting vitamin D deficiency
How FrailSafe addresses this	Home based interventions and groups based interventions will be suggested which can result in improvement in mobility and

parameter	functional ability. Also, resistance exercise is beneficial both in terms of preventing and treating the physical performance component of frailty (Turner & Clegg, 2014)
Background / Comments	There is emerging evidence that frailty increases in the presence of obesity particularly in the context of other unhealthy behaviours, such as, inactivity, a poor diet and smoking. An even more devastating condition in terms of frailty and subsequent morbidity is the so-called 'sarcopenic obesity', a combination of obesity and low muscle mass (Reinders, Visser & Schaap, 2017; Michel, Cruz & Cederholm, 2015; Kelaiditi, Van Kan & Cesari, 2014; Turner & Clegg, 2014; Motl & McAuley, 2010; Peterson et al, 2009; Fried et al, 2001; Newman et al, 2001;) Social vulnerability has been shown to correlate with frailty and mortality. Social factors play an important role in modulating the adverse outcomes of frailty (Fried et al, 2001) Social factors thus appear to influence health outcomes at a number of levels – biological, health behaviours (including diet, exercise, and smoking), availability of social support, and access to quality healthcare (Turner & Clegg, 2014)
European guidelines	14. Falls/Risk of falls Recommendations for physical exercise are vital (Turner & Clegg, 2014)
Target group	▪ Users ▪ Clinicians ▪ Researchers
Guideline implementation examples	Using aiding tools for individuals who have difficulties due to pathological reasons (hip replacement etc). Recommendations for individuals who do not need aiding tools include regular physical exercise, a balanced diet (vitamins etc). Also, recommendations for re-evaluation of their medicines, as some drugs are linked with falls (mentioned above)
How FrailSafe addresses parameter	Sensorized strap/vest (IMU measurements) Detection of falls and of fall of risk Activity classification
Background / Comments	Many drugs are associated with adverse outcomes in frailty (Turner & Clegg, 2014). Examples are: Antimuscarinics in cognitive impairment Long active benzodiazepines, other sedatives and hypnotics increase risk of falls

	Some opiate based increase the risk of delirium and confusion Preventative chronic disease medication such as statins and warfarin for atrial fibrillation and sedatives and antihypertensive
European guidelines	15. Fried's criteria (Fried et al, 2001)
Target group of guidelines	▪ Clinicians ▪ Researchers ▪ Users ▪ Family / caregivers
How FrailSafe addresses this parameter	Sensorized strap/vest (IMU measurements) Detection of falls and of fall of risk Activity monitoring Distances covered Gait speed Calculates Respiratory Rate and Breathing Amplitude, in clinical terms, reflect mainly on medical and physical/functional aspects of frailty GPS logger Gait speed Activity pattern
Background / Comments	A feature of frailty is loss of skeletal mass and function (sacropenia, Fried's phenotype model). Therefore, recommendations for physical exercise are vital. The Fried's Phenotype model describes a group of characteristics which are unintentional: weight loss, reduced muscle strength, reduced gait speed, self-reported exhaustion and low energy expenditure The first score elaborated and widely used was the Fried's clinical operational definition (Fried et al, 2001) which includes Weight loss: self-reported weight loss of > 4.5kg or recorded weight loss of ≥ 5% per year. Self-reported exhaustion: self-reported exhaustion on Centre for Epidemiologic Studies depression scale (3-4 days per week or most of the time). Low energy expenditure: energy expenditure < 383 kcal/week (for men) or < 270 kcal/week (for women). Slow gait speed: standardised cut-off times to walk 4.57 m, stratified by sex and height. Weak grip strength: grip strength, stratified by sex and body mass index (Waters & Baumgartner, 2011; Fried et al, 2001)

European guidelines	16. Encouraging healthy behaviours Two integrating dementia risk reduction prevention policies: In strategy documents include dementia aimed at preventing and other non-communicable chronic diseases such as type 2 diabetes, stroke and chronic obstructive-pulmonary disease) Recommendations for health behaviours include: stop smoking, reduce alcohol consumption, adopt a healthy diet and have a healthy weight and be more active physically (NICE, 2015)
Target group	▪ Clinicians ▪ Researcher ▪ Family / caregivers
How FrailSafe addresses parameter	The FS system will send recommendations to users to: ▪ Quit smoking ▪ Reduce alcohol consumption ▪ Maintain a healthy diet and healthy weight ▪ Be more physically active
Background / Comments	Evidence has shown that there is a link between smoking and dementia, frailty and disability. The same link exists for alcohol consumption (NICE, 2015) Physical activity reduces the risk of illness both in short and long term, it preserves memory and cognitive ability, it reduces the risk of falls and improving quality of life and health (Michel, Cruz-jentoft & Cederholm, 2015) Unhealthy behaviours can increase the risk of dementia (NICE, 2015)
European guidelines	17. Cognitive and psychological domains Individuals with scores outside the pre-set normal values should be referred to a doctor for further examination and/or medication prescription. Additionally, a cognitive enhancement program is recommended for training/stabilizing his/her cognitive abilities for the maximum time possible.
Target group	▪ Users ▪ Clinicians
Guideline implementation examples	Referral to a doctor for further examination and/or medication prescription. Additionally, a cognitive enhancement program is recommended for training/stabilizing his/her cognitive abilities for the maximum time possible. Also, recommend a referral for frail old age who have complex co-existing psychiatric problems as well as difficult behaviour in dementia

How FrailSafe addresses parameter	Recommendations for playing FrailSafe's games for cognition enhancement will be provided to users.
Background / Comments	Mini Mental state examination test (MMSE), Montreal cognitive assessment (MOCA) and Geriatric depression scale (GDS) Psychological, cognitive and social factors also contribute to this multidimensional condition. Together, these signs and symptoms seem to reflect a reduced functional reserve and consequent decrease in adaptation (resilience) to any sort of stressor and perhaps even in the absence of extrinsic stressors. Whereas both frailty and cognitive decline share common potential mechanisms, disentangling the relationship between cognition and frailty may lead to new intervention strategies for the prevention and treatment of both conditions (BGS, 2017;Turner & Clegg, 2014; Fried et al, 2001)
European guidelines	18. Co-morbidities Researchers are increasingly evaluating the interactions of concurrently present impairments, such as strength and balance or vision and hearing or bio mediators, such as interleukin-6 and insulin-like growth factor (NICE, 2015)
Target group of guidelines	▪ Clinicians ▪ Researchers ▪ Family / Caregivers
How FrailSafe addresses this parameter	FrailSafe is interested in co-morbidities especially for stroke, mild cognitive impairment and osteoporosis/osteoarthritis
Background / Comments	Researchers are increasingly evaluating the interactions of concurrently present impairments, such as strength and balance or vision and hearing or bio mediators, such as interleukin-6 and insulin-like growth factor-I Co-morbidity heightens the risk of disability and mortality, over and above the risk from individual diseases Particular pairs of chronic diseases are prevalent, and are synergistic in increasing risk for disability For example, the concurrent presence of heart disease and osteoarthritis of the knee increased the relative risk of developing mobility disability to 13.6, from a relative risk of 4.4 for those with osteoarthritis alone, or 2.3 for those with heart disease alone - compared to those with neither disease (NICE, 2015; Fried et al, 2001,20)
European guidelines	19. Physical exercise Recommendations include aerobic endurance training and

	resistance training (Aquirre & Villareal, 2015)
Target group of guidelines	▪ Clinician ▪ Researchers ▪ Family / Caregivers ▪ Users
How FrailSafe addresses this parameter	Regular exercise recommendation
Background / Comments	Longitudinal studies demonstrate that regular physical exercise extends longevity and reduces the risk of physical disability. Aerobic endurance training can significantly improve peak oxygen consumption by ~10–15%. Resistance training is the best way to increase muscle strength and mass (Aquirre & Villareal, 2015)
European guidelines	20. Management/prevention (RHC, 2013) Promoting physical activity and monitoring diet and bodyweight Monitoring and assessment using specific tools for data collection Use of the Geriatric Multidimensional Assessment method to avoid adverse events and progression to disability in hospitalized patients Personalized discharge planning (DP) when hospitalized Keeping updated frailty information
Target group of guidelines	▪ Clinicians ▪ Researchers
How FrailSafe addresses parameter	Personalized recommendations and guidelines will be provided to pre-frail and non-frail persons in order to prevent or slow down frailty
Background / Comments	Information on subjects' frailty should be updated and available, if possible, through a computer system covering each step of the healthcare network
European guidelines	21. IMI project SPRINTT (Bernabei et al, 2017) Whether frailty can be prevented by a treatment programme which combines: ▪ exercise ▪ dietary advice ▪ modern technologies
Target group of	▪ Clinicians

guidelines	▪ Researchers ▪ Users
Guideline implementation examples	Healthy diet and a balanced BMI Physical exercise
How FrailSafe addresses this parameter	FrailSafe will promote exercise, healthy diet and the use of technology for the prevention and management of frailty, and it might create a synergy with the SPRINTT project
Background / Comments	Weight loss, values outside the normal standards of each individual and reduced exercise are linked with frailty (Fried et al, 2001; Newman et al, 2001)

4 COLLECTED DATA RELATING TO FRAILSAFE RECOMMENDATIONS / GUIDELINES

As described in Section 2, lifestyle information on older people is attained through the FrailSafe Data Acquisition using specifically (a) nutritional/diet questionnaire and (b) physical activity monitoring though embedded smart phone sensors and apps (FrailSafe GPS logger) as well as tracking systems (WWBS containing linked IMUs). Furthermore, psychological and cognitive morbidity is assessed using validated assessment tools (i.e. Mini Mental State Examination and Montreal Cognitive Assessment).

Questionnaires, surveys and focus groups are conducted to investigate the FrailSafe metrics and get feedback from end-users. Collection of feedback is an on-going and continuous task in FrailSafe. User feedback is an essential parameter taken into account when designing and conducting the pilot studies in conjunction with the way they will be organized, supported and managed throughout the duration of the project. The main goal is to ensure reliable and ongoing feedback as part of the co-design method, as well as a safe and ethical procedure for the participants (WP7). Existing recommendations were also considered in the design of the clinical assessment battery which is under analysis in this deliverable.

For the purposes of the current deliverable, the data collected from the so far trials in the project, will be analyzed to provide indications on the parameters for which guidelines should be created. The guidelines will be targeting then, the quantification of frailty and the implementation of the prediction framework, specifying on the identification of the most appropriate recommendations to be sent to the patients, healthcare professionals and caregivers through the FrailSafe notification system (e.g. VPM). The Clinical Evaluation undertaken by all of the participants in the project has been organized according to ten different domains:

1. Medical Domain
2. General Condition Domain
3. Lifestyle Domain
4. Physical Condition Domain
5. Functional Capacity Domain
6. Nutrition Domain
7. Cognitive Domain
8. Psychological Domain
9. Social Domain
10. Environmental Domain
11. Wellness Domain

Data collected for the assessment of each one of the abovementioned domains have been analyzed to reveal whether there are any correlations or other associations with frailty. Univariate analysis according to the identified frailty level is used to signal a possible relationship of the parameter and examination and frailty Furthermore, linear multiple regression was conducted to examine which of the tests/parameters used in clinical analysis significantly predict frailty.

4.1 Medical Domain

Tests and measures falling under the medical domain used are:

- The number of co-morbidities a person suffers from
- Co-morbidity's impact

- Polymedication
- Hospitalizations
- Orthostatic Hypotension
- Visual Impairment
- Hearing Impairment

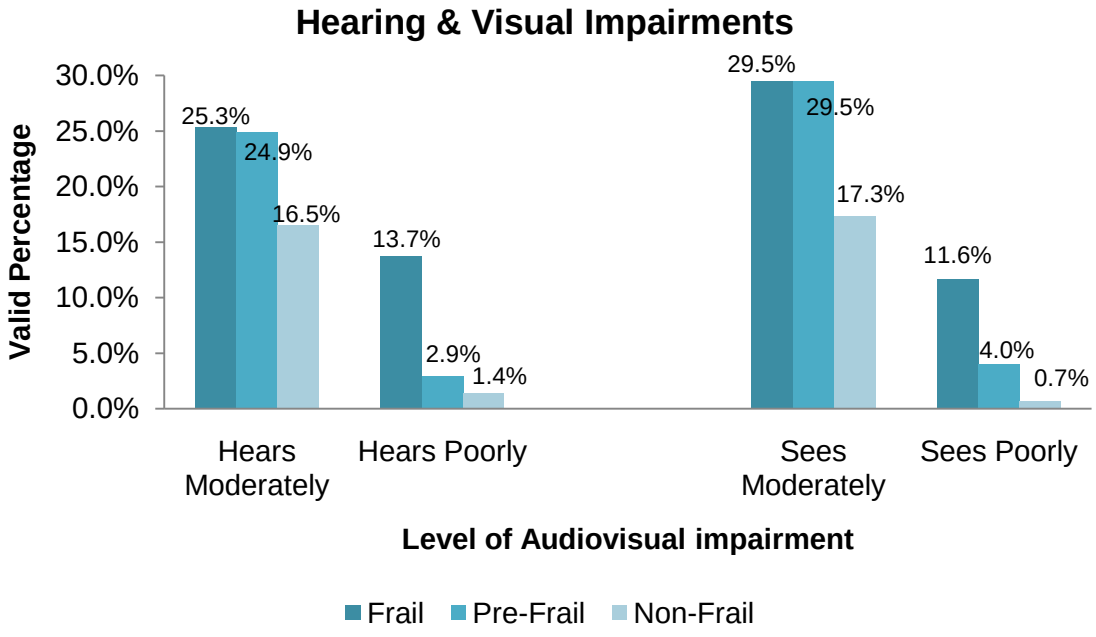
In terms of co-morbidities results do not show notable differences between frail, pre-frail and non-frail people, even though frail people seem to be under polymedication (75.7% take more than three different medications) more frequently than pre-frail (71.1%) and non-frail (70.8%) people.

Forty one percent (41%) of frail people seem to have been hospitalized in the past three years, whereas 37% of pre-frail and 25.7% seemed to have done so. Therefore, results indicate that frail people need to stay in the hospital more frequently than the other two groups.

Orthostatic hypotension seems to also have some impact on frailty as results show that 15.8% of frail people were found to suffer from it, whereas 13.9% of pre-frail and 12.9% of non-frail were found to have it.

Figure 1 shows the percentages of participants who hear and see moderately or poorly according to their frailty status. The results indicate that the hearing of frail people is more likely to be poor (13.7%) compared to pre-frail (2.9%) and non-frail (1.4%). Similarly, frail participants are more likely to have poor vision (11.6%) compared to pre-frail (4%) and non-frail (0.7%).

Figure 1: Hearing & Visual Impairments based on Frailty level



4.2 General Domain

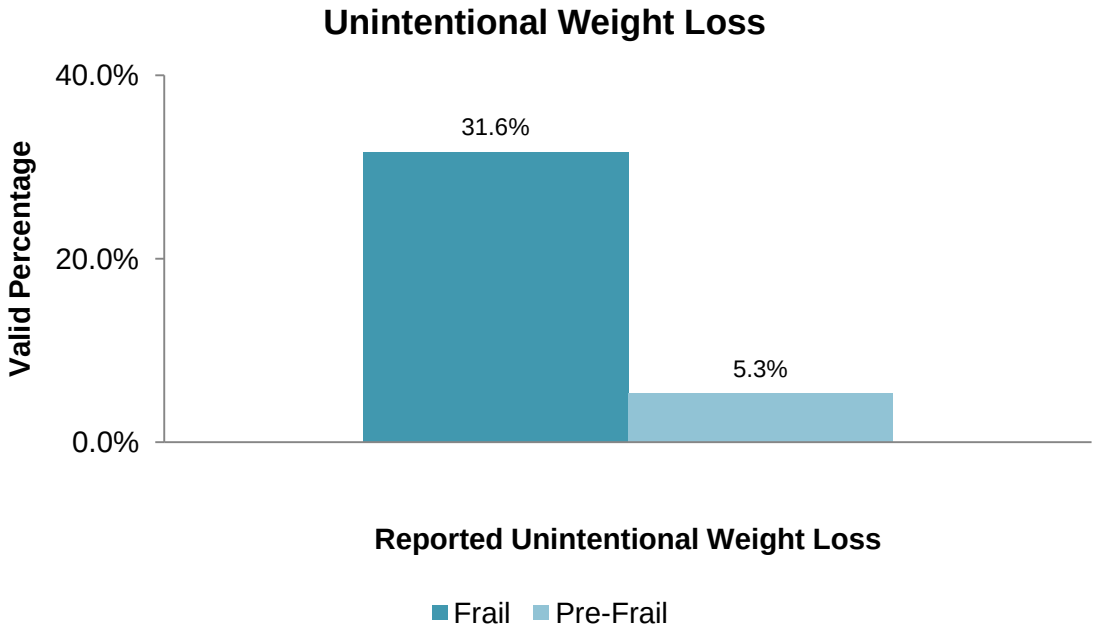
In the General Domain, the measures used (which are of utmost importance for Frailty recognition) and are part of the Fried's frailty phenotype criteria are:

- Self-reported unintentional weight loss

- Self-reported exhaustion

A great percentage (31.6%) of frail people reported unintentional weight loss while only 5.3% of pre-frail participants have unintentionally lost weight. From the results it seems that none of the non-frail participants have lost weight without intending to lose it.

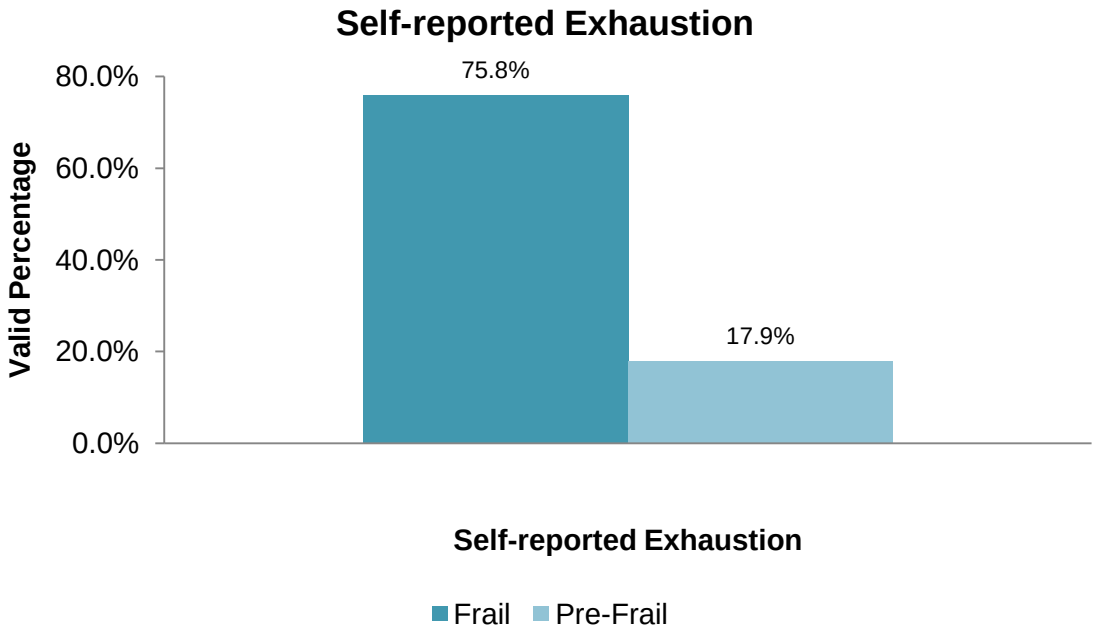
Figure 2: Self-reported Unintentional Weight Loss based on Frailty level



The vast majority of frail people (75.8%) self-reported exhaustion. Specifically, most of the frail people reported that most of the time or three to four days in a week they could not get going or felt that everything they did was an effort. Only 17.9% of pre-frail people reported feelings of exhaustion. Just like in unintentional weight loss, none of the non-frail participants reported feelings of exhaustion.

These results are consistent with the literature in that unintentional weight loss and exhaustion are main parameters of frailty.

Figure 3:Self-reported Exhaustion based on Frailty level



4.3 Lifestyle Domain

Part of the lifestyle domain for people constitute the daily habits and the way of life of each individual. In examining this parameter, FrailSafe included questions about:

- Smoking
- Alcohol Consumption
- Physical Activity

There are no important findings in the relation between frailty status and smoking as well as frailty status and alcohol consumption. However, a much bigger percentage of non-frail (63.3%) people seem to consume alcohol compared to pre-frail (47.7%) and frail (47.4%)people, a probable indication that people who start to see signs of frailty, reduce or even stop drinking alcohol. It is yet however to be investigated in the project, the possibility of smoking and drinking being causes of frailty.

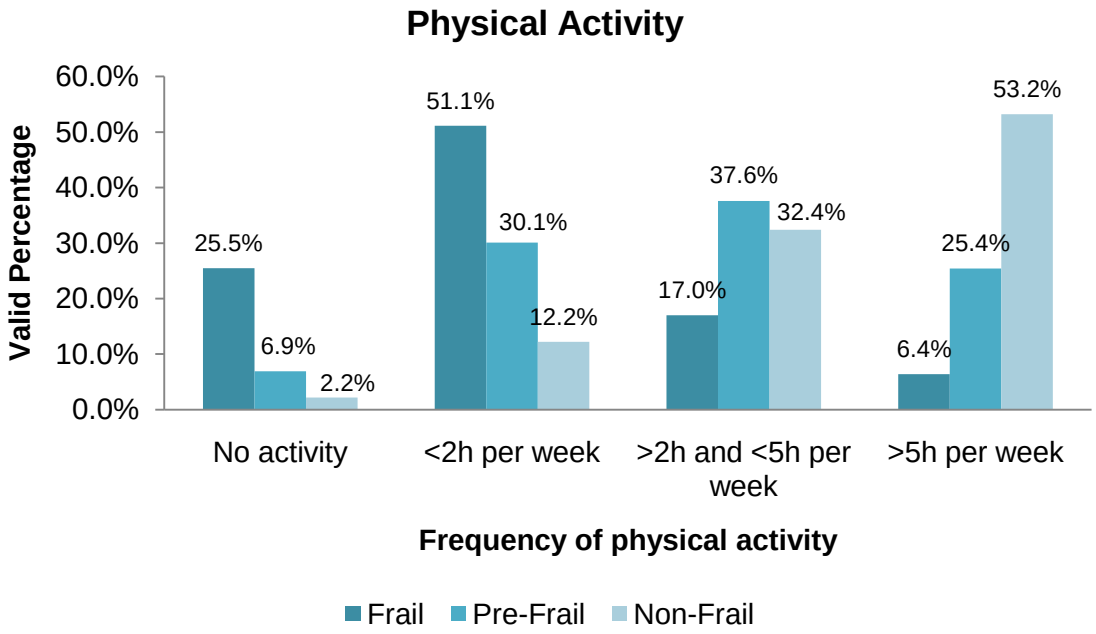
Participants in the study were asked to report on whether they regularly undertake physical activities such as walking, gardening, cleaning specifying on the approximate hours these are done per week.

As shown in figure 4, 25.5% of frail people are doing no physical activities with the biggest percentage (51%) of them reporting doing such activities for less than two hours per week.

Pre-frail participants are somewhere in the middle with 32.4% of those reporting doing physical activities for two to five hours per week, another 30.1% reporting doing them for less than two hours per week, and 25.4% doing such activities for more than five hours per week.

On the contrary, 53.2% of the non-frail report doing physical activities for more than five hours per week, with another 32.4% of them reporting somewhere between two to five hours and only 12.2% reporting such activities for less than two hours per week.

Figure 4: Frequency of physical activity based on frailty level



4.4 Physical Condition Domain

The physical condition of the participants is assessed through various tests focusing on balance, gait speed and grip strength. Specifically, they are checked on:

- Balance (Single foot standing)
- Gait Speed (4 metres)
- Gait Speed (Timed Get Up and Go test)
- Lower limb strength
- Grip strength
- Reported low physical activity

In every Clinical Evaluation, participants are asked to stand on one foot for as long as they can. Results from the test indicate that 40% of frail participants were not able to undertake the test at all, whereas only 25.3% of them were able to stand for more than five seconds. On the other side, the majority of pre-frail (60%) and non-frail (79%) participants were able to stand on single foot for more than five seconds.

Participants were also asked to walk at their normal pace, a 4 metres straight distance. Abnormal values for walking 4.57 meters are signalled as follows:

[Men]
≥7seconds for height ≤ 173cm

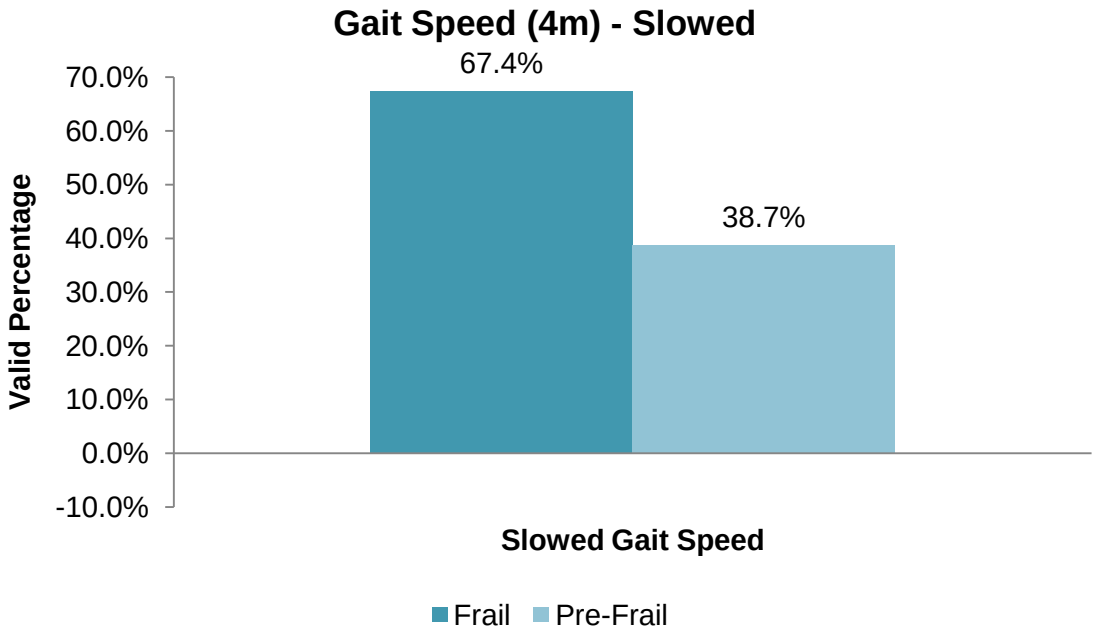
≥6seconds for height > 173cm

[Women]
≥7seconds for height ≤ 159cm

≥6seconds for height > 159cm

As presented in figure 5, 67.4% of frail participants and 38.7% of pre-frail participants showed slower than normal walking speed. None of the non-frail participants showed slowed walking speed.

Figure 5: Slowed gait speed of frail and pre-frail participants



A second test for measuring the participant's gait speed that is being used is the Timed Get Up and Go test on which participants are asked to get up from the chair, walk a 3 metres distance (to a mark), turn around, walk back and sit again on the chair. The time taken is combined with the 4 metres straight walk test for estimating whether slowed gait speed is present.

Testing the strength of lower limbs, participants are asked to get up and sit back on the chair for five times in a raw without using their hands. Results obtained reveal that 41.9% of frail participants required more than 15 seconds, which is the maximum normal time one can have to complete the test, while only 6.9% of pre-frail and 0.7% non-frail required more than the normal time.

For measuring grip strength, participants were given a dynamometer, which they had to use for three times in a row. The average value of the three attempts was the strength they had measured in kg. Normal values are checked as follows:

Normal values:

[Men]
>29kg for BMI≤24

>30kg for BMI 24.1-28 and

>32kg for BMI >28

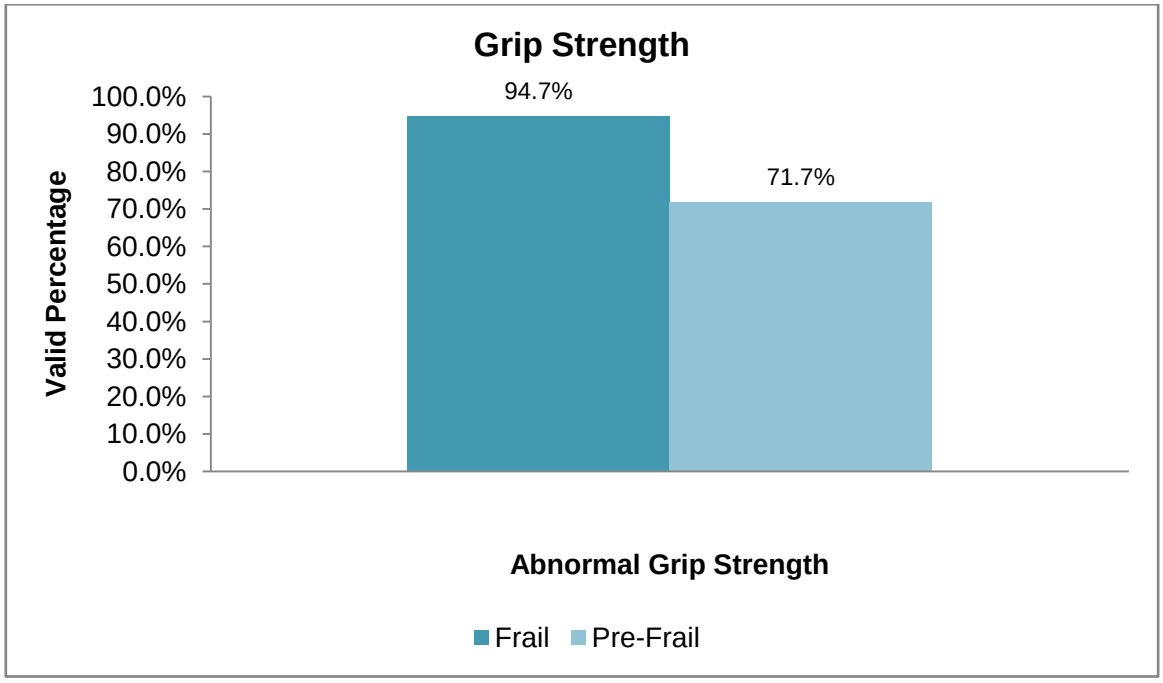
[Women]
>17kg for BMI≤23

>17.3kg for BMI 23.1-26

>18kg for BMI 26.1-29

>21kg for BMI >29

Figure 6: Percentage of abnormal grip strength values among frail and pre-frail participants



The results obtained indicate that 94.7% of frail participants and 71.7% of pre-frail participants showed abnormal values on grip strength.

Last, 57.9% of frail participants reported that they walk less than ten minutes per day while only 9.2% of pre-frail participants reported doing so. Reported low physical activity is another one of the five criteria from Fried's frailty phenotype.

4.5 Functional Capacity Domain

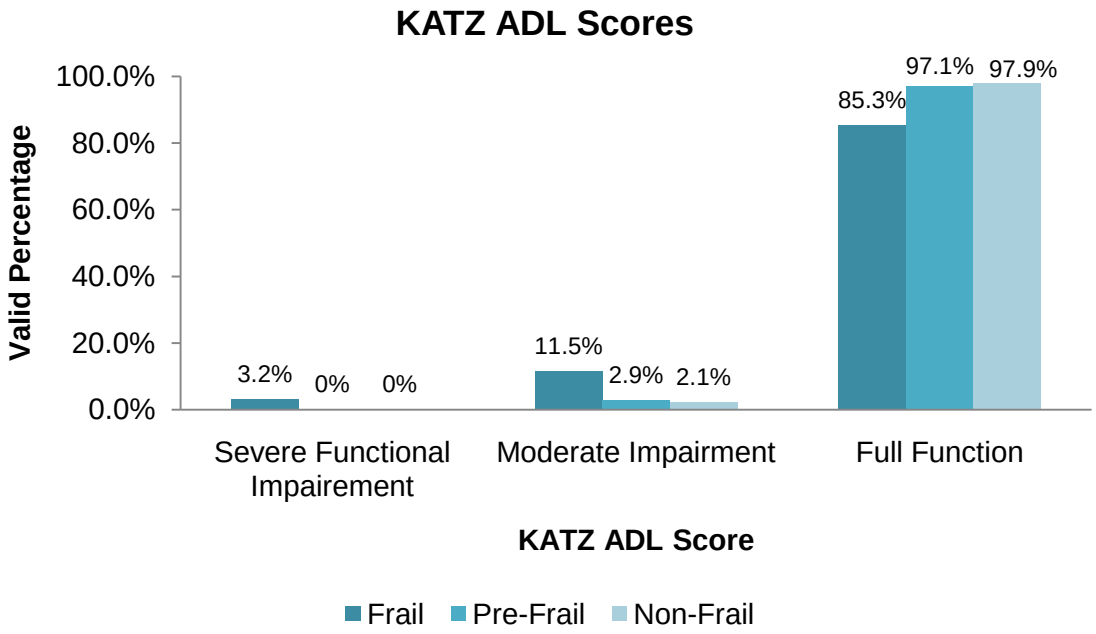
For the assessment of the functional capacity of the participants the tools chosen for FrailSafe are the:

- Katz Index of Independence in Activities of Daily Living (KATZ ADL)
- Instrumental Activities of Daily Living (IADL)

Participant's scores on KATZ ADL (Figure 7) indicate that the ability to live independently deteriorates as age increases. Comparing KATZ ADL and Fried's Scores, results indicate a statistically significant negative correlation (r=-.156, p=.002) which means that frail participants (14.7%) are more likely to have moderate or severe functional impairment than pre-frail (2.9%) and non-frail (2.1%).

Similar results are shown when comparing the IADL tool with frailty supporting therefore the results of KATZ ADL as well as the current literature.

Figure 7: KATZ ADL scores based on frailty level



4.6 Nutrition Domain

The main tool used for assessing the participant's nutritional status is the

- Mini Nutritional Assessment (MNA).

Other indicators for poor nutrition checked on FrailSafe are:

- Too low BMI
- Too high BMI
- Waist circumference and
- Lean body mass.

Results from the MNA score indicate that three participants were found to be malnourished, 37 were at risk of malnutrition while all the rest had normal nutritional status.

Comparing nutrition with frailty, 68.4% of the frail participants, 91.9% of pre-frail participants and 92.2% showed a normal nutritional status, showing once more that frail participants are more likely to become malnourished.

4.7 Cognitive Domain

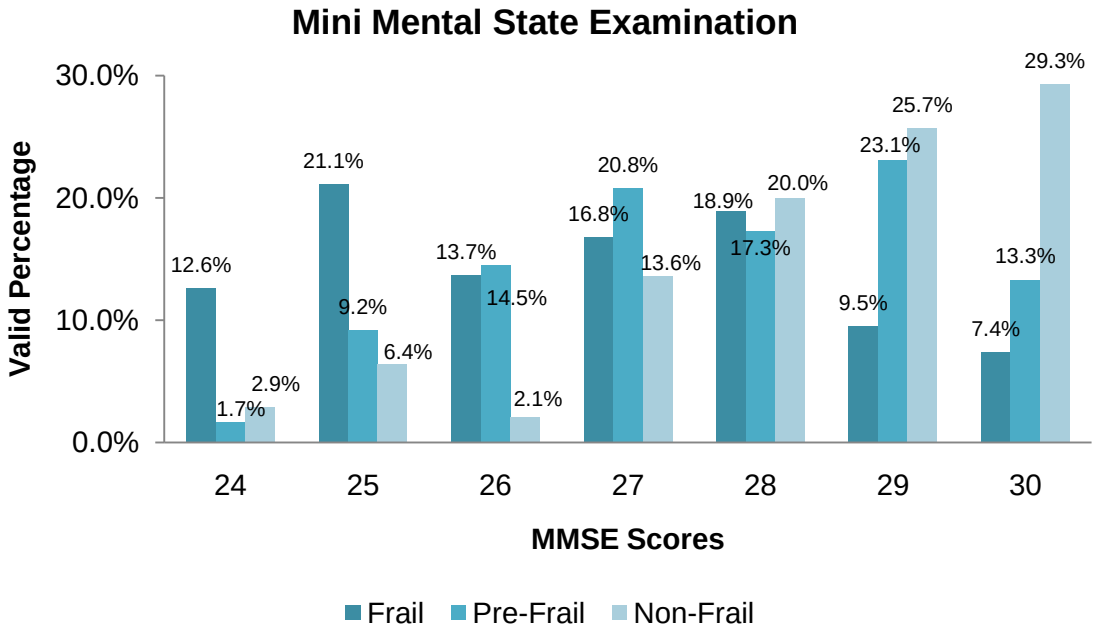
In order to assess the cognitive status of the participants, FrailSafe used the following tools:

- Mini Mental State Examination (MMSE)
- Montreal Cognitive Assessment (MOCA)

The MMSE tool was a pre-requisite to have scores above the cut-off (>24) for constituting a person eligible to participate in the study. As shown in the figure below, frail people tend to score lower than pre- and non-frail people on cognitive function tests.

Consistently with the current literature MMSE and MOCA tests are positively correlated to frailty (r=.356, p<.001 for MMSE and r=.437, p<.001 for MOCA).

Figure 8: MMSE scores separated by the level of frailty

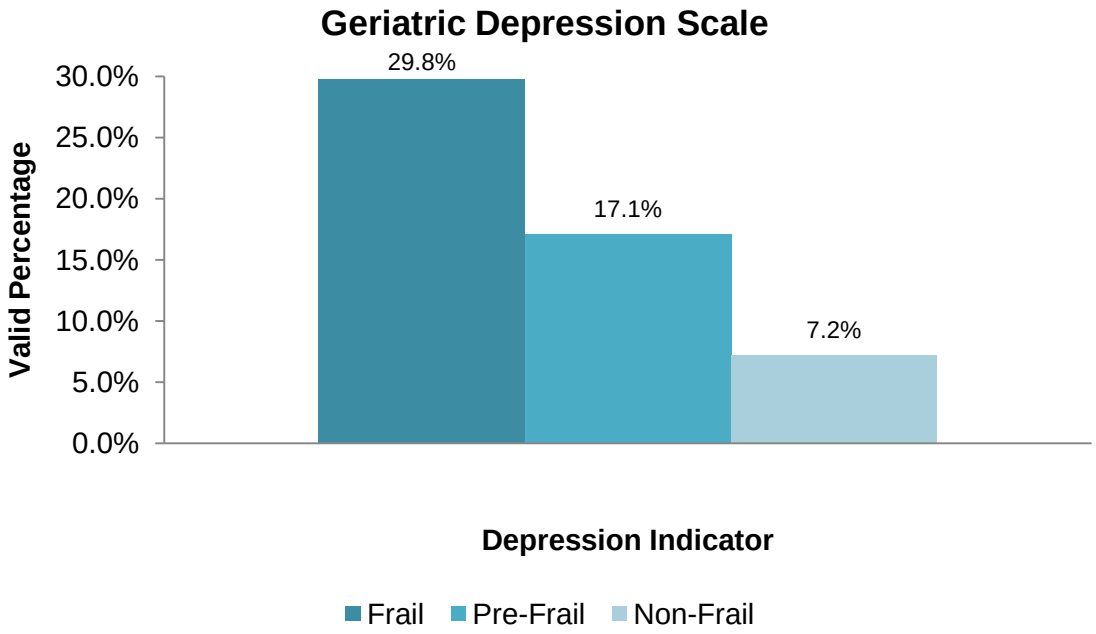


4.8 Psychological Domain

For assessing the psychological status of the participants, FrailSafe used the Geriatric Depression Scale (GDS).

Results indicate that frail participants are more likely to be depressed (29.8%) than the other groups (Figure 9) with the depression percentages being much higher for frail people than the rest. Further investigation on the depression scale is needed in order to examine whether depression is one of the outcomes of frailty or a cause to it.

Figure 9: Indicators of depression among frail, pre-frail and non-frail participants



4.9 Social Domain

For the Social Domain, participants in Clinical evaluations were asked to provide the following information:

- Living conditions
- Leisure activities (Number of times a person goes out of the house per week)
- Membership of a club
- Number of visits and social interactions per week
- Number of telephone calls exchanged per week
- Approximate time spent on phone per week
- Approximate time spent on videoconference per week
- Number of written messages sent by the participant per week

In the Clinical Evaluations participants are asked to respond on whether they live alone or with spouse/relatives, as this might play a role on frailty.

From the data collected, there are no major differences in the living conditions among the three groups with 30.5% of frail people, 43% of pre-frail people and 34.3% of non-frail people reporting that they live alone.

Responding to the question of how many times per week participants go out of their house 21.1% of frail people reported that they don't go out at all. Likewise, 4.1% of pre-frail and 1.4% of non-frail reported the same.

Investigating whether the participants are members to some sort of club or association results show that much less frail people (35.8%) are members, compared to 65.7% of pre-frail and 75% of non-frail participants.

A greater percentage (13.7%) of frail participants than that of the other two groups said they are not exchanging visits with other people at all, enhancing the belief that people who feel incapacitated end up being socially isolated.

Most of the FrailSafe's participants have reported that they talk on the phone at least once per week with a person close to them.10.5% of frail, 5.2% of pre-frail and 1.4% of non-frail are the percentages of those who said they do not exchange any phone calls with people close to them when examined under their identified level of frailty.

For people who are using the phone, participants are asked to respond on the approximate time spent talking on the phone per week. Results indicate that 9.5% of frail participants, 7% of pre-frail and 3.6% of non-frail participants mentioned not talking on the phone at all, while a great percentage of frail people 24.4% were not able to answer the question and responded "I don't know".

The majority of the participants are not using new technologies (i.e. videoconferencing) to communicate with other people, as around 90% of all the participants reported 0 minutes spent per week on videoconferencing.

Similarly, older participants seem to not use text messages all that much as 76.8% of frail, 64.3% of pre-frail and 42.1% of non-frail reported not using text messages for communicating at all. For this and all of the results in the social domain, it is important to be noted that frailty level might not significantly influence results, as the reason non-frail people seem to be more active in the social domain might be explained by the fact that frailty increases with age, thus non-frail participants are at the lowest level of the participant's total age range.

4.10 Environmental Domain

Participants were furthermore asked to evaluate the suitability of their housing environment for successfully satisfying their daily needs. The suitability was assessed by the clinician onsite. Specifically, for assessing the environmental domain the following information was collected:

- Subjective suitability of the housing environment according to participant's evaluation
- Subjective suitability of the housing environment according to investigator's evaluation
- Number of steps to access house

Almost all of the participants consider their house suitable and adapted to their needs, a view that coincides with the assessment made by the clinicians of the three centres. Additionally, for the majority of participants, their house either does not contain any stairs or has a small number (3-5) of stairs to access it.

4.11 Wellness Domain

For examining the wellness domain, participants were asked to rate their:

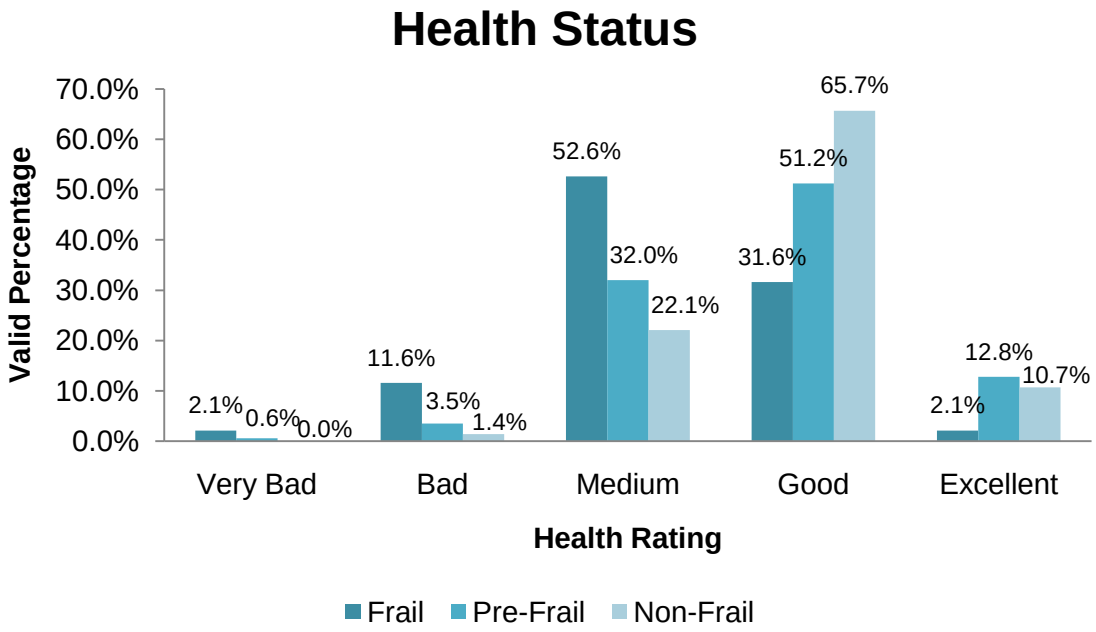
- Quality of life
- Perceived health status
- Perceived change in health since last year
- Level of anxiety
- Level of pain

On a scale from zero to ten, where zero would mean very bad quality of life and ten excellent quality of life, participants were asked to rate their quality of life in the overall and not just by

thinking their health status. The mean for this question was 7.1 (SD 2.04) for frail participants, 7.7 (SD1.78) for pre-frail participants and 7.9 (SD1.39) for non-frail participants.

Figure 9 illustrates the health status of the participants as rated by them. Results show that the vast majority of frail people think their health status is medium (52.6%) whereas the majority of pre-frail think their health status is good (51.2%). Most of non-frail participants also rated their health status as good (65.7%).

Figure 10: Perceived health status based on frailty level



When asked to compare their health with last year, 42.1% of pre-frail said about the same and 33.7% of them said a little worse. About the same (62.2%) was the most popular response of pre-frail participants as well with 23.3% choosing “a little worse” as an answer. Last, 64.3% of non-frail responded that their health is at about the same levels as last year while 21.4 said it’s a little worse this year.

4.12 Frailty Prediction

The data were analyzed using the Statistical Package for Social Sciences (SPSS). Linear multiple regression was conducted to signify the predictors of frailty (scored and categorized according as frail, pre-frail or non-frail). The model explains 55.9% of the variance and it appears to be significant ($F=12.857$, $df=33$, $p<.001$).

Table 4 shows those variables that significantly predict frailty. As it can be seen, frailty can be predicted by the frequency of exercising reported from the participants ($beta=-.219$, $t(234)=4.177$, $p<.001$). This result suggests that people who exercise less or not at all are more likely to be frail.

On a similar note, frailty can be also predicted from the scores obtained in the Mini Nutritional Assessment (MNA) test ($beta=.182$, $t(234)=3.762$, $p<.001$). Therefore, it is suggested that participants whose nutrition is not appropriate and balanced are more likely to have frailty.

Another predictor of frailty according to the Clinical Assessment data collected is the amount of time it takes participants to rise from the chair five times without the help of the arms (beta=-.193, t(234)=-3.210, p=.002). This indicates that the slower the participants are in their effort to rise from the chair five times, the greater the likelihood of being frail.

Similarly, hearing levels seem to be predicting frailty (beta=-.146, t(234)=-3.098, p=.002) suggesting that the lower their level of hearing is, the more likely they are to have frailty.

An important predictor of frailty seem to also be the participant's psychological status (beta=-.152, t(234)=2.863, p=.005). Participants who showed more depressive symptoms on the Geriatric Depression Scale (GDS) seem to be at greater risk for having frailty than those without depressive symptoms.

The number of co-morbidities a person is suffering from, seems to also predict frailty (beta=-.141, t(234)=-2.388, p=.018), indicating that the higher co-morbidities are associated with increased possibilities of having frailty.

The last predictor of frailty concerns the cognitive function of the individuals. Participants were tested using the Mini Mental State Examination (MMSE) which seems to also predict frailty (beta=.112, t(234)=2.271, p=.024). This result suggests that the lower the participant's score is on MMSE; the higher the chances are for that participant to be frail.

Table 4: Linear Multiple Regression for predicting frailty

	Unstandardized Coefficients		Standardized Coefficients		
Model	B	Std. Error	Beta	t	Sig.
Regular Activity	,163	,039	,219	4,177	,000
Hearing	-,178	,058	-,146	-3,098	,002
Co-morbidities	-,033	,014	-,141	-2,388	,018
GDS	-,042	,015	-,152	-2,863	,005
MMSE	,045	,020	,112	2,271	,024
Rise from Chair Time	,000	,000	-,193	-3,210	,002
MNA	,081	,021	,182	3,762	,000

a. Dependent Variable: Fried

5 CLINICAL GUIDELINES FORMALIZED

The aim of the current deliverable is to develop a list of clinical guidelines to be used as recommendations in the Virtual Patient Model after examining the scientific literature and analyzing the so far collected data. Consistently with the literature, the results indicated that the Lifestyle, Medical, Psychological, Cognitive, Physical Condition and Nutrition Domains are the prime predictors of frailty. Therefore, in order to be able to prevent, slow down or

reverse frailty, the users of the FrailSafe system will need to receive guidance on what aspects of their life will be good to alter to ensure a frailty-free and prosperous life.

5.1 Cognitive Domain Recommendations

Depending on the score received on the MMSE test, the VPM should suggest the following to the participant:

Table 5: Guidelines and Recommendations for Cognition

Guideline	Recommendation
If score is under the normal values	A visit to the neurologist is recommended for providing a more comprehensive evaluation of your cognitive level
If score is 24 (cut-off point)	Participation to a cognition enhancement programme is encouraged.
If score is 25 and above	To increase your cognitive level in an entertaining way, playing FrailSafe's "Memory", "Simon" "Supermarket" or "Reflex" games frequently is recommended

The same recommendations should be provided for MOCA scores, using however its cut-off which is at 26 points.

5.2 Lifestyle Domain Recommendations

The lifestyle of a person can have a major impact on his/her health. One of the most important aspects found both in the literature and in the results is the fact that seniors exercise less and less as they age and many of them do not exercise at all. The guidelines and recommendations that the VPM should deliver to the FrailSafe users are described in the table below:

Table 6: Guidelines and Recommendations for Lifestyle

Guideline	Recommendation
If the person is smoking	▪ Smoking deteriorates health and weakens the immune system. Consider replacing it with exercise ▪ There are plenty of programs available aiding people to quit smoking. Choosing one of them is encouraged *(maybe add a list per country?)*
If reported low or no physical	▪ Exercise can not only prevent but reverse frailty.

activity or if GPS Logger doesn't show a satisfactory outdoor walking activity (in terms of distance and duration)	Consider joining an aerobics and resistance exercise program ▪ The following videos provide valuable exercises for home workout. Give them a try. ▪ Walking for at least 2.5 hours per week can increase endurance and benefit your health ▪ Play FrailSafe's "Redwings" game to strengthen your grip
If the person is consuming an excessive amount of alcohol (recommendation based on unit reported)	▪ Alcohol can cause severe damages to the liver. Consider lowering consumption. ▪ There are groups helping people stop drinking alcohol ▪ One glass of red wine per day is the only healthy alcohol consumption option

5.3 Medical Domain Recommendations

The Medical Domain is also a crucial domain for the prevention and management of frailty as there are multiple reasons a person might become frail such as the presence of co-morbidities, possible effects from polymedication or the presence of orthostatic hypotension. Recommendations for users and/or clinicians are presented in the table below:

Table 7: Guidelines and Recommendations for Medical Record

Guideline	Recommendation
If Blood Pressure is consistently high	Consider visiting your GP for regulating your blood pressure
If more than 3 co-morbidities	Consider medication list review according to pre-defined criteria (e.g. STOPP/START) Consider modification of prescribed drugs according to the functional status of the patient for minimizing possible effects resulting to frailty
If presence of Orthostatic Hypotension	In order to avoid dizziness from orthostatic hypotension consider getting up from the chair, bed or other sitting posture slowly If dizzy at any point, sit down, lower your head towards your legs and breathe slowly

5.4 Psychological Domain Recommendations

Depression, as well as other psychiatric / psychological conditions is highly impacts people's mental health. Seniors are much more vulnerable in suffering from depression, which in turn was found to be a predictor of frailty. Thus, recommendations for actions to depressed users are really important and are shown in Table 8:

Table 8: Guidelines and Recommendation for Depression

Guideline	Recommendations
If score is greater than 5	▪ Consider visiting a neurologist or psychologist to discuss about the issues in your life that make you sad ▪ A smile can always make a day better ▪ Meeting with friends is a helpful habit ▪ For clinicians: Consider referral of the person to a psychiatrist, or neurologist for medical, psychological intervention

5.5 Nutrition Domain Recommendations

Another vital parameter for good physical and mental health concerns the nutrition each person has. Malnourished people have low muscle mass which is a criterion for frailty, but even obese people are at risk of suffering from sarcopenic obesity, which is also a component associated with frailty. Table 9 presents the recommendations to be provided for improving nutrition through the VPM:

Table 9: Guidelines and Recommendations for Nutrition

Guideline	Recommendations
If BMI too high	▪ Consider a healthy diet for achieving a balanced weight. Eat plenty of fruits, vegetables and protein ▪ Aerobic exercise not only helps cardio function but also helps in losing weight
If BMI too low	▪ A visit to the GP for investigating the low BMI is recommended ▪ An enriched and nutritional diet is recommended. Consider visiting a nutritionist ▪ Resistance exercise helps in increasing muscle mass and it is a perfect way of remaining physically healthy.
If malnourished on MNA	▪ Visit a nutritionist ▪ Resistance exercise increases muscle mass and

	improves appetite ▪ Investigate cause of malnourishment (for clinicians) ▪ Consider taking nutritional supplements

5.6 Physical Condition Domain

The physical condition of a senior person is the primal component for having or not having frail. Gait speed and grip strength are the most important symptoms of frailty but can fortunately be improved with exercise, which makes scientists confident that the frailty syndrome is reversible. Table 10, presents the recommendations for users and clinicians regarding the improvement of balance, gait speed, limb strength and grip strength:

Table 10: Guidelines and Recommendation for Physical Condition

Guideline	Recommendations
If balance on single foot standing <5 seconds	▪ Try to hold on to a stable object and stand on single foot for 1 minute. If unsuccessful try it as often as possible until you achieve it. When it is achieved try slowly removing hands from the object.
Slow gait speed	▪ Try walking for 2 minutes every day increasing the time as walking becomes easier
Low lower limb strength	▪ Exercise can help increase limb strength. Consider a home workout
Low grip strength	▪ Suggestion for reviewing medication (if medications taken might be the cause of low grip strength) ▪ Resistance exercise is extremely helpful for strengthening grip thus reducing one of the main symptoms of frailty ▪ Playing FrailSafe's "Red Wings" or "Force Analyzer" games two or three times a week can help in increasing grip strength
If low muscle mass and poly-medication exists	▪ Send recommendation to the clinician to prescribe medication that increases muscle mass

6 CONCLUSIONS

Deliverable 2.3 expanded on the D2.2's literature review of the European healthcare advices for frailty and analyzed FrailSafe's collected data in order to derive to guidelines and recommendations to be used in the Virtual Patient Model and possibly other modules of the FrailSafe system.

Recommendations are directed mainly to older adults, clinicians, researchers, doctors and families/caregivers. Moreover, formalized clinical guidelines were created both for prevention and for intervention purposes. The so-far collected data from the FrailSafe trials were firstly examined using a univariate analysis for identifying associations between the different parameters and the frailty status of the participants.

In order to check which of the FrailSafe's collected data can predict frailty, linear multiple regression was conducted. Results indicated that regular activity, hearing impairments, the presence of co-morbidities, depression, cognitive function, lower limb strength and nutrition significantly predict frailty, an outcome consistent with the current scientific literature.

Based on those outcomes, formalized guidelines and recommendations were prepared in order to be used by the Virtual Patient Model and possibly other components of the FrailSafe list. The developed list is not exhaustive and it is expected to be enriched as the project progresses.

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