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EXECUTIVE SUMMARY

The key objective of the first work package (WP1) of the FrailSafe project, entitled by "Requirements, Use Cases, Architecture and Specifications", is the fundamental definition of the overall user needs, architecture, and system specifications of the FrailSafe infrastructure that will be able to satisfy existing and future users' requirements by exploiting all medical, regulatory, and technological perspectives on a User Centred Design (UCD) methodology basis. A comprehensive analysis and review of the user and system level requirements will be subsequently conducted to define and deliver a number of representative use cases and user scenarios that will highlight the novelties of the FrailSafe framework. Throughout its lifetime, FrailSafe will contribute significantly in a multitude of scientific and technological facets pushing the boundaries of current care delivery systems for older people.

The first deliverable (D1.1) of WP1, entitled by "Analysis of current practices", offers the baseline description of the solutions and methodologies for commencing the work of the project, by reporting and benchmarking on the latest well-established developments that have already been studied in the specific areas where the FrailSafe framework aims to significantly contribute. Without loss of generality, the presented work can be divided into five parts that cover the current advances in the main fields of: (i) frailty quantification and relation to other co-morbidities & disabilities, (ii) sensing systems for monitoring frail-related features, (iii) older people-based virtual patient modeling and data management & mining, (iv) virtual and augmented reality rehabilitation programs and games for older people, and finally (v) personalized guidance systems via information visualization interfaces.

Frailty, co-morbidity, disability and sarcopenia are key issues for older people with major health care and consequently into society implications; considered as distinct entities, but they often co-exist, interact, share similar risk factors and lead to similar adverse outcomes. To this end, we initially provide a short summary of the available symptoms and signs that are frequently used to characterize frailty as an independent entity, which can be grouped in the physical, cognitive, functional, and social domain. Of these the former domain is widely studied in the literature, whereas the role of the rest ones is still elusive. This summary is then complemented by shading light to the correlation of the aforementioned entities with the aim of untangling the overlapping complexity between them.

The second part of this deliverable is devoted on the review of the sensing systems responsible for the continuous, indoors and outdoors, monitoring of key physiological parameters, behavioral changes and domicile activities, which are usually detected through the exploitation of complex signal processing methodologies that provide the value set of frailty-related indicators such as heart and respiratory rates, posture, gait, physical activity and several environmental parameters.

The early identification and detailed conceptual definition of the entities/concepts of interest for older people allows the personalized adaptation of the patient feedback /user interfacing/intervention strategies as well as makes the data analysis/mining and feature extraction more efficient due to the machine readable representation format. Initially, a large amount of studies on the domain of static and dynamic patient modelling representation is briefly covered, followed by an analytical description on the recent formats developed in previous projects (e.g. VERITAS) which will be the heart of the FrailSafe patient model representation. In the context of data management and knowledge discovery, we provide the main challenges coming from the streaming nature of dynamic sensor data and offer the state-of-the-art techniques responsible for indexing and fusing multidimensional data from different modalities.

The fourth part focuses on the different types of gamification software that have been strategically explored to affect a number of issues in health among older adults. Specifically, we will show how exploiting haptic and vision technologies from Virtual Reality (VR) and Augmented Reality (AR) games can offer clinical assessment, diagnosis support and rehabilitation options by improving the physical and cognitive level of the patients.

Last but not least, we offer a review on the personal guidance applications and virtual community platforms that could be essential utilized for producing healthcare-oriented systems. A short description of the different interactive information visualization techniques that allow the representation of medical information and the end-users (patients, care-givers) interaction with the system is subsequently presented. A summarization of the different cloud-based software modules that can ensure the effective communication, collaboration and control of frailty-status between patients and their caregivers is further introduced. Finally, this section is concluded by providing the existing cross-platform sensing infrastructures that outline the basic architecture for the collection of measurements.

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Abstract (for dissemination)	This deliverable offers the baseline description of the solutions and methodologies for commencing the work of the project, by reporting and benchmarking on the latest well-established developments that have already been studied in the specific areas where the FrailSafe framework aims to significantly contribute. The examined solutions cover the areas of (i) frailty quantification and relation to other co-morbidities & disabilities, (ii) sensing systems for monitoring frail-related features, (iii) older people-based virtual patient modeling and data management & mining, (iv) virtual and augmented reality rehabilitation programs and games for older people, and finally (v) personalized guidance systems via information visualization interfaces.			
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LIST OF ABBREVIATIONS AND ACRONYMS

(*in alphabetic order*)

ADL	Activities of Daily Living
ALFRED	Personal Interactive Assistant for Independent Living and Active Ageing
APCA	Adaptive Piecewise Approximation
AR	Augmented Reality
BSBL	Block Sparse Bayesian Learning
CES	Consumer Electronics Show
CGA	Comprehensive Geriatric Assessment
CS	Compressed Sensing
CVD	Cardiovascular Disease
DFT	Discrete Fourier Transform
DOREMI	Decrease of cOgnitive decline, malnutRition and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion
DSS	Decision Support System

DTW	Dynamic Time Warping
DWT	Discrete Wavelet Transform
EC	European Commission
ECG	Electrocardiogram
EEG	Electroencephalogram
eHealth	Electronic Health
EU	European Union
EHR	Electronic Health Record
FI	Frailty Index
FI-CGA	CGA-based Frailty Index
FTSS	Five Times Sit to Stand
GFST	Gerontopole Frailty Screening Tool
GRACE	Geriatric Research in Ambulatory and Cognitive Excellence
GPS	Global Positioning System
GUI	Graphical User Interface
HCI	Human Computer Interaction
HR	Heart Rate
IADL	Instrumental Activities of Daily Living
ICD	International Classification of Diseases
ICF	International Classification of Functioning, Disability and Health
ICT	Information and Communication Technologies
IHME	Institute for Health Metrics and Evaluation
IMU	Inertial Measurement Unit
LCSS	Longest Common Subsequence
mHealth	Mobile Health
MEMS	Micro Electro Mechanical Sensors
MIRACULOUS-LIFE	Miraculous-Life for Independent Elderly Living

MoVA	Mobile network Visual Analytics
MRI	Magnetic Resonance Imaging
NLM	Nonlocal Means
OWL	Web Ontology Language
PAA	Piecewise Aggregate Approximation
PCA	Principal Component Analysis
PHM	Personal Health Monitor
SAA	Symbolic Aggregate Approximation
SE	Shannon Entropy
SES	Socio-Economic Status
SOCP	Second-Order Cone Program
SP	Spectrogram
SPPB	Short Performance Physical Battery
STFT	Short Time Fourier Transform
SVM	Support Vector Machines
TFR	Time Frequency Representation
TUG	Timed Up and Go
UI	User Interface
UWB	Ultra Wide Band
VAP	Visual Analytics Platform
VR	Virtual Reality
VSP	Virtual Support Partner
WBAN	Wireless Body Area Network
WWS	Wearable Wellness System
XML	Extensible Markup Language

1 INTRODUCTION

FrailSafe is proposing a novel frailty management system based on a patient-specific approach that is part of a comprehensive plan to managing and support frailty older people, as well as exploring different causes of frailty manifestation. The system focus on monitoring older people's everyday life in order to capture manifestations related to frailty, and through augmented reality combined with state-of-the–art data mining techniques, it builds a self-adaptive personalized virtual patient model, aiming to unobtrusively help older people improve and/or prevent being frail. 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. In detail, 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. The system will leverage the ongoing integration and miniaturization of sensors to build an integrated holistic frailty self-management framework. The aim of this deliverable is to provide the baseline definition for conducting interdisciplinary research in each of the scientific and technical innovation areas targeted by this project. We report on the recent advances and developments; highlighting features and trade-offs; pointing out hardware/implementation details and light-weight modifications that can be explored to guide the decision of which system/model/game/tool to employ in a given setting. Without loss of generality, the rest of this deliverable is organized as follows:

Section 2 offers a comprehensive overview of the existing frailty measurements in terms of identified symptoms, signs, states and deficits that an older person may experience. These characteristics can be classified in a physical, cognitive, functional, and social domain; where the physical is widely studied and the rest ones have been substantially unexplored. While frailty, sarcopenia, co-morbidities and disabilities are distinct conditions, several works have showed how they coexist, interact, share similar risk factors as well as possibly similar pathophysiological mechanisms and thus may lead to similar adverse outcomes.

Section 3 provides a short technical summary of the available sensing technologies; wearable and/or implanted sensor devices for monitoring the physiological status of the patient as well as ambient sensors for monitoring physical activities and environmental parameters. Furthermore, a careful investigation of the signal processing algorithms most closely to the project’s requirements is also provided.

Section 4 presents the research work conducted during the latest few years to develop virtual patient models, covering a wide range of population groups and especially focusing on groups in risk of exclusion (older people, people with disability, people with co-existent condition); paired with a comprehensive insight of the heterogeneous electronic health record requirements from various domains involving different target stakeholders. An extensive overview of the state-of-the-art real-time data management and data mining techniques explored in previous health-oriented problems for the effective decision assessment, risk detection and alarm triggering scenarios is finally given.

Section 5 shows how new and emerging advances in gamification area have been applied to improve the health, welfare and quality of life for older people. These include virtual and/or augmented reality games/exercise programs that allow both clinical assessment alternatives and rehabilitation options.

Finally, Section 6 is devoted to the core parts of the self-support management and personal guidance systems for old patients. It initially presents a number of different information visualization techniques and health support tools that provide the intuitive representation of a variety of medical information as well as offer help interaction platforms responsible for communication between the system's end users (patients and caregivers). Different cloud-based software modules responsible for the customization and co-design of the frailty-aware personal guidance system and virtual community platform are also provided.

2 FRAILTY QUANTIFICATION, CO-MORBIDITIES & DISABILITIES

In 1990, an American Medical Association white paper concluded that ''*one of the most important tasks that the medical community faces today is to prepare for the problems in caring for the older people in the 1990s and the early 21st century*'' [1]. A particular emphasis is the growing population of frail, vulnerable older adults, ''*the group of patients that presents the most complex and challenging problems to the physician and all health care professionals*''. The vulnerable subset of the older population has also been identified as (a) those older adults with multiple chronic conditions or comorbidities [2, 3], or (b) those who are disabled or dependent [4]. In fact, these three terms, (i) disability, (ii) frailty, and (iii) comorbidity are often used interchangeably to identify the physically vulnerable subset of older adults requiring enhanced care. However, recent research supports geriatricians' perceptions that these are distinct clinical entities, although interrelated, and that clinical management of each of these has its own unique content and challenges. Improved clarity as to definition and criteria for distinguishing these three conditions could improve diagnostic accuracy and development of effective, targeted strategies for prevention and treatment.

In the following sections we will provide definitions, descriptions and evidence of translational applications of comorbidity (Section 2.1), disability (Section 2.2) and frailty (Section 2.3). The first part of Section 2.3 is devoted in describing the definitions and mechanisms of frailty, while in the second part the two main frailty models will be described. In the third part of this section, some important frailty components will be presented (sarcopenia, polymedication, cognitive and psychological aspects as well as social dimension). Section 2.4 refers to frailty metrics. A brief mention to frailty assessment instruments, as well as the role of comprehensive geriatric assessment, will be done. Finally, in Section 2.5 the rational of the FrailSafe project, from a clinical point of view, is explained.

2.1 Comorbidity

At first blush, comorbidity should be the most straightforward concept to define medically, compared with disability and frailty. Its formal definition is the concurrent presence of two or more medically diagnosed diseases in the same individual, with the diagnosis of each contributing disease based on established, widely recognized criteria. In this sense, the concept of comorbidity could be viewed as an interface between the geriatric paradigm of health and the more traditional medical definition of disease.

With aging, the presence of comorbidity increases markedly, in large part because the frequency of individual chronic conditions rises with age. For example, after age 65, 48% of community-dwelling persons in the United States report arthritis, 36% hypertension, 27% heart disease, 10% diabetes, and 6% a history of stroke [2, 5]. As a result of these prevalences, 35.3% of the population in the United States at ages 65–79 reports two or more diseases, and this reaches 70.2% at age 80 years and older [5]. Analysis of Medicare claims data shows that two thirds of all beneficiaries aged older than 65 years have two or more chronic conditions, and one third have four or more [6]. Comorbidity is associated with high health care utilization and expenditures with 96% of annual Medicare spending attributable to beneficiaries with multiple chronic conditions [6].

Additionally, comorbidity heightens the risk of disability and mortality, over and above the risk from individual diseases [7, 8]. Particular pairs of chronic diseases are prevalent, and are synergistic in increasing risk for disability [9, 10, 11]. 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 [11]. Overall, of the 368 participants (of 4317) who were frail, 27% reported disability in one ADL (Activities of Daily Living), with or without comorbidity, and 68% reported having two or more chronic conditions (with or without disability) 21% of those who were frail were also disabled and had comorbid disease [12]. Thus, these data offer distinction of these conditions and evidence for their co-occurrence.

Recent work developed in clinical geriatrics suggests that comorbidity could be thought of as occurring at multiple physiologic/pathophysiologic levels, beyond just that of clinically diagnosed diseases. For example, researchers are increasingly evaluating the interactions of concurrently present impairments, such as strength and balance [13] or vision and hearing [14], or biomediators, such as interleukin-6 and insulin-like growth factor-I [15], in contributing to downstream outcomes of frailty and disability. In fact, it is also possible that a clinical disease can be undiagnosed due to atypical or silent presentation or subclinical status, but contribute substantially to the burden of comorbidity. As a consequence of this work, we are starting to understand that current definitions of comorbidity based on diseases that are fully manifest should be revised. If the value of considering comorbidity as capturing the synergistic interactions that lead to worsened outcomes than would be found due just to the additive effects of the individual conditions alone, then comorbidity should, theoretically, involve interactions between any two conditions, even of clinical or subclinical diseases with impairments or physiologic biomediators. This issue leads to more questions than answers at this point.

However, given that both frailty [12] and comorbidity [9, 10, 11] are independent risk factors for disability, perhaps at this time we can think about comorbidity as the aggregation of clinically manifest diseases present in an individual, and frailty as the aggregate of subclinical losses of reserve across multiple physiologic systems.

2.2 Disability

Disability is an umbrella term1, covering impairments (somatic dysfunction), activity limitations (difficulty in the execution of a task or action), and participation restrictions (the gap between a person's capabilities and the demands of the environment). Thus, disability is more than a medical issue; it involves social, public health, economical and even moral dimensions [4].

Although the term disability could embed multiple aspects, physical disability, as is more frequently presented by mobility restriction, has been mostly studied and approached by several screening methods. It is mainly diagnosed by self-report of difficulty in specific tasks, but more systematized, performance-based questionnaires about functional abilities also exist. 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 people over the age of 70 and tools destined to identify older adults in higher risk of disability also exist [16, 17, 18]. This is justified by the fact that physical disability risk rises steadily with age among those aged 65 years and older [5] and thus is especially frequent in older adults. An estimated 20%–30% of community-dwelling adults aged over 70 years report disability in mobility, IADLs and/or ADLs.

Approximately half of disability in older adults develops chronically and progressively in association with underlying severity of disease, comorbidity, and frailty; the other half develops acutely, or catastrophically, in association with acute clinical events such as hip fracture or stroke [19].

[1] http://www.who.int/topics/disabilities/en/

Physical disability in late life is, primarily, an outcome of diseases and physiologic alterations with aging, with the impact of these underlying causes modified by social, economic, and behavioural factors as well as access to medical care. Individual diseases, specific pairs of comorbid conditions, co-existing impairments (such as muscle weakness and balance decrements or decreased exercise tolerance), and frailty itself are identified risk factors for physical disability [7, 8]; these may act independently or, more often, in synergistic combinations.

While disability itself is an adverse health condition, it is also a risk factor for further unfavourable outcomes. Motor disability predicts subsequent deficiency in IADLs and ADLs [20, 21] and this restriction implies a loss of independency and even personal autonomy. This is particularly important for the most disabled, dependent subset of older adults, who reside in nursing homes: approximately 5% of those aged 65 years and older. Further, disability defined as difficulty in tasks of ADL and IADL, independently of its causes, is associated with an increased risk for mortality [22], hospitalization, need for long-term care [7, 8], and higher health care expenditures [23].

2.3 Frailty

2.3.1 Definitions and mechanisms

Identifying frail older patients objectively and quickly has been proved neither evident nor straightforward. The theoretic definition of frailty describes a “clinically recognisable state of increased vulnerability, resulting from age-associated decline in reserve and function across multiple physiological systems such that the ability to cope with every day or acute stressors is compromised” [24]. These stressors can be perturbations of various kinds like extremes of environmental temperature, exacerbations of a chronic disease, an acute illness, or an injury.

While most of the clinicians find this definition comprehensive and acceptable, there is a lack of consensus regarding the operational definition of frailty for use in everyday clinical practice [25]. This makes it difficult to create validated basic screening tools, and current practice often relies on clinical discretion.

The American Medical Association has stated that as many as 40% of adults aged 80 years and older are frail [1]. It is also thought that the vast majority of the 1.6 million older people nursing home residents in the United States are frail [26]. Thus, frailty occurs in a significant subset of older adults; conveying some notion of its import.

The fact that frailty and disability can be implicated in causal relationships between each other and also result to other health outcomes, together with the important frequency of their co-existence, has emerged much definitional confusion between frailty and disability/dependency. However, there is increasing consensus that differentiating frailty from disability may improve our understanding of the aging process and offer new opportunities for prevention and care in clinical geriatrics.

Establishing a definition for the frailty syndrome would improve our ability to characterize the heterogeneity of health and functional status observed in older persons as well. Moreover, it would help identify a subset of vulnerable older adults at risk of experiencing adverse outcomes. This can be of particular value in evaluating non-disabled older persons with chronic diseases such as cancer or cardiovascular disease, where the presence of frailty can have important implications in treatment decision-making and care management [27].

The central problem with frailty lies in the potential for serious adverse outcomes after a seemingly minor stressor event or change. This could mean anything from a simple episode of flu to a major intervention like a joint replacement. Even apparently simple interventions like a move to a short term residential placement, a trip to the local emergency department after a fall or the trial of a new analgesic can have unforeseen and adverse outcomes [28] (see Figure 1). Susceptibility to stressors is also influenced by biological, behavioural, environmental, and social risk factors, with the main consequence being an increased risk for multiple adverse health outcomes, including disability, morbidity, falls, hospitalization, institutionalization, and death.

Thus, for an individual the knowledge that they are prone or present established frailty can help health and social care professionals to tailor their approach and interventions, and to start a pathway of care to address the issues contributing to frailty.

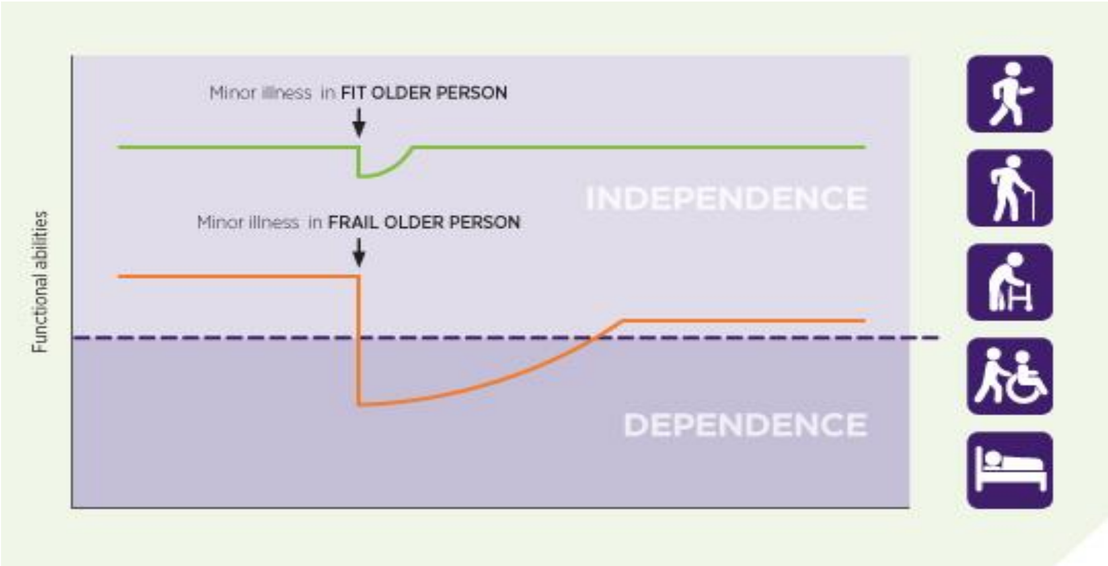

Figure 1. Frail older people display low resilience to minor stressors (e.g. urinary tract infection) [28].

In the pathophysiological point of view, there are numerous organic systems in which physiologic decrements in mass or function have been demonstrated with age, including sarcopenia, osteopenia, dysregulation of the hypothalamic axis, of inflammation and of immune function [29]. Several experts in the field of frailty propose that the immune-endocrine changes with ageing could be the common substrate of the parameters composing the frailty syndrome [30]. Another approach is to consider frailty as an accumulation of deficits of different origin without necessarily a common underlying mechanism. Thus, aggregate expression of risk resulting from age- or disease-associated physiologic accumulation of subthreshold decrements affects multiple physiologic systems. Still, it is a dynamic process, represented as an auto-feedback process influenced by multiple endogenous and exogenous factors that affect both the onset and trajectory over the lifetime of the individual [31].

Although the early stages of this process may be clinically silent, when the losses of reserve reach an aggregate threshold that leads to serious vulnerability, the syndrome may become detectable by looking at clinical, functional, behavioural, and biological markers. Central to the clinical definition of frailty has been the concept that no single altered system defines this state, but that multiple systems should be involved. The hypothesized subclinical dysregulations of frailty, as above, are under active investigation [32, 33]. However, it appears that these multisystem dysregulations become clinically apparent either when unmasked by stressors or in a clinical phenotype of a final common pathway [29].

It seems that a critical mass of impairments or geriatric conditions adding up to the phenotype of frailty, indicate that frailty is a distinct entity, and as such should be recognized by clinicians, with multiple possible causal components and manifestations and no single one, by itself, being sufficient or essential in its presentation. This definition is consistent with that of a medical syndrome.

While there is consensus on the general definition of frailty, translation into practice has been more problematic. Building on the clinical consensus and research evidence to date, a clinical phenotype of frailty was operationalized by Fried et al. in 2001, based on the presence of a critical mass of three or more core ‘‘frail’’ elements, with the core entities being weakness, poor endurance, weight loss, low physical activity, and slow gait speed [29, 12]. The latter operational definition was tested in the Cardiovascular Health Study, a sample of 4317 community-dwelling adults aged 65 years and older who lived in four communities in the United States [12]. Seven percent of community-dwelling adults aged over 65 years in this population were frail; the proportion increased steadily with age, up to 30% of those aged 80 years and older. To offer criterion validity for this definition, it was demonstrated that the presence of frailty significantly predicted disability and other adverse outcomes in older adults. Frailty predicted 3-year incidence or progression of disability in both mobility and ADLs, independent of comorbid diseases, health habits, and psychosocial characteristics [12].

In 2008, Bergman et al. extended the frailty phenotype definition using a life course approach, which incorporates biological, social, clinical, psychological, and environmental determinants. Bergman and colleagues' definition thus identified seven markers of frailty – nutrition, mobility, activity, strength, endurance, cognition, and mood [34].

2.3.2 Frailty Models

There are two broad models of frailty. The first is the Fried’s Phenotype model which describes a group of characteristics which are unintentional: *weight loss*, *reduced muscle strength*, *reduced gait speed*, *self-reported exhaustion* and *low energy expenditure* [12]. Presence of these factors was used to categorise subjects into frail (*three or more characteristics*), pre-frail (*one or two characteristics*) or not frail (*none characteristics present*). Based on this frailty model, outcomes like death, hospitalisations, falls, mobility and functional decline were assessed in three and five years’ time. The frail cohorts were significantly more likely to die or have an adverse outcome than the non-frail [12]. The model proposed by Fried and colleagues is limited by the fact that it lacks measures of cognition and mood, which improve the ability to predict adverse outcomes. However, this model is relatively easy and rapid to assess, and has shown its clinical prognostic interest in several epidemiological studies.

The second model of frailty is the Rockwood’s Cumulative Deficit model. The cumulative deficit approach to defining frailty is broader than the phenotype approach, encompassing co-morbidity and disability as well as cognitive, psychological and social factors. The potential causes are wider and include the multiple risk factors which are implicated in the various diseases and conditions. The model assumes an accumulation of deficits ranging from symptoms: *loss of hearing* or *low mood*, through signs such as *tremor*, to various diseases such as *dementia* which can occur with ageing.

In 2005, Rockwood et al. proposed the Canadian Study of Health and Aging (CSHA) Clinical Frailty Scale based on a Comprehensive Geriatric Assessment (CGA), with scores ranging from “very fit” to “severely frail” [35]. A more detailed evaluation quantifies health deficits in a Frailty Index (FI). A FI based on a CGA Frailty Index (FI-CGA) consists of a summary measure of deficit accumulation across functional, clinical, and physiological levels. Applied to a sample of 2,740 community-dwelling adults aged 65 to 102 in Canada, the FI-CGA estimated that 22.7% were frail, and that across all values of the FI, higher scores significantly increased the risk of death [36]. Indeed, using an empirically derived cut-off score, the FI-CGA identified a group of individuals with 100% mortality 19 months after the baseline assessment [37].

While the multidimensional approach of the FI-CGA more accurately reflects the multidimensional nature of frailty it difficult to apply in routine clinical practice. However, Rockwood and colleagues have suggested that deficits accumulate in a very orderly way and that frailty can be determined by counting up a smaller number of deficits with similarly robust results [38]. This model is more complete but also more complicate than de Fried's model and probably less specific for "frailty". Finally, one of the critiques of the FI-CGA model is that it does not incorporate pathophysiology.

2.3.3 Frailty components

2.3.3.1 Sarcopenia

While many clinical features have been recruited in order to define frailty, special attention has been paid for to the major determinant of physical frailty, *sarcopenia*, which is defined as the loss of skeletal muscle mass and strength that occurs with advancing age [39]. The strongest risk factor is age and, since prevalence clearly rises with age. There is also an effect of gender where the prevalence of sarcopenia in community dwelling older people is usually higher in women.

There is a growing body of evidence for beneficial interventions to address this aspect of frailty and this has been reviewed recently [40]. The benefits of exercise in older people with frailty show that home-based and group-based interventions result in improvement in both mobility and functional ability. Strength and balance training is a key component although a wide range of approaches have been employed and the optimal exercise regimen remains uncertain. The place of nutritional interventions also needs to be considered although evidence remains limited. Recommendations currently include optimising protein intake and correcting vitamin D insufficiency. A number of drug interventions have been proposed to improve muscle mass and function. Testosterone improves muscle strength but is also associated with adverse effects, particularly on the cardiovascular system. Growth hormone probably improves mass more than function. There is also interest in the idea of 'new tricks for old drugs', such as the angiotensin-converting enzyme inhibitors which appear to improve the structure and function of skeletal muscle. Currently there is not sufficient evidence for this to be translated into clinical practice. In terms of modifiable influences, the most studied is physical activity and more specifically resistance exercise, which is beneficial both in terms of preventing and treating the physical performance component of frailty. The evidence for diet is less extensive but a suboptimal protein/total calorie intake and vitamin D insufficiency have both been implicated.

On the other hand, there is emerging evidence that frailty increases in the presence of obesity particularly in the context of other unhealthy behaviors, 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 (and strength). Excess energy intake, physical inactivity, low-grade inflammation, insulin resistance and changes in hormonal milieu may lead to its development [41].

The main 2 clinical expressions of sarcopenia are low gait speed and diminished strength which are both extensively quantified for the detection of frailty. Slow walking speed (taking more than 5 seconds to walk 4m), has a fair sensitivity but only moderate specificity for identifying frailty. Grip strength (using a hand held dynamometer) may be useful in situations where it is not feasible for the patient to get up and walk [42].

2.3.3.2 Polymedication

Polymedication can be considered as one more frailty indicator [43]. In a study of 2015, the number of daily-consumed drugs was independently associated with physical frailty, and the consumption of medication for the cardiovascular system and for the blood and blood-forming organs explained part of the variance of total and physical frailty. The adverse effects of polymedication and its direct link with the level of comorbidities could explain the independent contribution of the amount of prescribed drugs to frailty prediction. Thus the added value of a simple assessment of medication was considerable, and it should be taken into account for effective identification of frailty [43].

2.3.3.3 Cognitive and Psychological aspects

Whereas physical impairment is the main hallmark of frailty, evidence suggests that other dimensions, such as 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 [44].

Cognitive and physical frailty interact: cognitive problems and dementia are more prevalent in physically frail individuals, and those with cognitive impairment are more prone to become frail. 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 [45].

There is little written in the geriatric literature about the concept of psychological frailty which encompasses cognitive, mood, and motivational components. In a parallelism to physical frailty, brain changes that are beyond normal aging, but not necessarily inclusive of disease, can result in decreased cognitive or mood resilience in the presence of modest stressors, and may eventually lead to negative health outcomes [46].

Moreover, as health deficits accumulate, a maladaptive response to the sense of self can be observed and is characterized as "frailty identity crisis". Additionally, frailty was associated with psychiatric conditions and low levels of psychological well-being, though its relation with the latter is unclear. Psychological well-being impaired by a frailty identity crisis may play an important role in defining subjective health in older adults [47]. Interestingly, maintaining a stronger sense of psychological well-being in later life seems to protect against the development of physical frailty. Future research needs to establish the mechanisms underlying these findings [48].

2.3.3.4 Social dimension

Finally, social vulnerability has been shown to correlate with frailty and mortality (85). Social factors play an important role in modulating the adverse outcomes of frailty. For example, a meta-analysis of 19 published studies showed that lower childhood socioeconomic position (SEP) was associated with reduced physical performance in late life [49]. Interestingly, social factors also appear to accumulate in a manner comparable to the way that health deficits do. 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. Yet despite strong evidence linking social factors to frailty, little is known about the interplay of molecular, clinical, and social factors, including how social stress could be expressed through epigenetic modulation or triggering of inflammatory processes throughout exposure to infectious agents [35].

2.4 Frailty Metrics

2.4.1 Frailty assessment instruments

The need for more extensive detection of frailty in older populations has led to the development of several shorter battery tools and scales in the form of short questionnaires in order to be administered in busy clinical settings by multiple health care practitioners, non-specialist physicians and even the patients themselves. The usefulness of any measure of frailty depends on the reason for which the assessment is being done. For example, an oncologist or general surgeon may wish to evaluate frailty in a patient to determine whether he or she can tolerate a specific treatment or procedure.

The first score elaborated and widely used was the Fried' clinical operational definition in 2001 [12]:

- *weight loss*: self-reported weight loss of > 4.5kg or recorded weight loss of ≥ 5% per year.
- *self-reported exhaustion*: self-reported exhaustion on Center 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.

In outpatient surgical settings, there is a lack of consensus on which tool should be used to identify frailty. Slow *Gait speed* (<0.8 m/sec) may help predict adverse outcomes, however, evidence is emerging for the use of the Edmonton Frail Scale [50]. The strengths of this tool include brevity, clinical feasibility and identification of aspects of frailty amenable to preoperative optimization. It is an easy to perform test which broadly assess function in a number of areas, including *functional dependence*, *mood*, *nutritional state* and *general health*. It is valid and reliable, and identifies the presence of frailty well, but does not give the diagnostic advantages that will occur with CGA.

The Groningen Frailty Indicator questionnaire - which is a 15 item frailty questionnaire that is suitable for postal completion. A score of > 4 indicates the possible presence of moderate-severe frailty.

The FiND questionnaire is a self-reported screening tool for detecting community-dwelling older persons with frailty syndrome in the absence of mobility disability [51]. It consists of five questions, two that are specifically targeted in identifying subjects with mobility disability and three assess components of the frailty syndrome: weight loss, exhaustion and sedentary behaviour.

Other instruments have been proposed as well, like the Gerontopole Frailty Screening Tool (GFST) which is applied by the general practitioners and contains also two items of their personal view about their patient's frailty level [52] and the G-8 scale that shows good screening properties for identifying older cancer patients who could benefit from CGA [53].

Physical performance measures such as the *Short Performance Physical Battery* (SPPB), which includes walking, balance, and chair stand tests, have also been used to assess frailty and predict negative health-related outcomes [54].

A growing body of evidence shows these instruments as able to capture the inner foundations of the frailty status beyond the mere evaluation of the physical status. Advantages of the physical performance tests are that they are extensively used in epidemiologic and clinical settings and can be performed easily and quickly, although some instrumentation and training are sometimes required. They represent extremely important screening tools for the overall health status, especially in community-dwelling and non-disabled older persons. For this reason, they may be particularly valuable for selecting subjects to enrol in interventional studies.

None of the aforementioned scales include social factors, such as *socio-economic status* (SES) and level of education, which also play important roles in the genesis and pathophysiology of frailty [55].

Since frailty is a multidimensional syndrome and frail older people so heterogeneous, a measure that captures such heterogeneity and the multiple phases of frailty has been difficult to establish. It is evident that the value of short frailty detection tools is mostly apparent in everyday clinical settings circumstances, where the lack of time and expertise do not permit a complete comprehensive geriatric assessment. Still, in case of problem detection and in order to organize management and prevention strategies for frailty, the comprehensive geriatric assessment remains the reference point up until now.

This lack of reliable and easy to apply tools to detect frailty, especially in earlier stages, corresponds to an unmet need in the field of geriatrics and gerontology, that translational research have been called to address.

2.4.2 Comprehensive Geriatric Assessment

Comprehensive geriatric assessment (CGA) and management is usually defined as a 'multidimensional diagnostic process focussed on determining a frail older person's medical, psychological and functional capability in order to develop a coordinated and integrated plan for treatment and follow-up' [56]. In this definition is reflected the global and holistic character of a clinical methodology, developed in the early 1970's, that was meant to become the cornerstone of geriatric medicine and gerontology. CGA is an analytic and synthetic procedure, can be time consuming and requires special skills and expertise. Therefore it is used as a second stage assessment for those patients identified as frail using simple and short frailty scales.

The main difference of the CGA in comparison to a typical medical evaluation is that it also incorporates the investigation of functional capacities, psychological and socio-environmental issues and quality of life aspects and often requires a multidisciplinary team approach [57]. It is a good representation of a holistic individualized healthcare approach aiming to more thoroughly explore the individual's problematic and needs, more accurately identify the potential risks and possible beneficial intervention fields and more effectively tailor a management strategy, which most of the times turns out to be not strictly medical.

Due to GCA, the clinical physician can avoid the trap or under-treatment and similarly the temptation of over-treatment in a way non cost-effective in clinical terms and unfavourable also in terms risk-real benefice balance. By pointing out what is really important for the well-being of each individual, CGA aims to safer and more effective interventions. It can be said that in the core of geriatric care, the CGA represents the model of a patient- rather than problem-centred approach.

During a standard CGA, specific elements of physical health are evaluated, like the nutritional, cognitive and emotional status, the functional capacities, the presence of pain, any vision and hearing impairments, presence of sphincter incontinence and mobility and balance disabilities. Autonomy maintenance is also a core concept for CGA and subsequent interventions. Most of them aim at the detection or the risk evaluation of several geriatric syndromes.

Because CGA is a particularly time consuming and complicated procedure, many tools have been tested and proposed in order to promote, facilitate and speed up its application in various clinical settings. Thus, well-validated tools and survey instruments for evaluating activities of daily living, hearing, fecal and urinary continence, balance, and cognition are an important part of the geriatric assessment. On the other hand, the component of clinical “intuition” and well-targeted in-depth evaluation remains valid.

Still, in order that extensive CGA results in cost-effective outcomes, it has to be well-targeted in the subpopulations that are most likely to draw the most of benefit, by excluding those who are too well (functionally independent) or too sick (terminal illness and advanced dementia) [56].

Data exist that show that CGA can improve outcomes for frail older people in various clinical settings [58]. There is also some evidence to support the use of CGA in the community setting for older subjects with frailty [59]. Benefits have also been displayed in several trials that tested CGA in the post-acute care period, for patients who have been hospitalized for many days or weeks [60, 61, 62].

In conclusion, CGA is an appreciated and effective method for evaluation, management guidance and follow up in several subgroups of older subjects and especially those in risk or clinically established frailty. Still, its requirements for time and expertise restrains its wider and “lege artis” implication.

2.5 Relation to the FrailSafe Project

Our understanding of frailty has markedly improved over the last five years, still there are many issues yet to be resolved. It has been emerged as a research priority the invention of frailty markers and the development of instruments that would be useful in various clinical settings. These tools will be relevant if they accompany effective health promotion, prevention, treatment, rehabilitation, and care interventions [27]. The FrailSafe study tempts to respond to this unmet need.

More analytically, from the clinical point of view, the FrailSafe project aims at:

- developing of hi-tech, clinically usable tools that would lead to an earlier identification of frailty or pre-frail conditions, and ultimately make feasible the application of early interventions to prevent worsening or reverse this condition components.
- establishing criteria to identify frail subjects and monitor frailty modifications.
- identifying biomarkers of frailty to improve screening, diagnosis, and prognosis of frailty in older individuals.
- contributing to the planning of health care services, by providing a practical, clinically applicable and widely understandable starting point for clinical assessment of frailty.
- identifying frail individuals, targeting them with interventions to reverse the condition or ameliorate their loss of functionality, carrying potential public health benefits.
- developing international collaborations to expedite research in this field and reach agreement in the currently controversial issues of frailty.

In order to obtain more valid information concerning frailty in older subjects, the FrailSafe system is applied on the top of the conventional CGA, yet with its added valued schematically depicted in three aspects (see Figure 2):

a) *ecological aspect*: information is obtained inside the patient's environment versus usual clinical settings.
b) *time frame*: multiple signals in real time conditions versus single shot evaluation.
c) *analysis capacity*: big data analysis, objectivity in the extrapolation versus limited data and subjective interpretation.

These aspects allow the possibility for feedback and improvement of the evaluation system itself and eventually generating more specific preventive strategies.

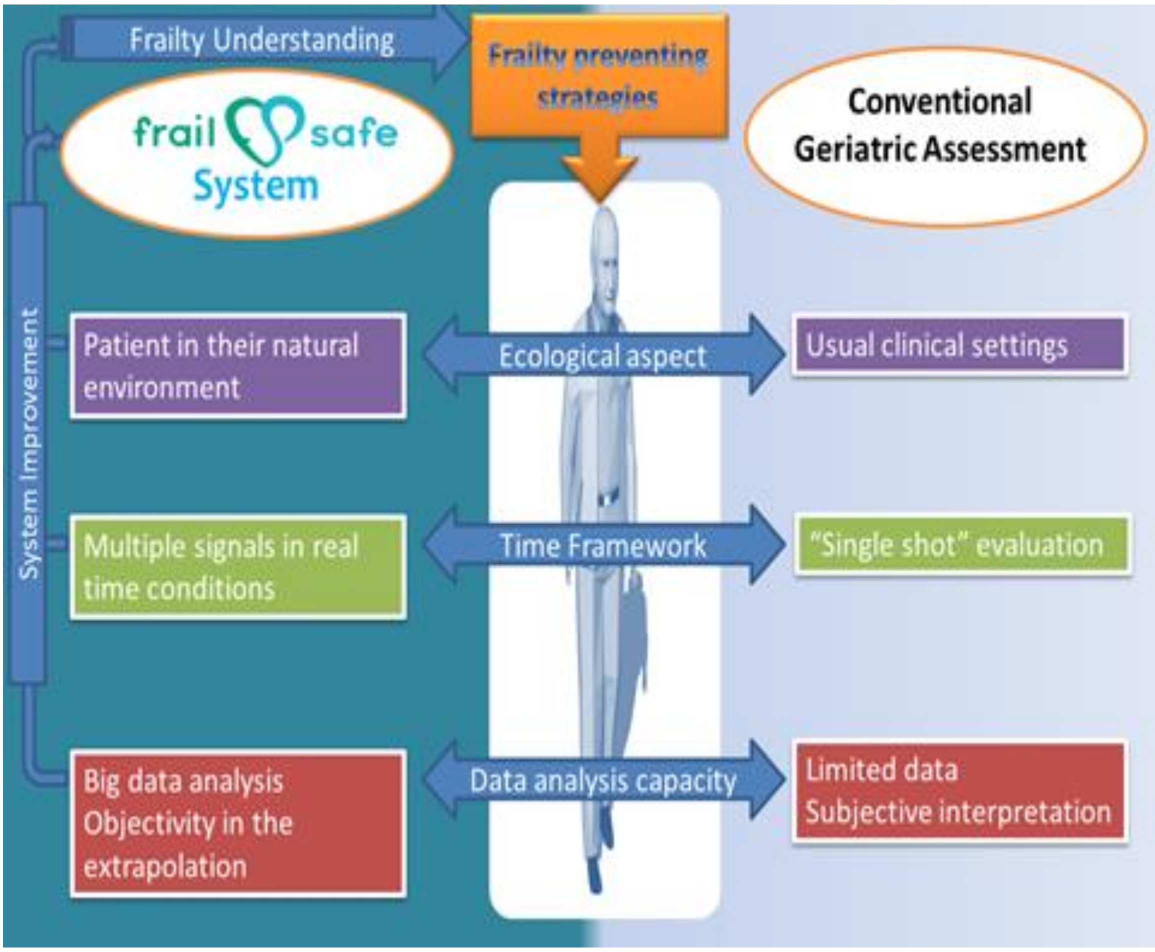

Figure 2. Frailsafe system overview.

3 SENSING SYSTEMS FOR MONITORING PHYSIOLOGICAL & BEHAVIORAL CRITICAL PARAMETERS

The core parameters which are of interest for the FrailSafe project as shown in Table 1. Those parameters can be monitored in hospital or at home, with hospital-like devices that can deliver recorded or real-time data to the hospital or to a monitoring center. These monitoring activities are usually limited in time (spot measurements), taken once a day for a few minutes or even less often.

In recent years several products have reached the market (with or without certification as medical devices) that can be used for longer periods, in order to generate a long-term collection of information and be used during normal life activities. These products, portable or wearable monitoring systems, can collect data in order to provide the users with clinical data or to analyze and classify lifestyle, fitness, sport performance or sleep quality.

As one can imagine, there are several overlaps between those two groups, and it is hard sometimes to strictly classify one device in one or the other group: the cardiac holter can be taken as an example. It is true that can be used at home during standard life, but it is necessary to go to a hospital to get it and to have a diagnosis, and there is also the need of specialized personnel (i.e. nurses) to place the electrodes correctly. Finally, no information is given directly to the users, as recorded data must be analyzed by a software own by hospitals and selected data checked by physician for final diagnosis.

As the goal of this project is medium-to-long-term monitoring that can be performed by the final user alone at home, only a quick analysis of hospital-like medical devices will be performed in the following section, and more space will be left to wearable and portable devices.

Parameter	Monitoring Frequency	Data Analysis	
		Offline	*Real-time*
Blood Pressure	Two sets of six measurements per day	✓	×
Weight	Once a day	✓	×
Strength	Once a day (plus use during serious games)	✓	×
ECG	Always	✓	×
Heart rate	Always	×	✓
Respiration signal	Always	✓	×
Respiration rate	Always	×	✓
Posture	Always	✓	✓
Activity classification	Always	✓	✓
Fine movement analysis using IMUs	Always	✓	✓

Table 1. Monitoring parameters, frequency ration and data analysis with regards to frailty.

3.1 Stationary devices

3.1.1 ECG monitors

There are many electrocardiograph devices in the market for hospital and outpatient use. They are used only on the spot (during a medical control) or in intensive care (if there is a high risk of heart attack). They are not useful for the type of monitoring requested by this project, both in terms of ease of use and of type of data collected: the level of signal analysis and self-diagnosis is very high, not focused on the need of this type of patient. The cardio holter are devices that stay in between: as written above, they are portable, but still the level of information too high for the scope of this project. Their cost starts from € 800, not including the cost of the software required for data analysis. Some portable/wearable solutions that could be of interest are described in the wearable paragraph.

3.1.2 Respiration monitors

The main device that is used in pulmonary medical checks is the spirometer. They are standard hospital and laboratory devices that, using different technical approaches (whole-body plethysmograph, pneumotachometer or fully electronic devices, as examples), allow to monitor some breathing parameters like lung volumes and maximum breath speed. These devices have different precisions, and they are commonly used to investigate pulmonary diseases, comparing spot measurements with standard parameters, and are not used for monitoring of breath rates and breathing behavior. There are some small portable devices in the market, but they are again used only in spot measurements. The real wearable ones are described below: they are more oriented in monitoring breath rates and ranges, but, even if some of them claim the possibility to measure lung volumes, it is likely that those devices must be calibrated every time before a measurement with a standard spirometer and anyway they will just provide the user with estimates.

3.1.3 Devices for fine movement analysis, reconstruction and/or rehabilitation

If the rules done at the beginning of this chapter must be strictly followed, no devices found for this application can be classified in the following section 3.2 , as none of them can be used at home by the end user alone. All solutions listed below need the presence of specialized personnel during the test to instruct the user and time of monitoring is limited to few seconds.

The best option for not-wearable systems are camera based. The most famous system is *Vicon*, a set of several cameras that uses markers (reflective spot) placed on joints to reconstruct body movement on PCs. They have several products, both hardware (cameras) and software, studied for many different applications. The cost may vary largely on the basis of selected options, in any case is always in the range of several tens of thousands of euros. Many similar products are now available on the market.

Movement reconstruction is of very high quality (with some limitations due to the positioning of the markers, that is not easy, standard and stable for all joints), but it requires a large dedicated laboratory, long time for setting any measurement and skilled technicians.

A second option is the use of several inertial measurement units (IMUs) placed all over the body or just in part of it (see Table 2): the most famous producer of this type of device is *Xsens*, but there are many other companies that are coming into this market at cheaper prices and with some slightly different approaches. In the case of Xsens, a full system is quoted at about € 30.000, but single IMUs can be purchased separately.

Some of them provide real time body position and movement reconstruction via avatar (Xsens, Synertial, ect.), while others provide quantitative figures but not in real time (Trigno), some can do both.

Company	Product	Country	Body Pos.	Application	EMG	IMUs
270 Vision	BPM Physio	UK	Wherever	Health/Fitness	-	Y
APDM	Opal	US	Wherever	Research	-	Y
Delsys	Trigno	US	Wherever	Health/Entertainment	Y	Y
DorsaVi	ViMove	Australia	Back or knees	Health	Y	Y

Heddoko	Smart Garment	Canada	Full body	-	-	Y
Noraxon	MyoMotion	US	Wherever	Health/Entertainment	-	Y
Synertial	IGS Cobra Suit	UK	Wherever	Health/Entertainment	-	Y
STT Systems	iSen	Spain	Wherever	Health/Entertainment	-	Y
Xsens	Several IMUs products	US	Full body	Health/Entertainment	-	Y

Table 2. IMUs overview.

Some of the systems above can make automatic calculations and elaborate gait analysis (see Table 3).

Company	Product	Country	Price	Body Pos.	Application	3D Acc.	IMUs	Pressure	GPS
3L Labs	Footlogger	South Korea	100.00 $	Feet	Fitness/Health	1	-	8	-
Moticon	OpenGo	Germany	1,180.00 €	Feet	Fitness/Health	1	-	13	-
Gait Up	Physilog	Switzerland	6,000.00 CHF	Feet	Health	-	Y	-	-
Kinematix	Tune	Portugal	200.00 €	Feet	Fitness	Y	-	Y	Y
Biosensics	Legsys	US	2,750.00 $	Leg bands	Health	-	Y	-	-

Table 3. Gait analysis systems overview.

To be correct, only systems with IMUs (e.g. Legsys and Physilog) provide the researcher/physician with true gait analysis (stride length and speed, gait cycles, etc.), while the other ones seems to be more fitness oriented. Legsys has already been used to classify frailty [63] (the version of the product used in that publication is the 5-sensor one, which costs US$ 5.000).

There is another product that is considered the gold standard for gait analysis without using cameras, that uses a completely different technology: GAITRite by CIR Systems (US). Full gait analysis is performed (again off line) using a sensorised walkway with pressure sensors.

3.2 Portable and wearable devices

There are three main classes of them: a group dedicated mainly to the monitoring of the heart, a second one more focused on activity tracking, included sleep analysis, and a third one on body or limb movement reconstruction; there are many systems that have overlapping features and a few with singularities.

3.2.1 Monitoring of physiological parameters

3.2.1.1 Heart rate (HR) monitors

These are the entry-level products; it just provides the user with heart rate (sometimes also energy expenditure, derived from heart rate), but not the electrocardiogram (ECG).

Table 4 lists those present on the market:

Company	Product	Country	Price	Body Pos.	Application	ECG	3D Acc.	IMUs	GPS
Garmin	Fascia Cardio Standard	Switzerland	50.00 €	Chest Strap	Fitness	-	-	-	-
Polar	H7	Finland	70.00 €	Chest Strap	Fitness	-	-	-	-
Garmin	HRM-run	Switzerland	100.00 €	Chest Strap	Fitness	-	Y	-	-
Medtronic /Zephyr	HxM Smart	US	50.00 €	Chest Strap	Fitness	Y	-	-	-
Adidas	Micoach HR Monitor	Multinational	60.00 $	Chest Strap	Fitness	-	-	-	-
Adidas	Micoach X_Cell	Multinational	70.00 $	Chest Strap	Fitness	-	Y	-	-
Wahoo Fitness	Tickr HR Monitor		50.00 $	Chest Strap	Fitness	-	-	-	-
Wahoo Fitness	Tickr X Workout Tracker		100.00 $	Chest Strap	Fitness	-	Y	-	-
4IIII	VIIIIVA	Canada	80.00 $	Chest Strap	Fitness	-	-	-	-
Decathlon	Geonaute SMART	France	40.00 €	Vest/T-shirt	Fitness	-	-	-	-
Apple	AppleWatch	US	370.00 €	Watch	Fitness/Health	Y	-	Y	-
Garmin	Forerunner 920XT	Switzerland	470.00 €	Watch	Fitness	-	Y	-	Y
Samsung	Gear2	South Korea	360.00 €	Watch	Fitness/Health	-	-	Y	-
Adidas	Smart Run	Multinational	400.00 $	Watch	Fitness	-	Y	-	Y
Polar	V800	Finland	400.00 €	Watch	Fitness	-	Y	-	Y
Garmin	VivoSmart	Switzerland	150.00 €	Watch	Fitness	-	Y	-	-
Asus	ZenWatch 2	Taiwan	180.00 €	Watch	Fitness/Lifestyle	-	-	Y	Y

Table 4: Heart rate monitions summary

All these products come with a chest strap with (usually) two fabric electrodes and an electronic device connected with two snaps. The systems without accelerometer just provide heart rate (no ECG): as all of them can be connected to a Smartphone with a dedicated app (sometimes apps are produced by third parties, like *Runtastic*[2]), they may provide other information like energy expenditure, step counter, distance, etc. using smartphone's accelerometer, GPS, etc.

The only product using a vest instead of a chest strap is the *Decathlon* one, *Kiprun Cardio*[3]: € 20 (€ 25 for a T-shirt), plus € 20 for the electronic device (*Geonaute*). The price of products in this first group is always below €/$ 100, when it is lower (like in the case above of the Decathlon product), this is due to the fact that there are strap and device only, without a watch to see signals, so you need to purchase it or to use a smartphone, when compatible. Soon after there are the second level products of both *Adidas (Micoach*[4]*)* and *Wahoo (Tickr*[5]*)*, that integrates a 3D accelerometer, with a little increase in price.

There is also a third level product, like *Garmin's and Polar's* ones (e.g. *VivoSmart*[6]), where the monitoring device is a watch that takes the HR for the wrist and can optionally integrated with a chest strap. They usually integrate also GPS and are more expensive, starting for € 150 for an entry level, but it is more likely to find a product of this group over € 400 (just two examples are listed in the table). Also *Suunto*[7] (the products of which are GPS monitors) entered this market sector (but probably the analysis from the HR is of lower quality).

Similar to this last group, but deserving a special mention for market penetration are the smart watches produced by *Apple*[8] and *Samsung*[9]: they provide the same type of information, but they can count on the tight connection with their respective smartphones and several dedicated apps. Starting prices are similar (from € 350, Asus one is cheaper: € 180). There are other products (see Table 5) that are interesting for the type of service they could offer (like the *Awatch*) but with severe limitation in use, due to battery consumption (less than 12 hours for Awatch).

As it is written below, there are some overlapping between this group of devices and those classified as activity trackers. One of the main issue is the reliability of the heart frequency: it is obviously accepted that devices using a chest strap (or a vest) are much more reliable than those tracking heart rate with an optical sensor[10].

Company	Product	Country	Price	Application	ECG	3D Acc.	IMUs	GPS
Apple	AppleWatch	US	370.00 €	Fitness/Health	Y	-	Y	-
Garmin	Forerunner 920XT	Switzerland	470.00 €	Fitness	-	Y	-	Y
Samsung	Gear2	South Korea	360.00 €	Fitness/Health	-	-	Y	-
Adidas	Smart Run	Multinational	400.00 $	Fitness	-	Y	-	Y

2 *https://www.runtastic.com/*

3 *http://www.decathlon.fr/tee-shirt-kiprun-cardio-id_8328859.html*

4 *http://www.adidas.com/us/micoach*

5 *http://eu.wahoofitness.com/devices/hr.html*

6 *https://buy.garmin.com/en-US/US/into-sports/health-fitness/vivosmart-hr/prod531166.html*

7 *https://www.suunto.com/Product-search/Products/?categories[]=12017*

8 *https://www.apple.com/watch/*

9 *http://www.samsung.com/us/mobile/wearable-tech/SM-R3810ZKAXAR*

10 *http://www.wareable.com/sport/optical-heart-rate-tech-the-experts-speak-9763*

Polar	V800	Finland	400.00 €	Fitness	-	Y	-	Y
Garmin	VivoSmart	Switzerland	150.00 €	Fitness	-	Y	-	-
Asus	ZenWatch 2	Taiwan	180.00 €	Fitness/Lifestyle	-	-	Y	Y

Table 5. Smart watches overview.

3.2.1.2 ECG and respiration monitors

Most products of this second group integrates heart with respiration and activity, using in most cases fabric electrodes for a full ECG plot (one lead), measurement of inductance for respiration and one 3D accelerometer, which some of them have also FDA/EC certification as medical devices (see Table 6):

Company	Product	Country	Price	Body Pos.	Application	FDA /EC	ECG	HR	Resp.	EMG	3D Acc.	Therm.
Medtronic Zephyr	Bioharness	US	630.00 $	Chest Strap	Fitness	-	Y	Y	Y	-	Y	-
Preventice	Bodyguardian	US	-	Adhesive Strip	Health	Y	Y	Y	Y	-	Y	-
Empatica	E4 Wristband	Italy	1,690.00 $	Wristband	Health/Lifestyle	-		Y	-	-	Y	Y
Carré Technologies	Hexoskin	Canada	400.00 $	Vest	Fitness/Lifestyle	Y	Y	Y	Y	-	Y	Y
Nuubo	nECG Minder	Spain	-	Vest	Fitness/Health	EC	3	Y	-	-	Y	-
OMSignal	OM Smart shirt		200.00 $	Vest	Fitness	-	-	Y	Y	-	Y	-
Qardio	QardioCore	US	-	Chest	Health	?	Y	Y	Y	-	Y	Y
Smartex	Wearable Wellness System	Italy	600.00 €	Vest	Fitness/Health	-	Y	Y	Y	-	Y	-
MAD Apparel	Athos	US	550.00 $	Catsuit	Fitness	-	-	Y	-	12 + 8	-	-
BTS Bioengineering	BTS Surface EMG	US	-	Leg bands	Health	-	-	-	-	Y	-	--
Gesture Logic	Leo		-	Leg strap	Fitness	-	-	Y	-	Y	Y	-

Table 6: ECG & Respiration products.

- *Hexoskin* seems to be the benchmark of this group in the fitness sector: the device is FDA/EC certified, it communicates via Bluetooth to both iPhone and Android devices and has a reasonable price. It promises to monitor not only respiration rate but also breathing volumes, which seems to be a little optimistic, taking into account that they just have a measurement of inductance. It monitors two breaths, at thorax and abdominal level. It has also a thermometer to monitor body temperature.

- *Smartex Wearable Wellness System (WWS)* is very close to Hexoskin; WWS uses a fabric piezo-resistive sensor instead of inductance for respiration, so it is again not able to give any information of breathing volumes, and has no temperature sensor. Device dimension and position is more ergonomic, instead. Both products provide customers with tools that enable personal analysis of data and integration in third party software.
- *OM Smart Shirt* is the last one of this group using a vest as sensor holder: its price is very attractive, but seems to be less professional in terms of data analysis (no ECG is visible, data are not open to third party analysis).
- *Bioharness***,** a second level product (after the HR monitor) by Zephyr, that uses again a strap (not a vest) but integrates the advanced knowledge developed for the health sector (which includes products for soldiers). Bioharness should have FDA/EC certification (to be investigated) and integrates several sensors, in order to be able to compare several signals without using a smartphone. It is the only device that integrates GPS. As Zephyr was purchased in 2014 by Covidien, which in turn was bought in February, 2015 by Medtronic, and so forming the largest medical device company of the world, their products will probably be the benchmark of wearable solutions in the medical sector.

The last three products are completely different from the group above and among themselves:

- *Bodyguardian*[11] is a certified medical device sold directly by the producer, Preventice, that sell also the medical service of prevention and control. From a technical point of view, the electronic device must be connected to a sticking plaster and then fixed on the thorax; no information is available on price and on the possibility to purchase it independently from the service. The product has a microprocessor produced by ST and has FDA certification.
- *QardioCore*[12] is a new product (still under development, not already on the market) strongly oriented to the medical market, that has been presented at Consumer Electronics Show (CES) 2014 and 2015.
- *E4 Wristband*[13] is completely different from all the other devices of this group, both in terms of technology and price. It is a watch, using photopletysmography for HR monitoring (no ECG), electrodermal activity, movement (3D accelerometer) and peripheral skin temperature. It is produced by an Italian company with liaison with the out-of-commerce QSense by Affectiva. It is difficult to position this product in a clearly way so far.
- *Nuubo* is one of the first cardiac holter that uses fabric electrodes and a vest to collect 24h 3-lead ECG signals.
- There are 3 products that have been developed for s-EMG monitoring: Gesture Logic's *Leo* is a thigh strap to be used for sport monitoring; *BTS Engineering* produces some EMG products; MAD Apparel's *Athos* is a composed by a long-

[11] *http://www.preventicesolutions.com/services/body-guardian-heart.html*

[12] https://www.getqardio.com/qardiocore-wearable-ecg-ekg-monitor-iphone/

[13] https://www.empatica.com/e4-wristband

sleeve shirt and a pair of shorts and monitors heart rate and muscle activity: there are (in the full system) 20 EMG sensors.

- Other similar products can be found on the web, but with little (if any) information of technical aspect and commercial offer; one example is *CitizenSciences's D-shirt*[14].

3.2.2 Wearable activity trackers

There are many devices (mainly bracelets) that monitor activity (and sleep). They are simpler than the watches described above, and do not monitor heart or respiration. In this group (see Table 7) there is the best seller *FitBit*[15], and also *UP*[16], *Misfit Shine*[17], *Withings's Pulse Ox*[18], etc. This group is having a great commercial success (with some big flops as well, as it happened with UP first round of commercialization) but the level of signal quality is far away from what it is required by FrailSafe requirements as well as there are big doubts on the reliability of the analysis of movement and (mainly) sleep quality they can provide the user with [64].

The fact that they just rely on one 3D accelerometer, usually placed in a watch or a bracelet, make the automatic classification of activity really difficult: some of them have found a solution in specialising in a few activities, like Atlas, that is thought to monitor and classify only the workout you do in a gym (so don't use it outside), otherwise the producer takes the risk to get many negative feedbacks in dedicated Internet *fora*.

There are already on the market some products dedicated to senior people living alone, monitoring activity thanks to a watch/bracelet with a 3D accelerometer, together with a set of beacons to monitor movement in their house and providing an automated alert if collected data show a significant change in user's behaviour. One example is Tempo, produced and distributed by Carepredict. In other cases, they are just GPS devices (like *LG Gizmopal*).

In the last years several promising products or company have closed, as a sign of the strong competition for this market; as examples that can be mentioned: *Lark, Jaybird Reign, BodyMedia.*

Company	Product	Country	Price	Body pos.	Application	HR	3D Acc.	IMUs	GPS
Adidas	Micoach Speed Cell	Multinational	70.00 $	Feet	Fitness		1		
Amiigo	Fitness Band	US	180.00 $	Bracelet	Lifestyle	Y	Y		
Atlas	Atlas WristBand	US	200.00 $	Watch	Fitness	Y		Y	
BIA	BIA Sport watch	US	270.00 $	Watch	Fitness	Y	Y		Y
Bionym	Nymi	-	100.00 $	Bracelet	Lifestyle	Y		Y	
Bragi	Dash	Germany	300.00 €	Ear	Fitness/Lifestyle	Y		Y	

[14] http://www.cityzensciences.fr/en/

[15] https://www.fitbit.com/eu

[16] https://jawbone.com/

[17] http://misfit.com/products/shine?locale=en

[18] http://www.withings.com/us/en/products/pulse

Catapult	Nanotrak	Australia	300.00 $	Wherever	Prof sport			Y	Y
Cogito	Pop	-	100.00 €	Watch	Lifestyle		Y		
DigitSole	SmartSole/Shoe	France	200.00 €	Feet	Lifestyle		1		
Epson	Pulsense PS-500	Japan	290.00 $	Watch	Fitness/Lifestyle	Y	Y		
Epson	Runsense SF-810	Japan	300.00 $	Watch	Fitness/Lifestyle	Y	Y		Y
FatigueScience	ReadyBand	Canada	-	Bracelet	Lifestyle		Y		
Fitbit	Fitbit Blaze	US	230.00 €	Bracelet	Lifestyle	Y	Y		
Fitbit	Fitbit One	US	100.00 €	Bracelet	Lifestyle		Y		
Fitbit	Fitbit Surge	US	250.00 €	Watch	Lifestyle	Y		Y	Y
Fitbit	Fitbit Zip	US	50.00 €	Clip	Lifestyle		Y		
Fitbug	Orb	UK	50.00 $	Bracelet	Lifestyle		Y		
FlyFit	FlyFit	US	120.00 $	Ankle	Fitness/Lifestyle		Y		Y
Free Wavz	Free Wavz	US	220.00 $	Ear	Fitness	Y	Y		
Gait Up	Activity monitoring	Switzerland	4,500.00 CHF	Chest	Health			Y	
Geopalz	Ibitz	US	50.00 $	Clip	Lifestyle		Y		
Healbe	Gobe	-	250.00 $	Bracelet	Fitness/Lifestyle	Y	Y		
Heapsylon	Sensoria	US	200.00 $	Vest + Socks	Fitness	Y			
Huawey	Watch	China	500.00 $	Watch	Lifestyle	Y		Y	
iFit	Act	-	30.00 $	Bracelet	Lifestyle		Y		
iFit	Vue	-	80.00 $	Bracelet	Lifestyle		Y		
iHealth	Edge	US	70.00 $	Bracelet	Lifestyle		Y		
InBody	InBody Band	US	180.00 $	Bracelet	Lifestyle	Y	Y		
Jawbone	UP Move	US	50.00 $	Bracelet	Lifestyle		Y		
Jawbone	UP3	US	130.00 $	Bracelet	Lifestyle	Y	Y		
Ki Performance	Ki Fit	UK	280.00 £	Bracelet	Lifestyle		Y		
LG	HRM Earphones	-	180.00 $	Ear	Fitness/Lifestyle	Y	Y		

LifeBeam	Smart Hat	US	100.00 $	Hat	Fitness	Y	Y		
Misfit	Shine	US	70.00 $	Watch	Fitness		Y		
Wethings	Pulse Ox	France	100.00 €	Hand/pocket	Lifestyle	Y	Y		
Wethings	Pulse Ox	France	170-200 €	Watch	Lifestyle		Y		

Table 7. Wearable activity trackers summary.

3.3 Signal processing algorithms for the real-time monitoring of informative indicators

Several experts in the fields of healthcare information and communication technologies (sensing, signal processing, wireless communication, HW/SW design) focus on developing novel mHealth systems that allow ubiquitous and personalized health monitoring of patients. Such systems are especially useful in monitoring the health condition of older people, since they often need a continuous monitoring, without having the ability to regularly visit the doctor. To this end, wireless sensor and wearable sensor technologies have proven invaluable. The authors of [65] provide a review of current practices for ECG monitoring in older adults, using wearable and wireless technologies. Current systems mostly follow the layered architecture of Figure 3, with the body sensors being in the lower layers, the small-area communication protocols in the middle layers and the large-area communication services connecting the patient to the doctors and medical centres, to the higher levels.

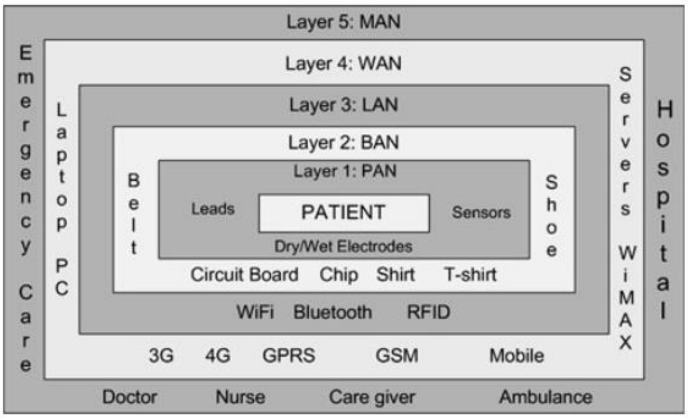

Figure 3: Layered architecture of current wearable and wireless sensor networks used in healthcare monitoring of older adults. The image is from [65].

The increase in the computational capacities of mobile devices has facilitated the use of smartphones as the aggregators of the signals originating from the multiple sensors. The authors of [66] propose an event-based middleware targeting such smartphone-based architectures. Although the healthcare sensor networks mostly rely on clinical signals acquired by wearable sensors, other types of sensors applied on the environment of the user's daily activities are also useful. An example is the work of [67], where the authors use household appliances connected to sensors in order to extract indicators of wellness of older people.

Within FrailSafe, both wearable and environmental sensors, in combination with questionnaires and games, will be used in order to monitor the older user's clinical condition, activities and cognitive state. Table 8 contains a list of the raw signals collected from a patient and meant to be used within the context of FrailSafe, for analysis and extraction of frailty metrics. These signals are acquired using sensors attached both to the patient's body, in the FrailSafe vest, and in the environment. Some of these signals are automatically acquired, without the requiring the attention of the user, apart from wearing the sensor, such as the respiration signal or the indoor coordinates. Others require the user attention, such as the weight signal, which requires the user to use the scales. There are also signals acquired through the use of questionnaires or games that the user needs to fill or play.

Table 8: Raw FrailSafe signals collected from a patient.

Clinical signals
Electrocardiogram
Heart rate
Respiration, acquired from piezoresistive sensor
Blood pressure
Arterial stiffness, acquired from mobilograph
IMUs signals
Weigh, acquired from scales
Strength, acquired using the dynamometer
Activity signals
Accelerometer signal
Steps per minute
Instability / falls signals
Posture
Indoor room location
Indoor coordinates
Outdoor coordinates
Data acquired through questionnaires/games
Indoor/Outdoor activity index
Nutrition index
Social interaction index
Cognitive state index
Freid Frailty Index

However, the common characteristic of all these signals is that they are time-based. They are continuously collected through regular (or sometimes irregular, as in the case of questionnaires and games) time intervals. The frequency of the data acquisition differs for the various sensors used. For instance, the electrocardiogram signal is sampled with a frequency of 250Hz, the respiration rate is sampled at 25Hz, while the steps per minute signal is acquired once every 15 seconds. In all cases, the signals form time series, which can be analyzed in order to extract information regarding the health condition of the user and frailty indications.

In the following sections, state-of-the-art methods will be reviewed that address two general topics:

- The problem of signal transmission from a wireless body-area-network, such as the one employed for data acquisition in FrailSafe, to the data collection unit, which can be a smartphone or a PC, in a fast and energy-efficient manner.
- The problem of pre-processing the acquired signals, in order to remove noisy components, which are always present in measured data, as well as robustly extract basic information, such as peaks and rates, from the signals.

3.3.1 Signal compression/recovery

Signal compression is necessary in order to reduce the size of data transferred from the smartphone to the central processing unit/database, as well as the transmission time, since most of the energy in the process is consumed during the transmission.

3.3.1.1 Compressed Sensing (CS)

Compressed Sensing (CS) approaches for signal compression/reconstruction offer an affordable solution for wireless sensor networks [68], by allowing the reconstructing of signals from a small number of random linear observations. Compressed sensing is invaluable for the design of body-area-network signal acquisition systems, by allowing the collection of signals at a sampling rate lower than the Nyquist and accurately reconstructing the signals, thus achieving low power consumption. Within the context of FrailSafe, CS-based compression/reconstruction schemes have benefits for the efficient tele-monitoring of frailty-related signals in wireless body area networks (WBANs). According to the initial idea of the classical CS approach, a vector $\boldsymbol{s}$ may be recovered from $\boldsymbol{y}$ by solving the problem:

$$\min_{\boldsymbol{s}} \left\{ \|\boldsymbol{s}\|_0 : \left\|\boldsymbol{y}_q - \boldsymbol{A\Psi s}\right\|_2^2 \leq \varepsilon \right\}, \tag{1}$$

where the parameter ε corresponds to the predefined error tolerance and $\|\cdot\|_2$ is the l_2-norm of the input vector, respectively. The above optimization problem is computationally intractable and cannot be used for practical applications. CS suggests replacing the l_0 quasi-norm by the convex l_1-norm and solving the following problem:

$$\min_{\boldsymbol{s}} \left\{ \|\boldsymbol{s}\|_1 : \left\|\boldsymbol{y}_q - \boldsymbol{A\Psi s}\right\|_2^2 \leq lon \right\}, \tag{2}$$

where $\|\boldsymbol{s}\|_1 = \sum_{i=1}^{N} |s_i|$. Lagrange relaxation allows us to efficiently approximate the solution of the aforementioned problem by solving the problem:

$$\hat{\boldsymbol{s}}_L \coloneqq \arg\min_{\boldsymbol{s}} \left\|\boldsymbol{y}_q - \boldsymbol{A\Psi s}\right\|_2^2 + \lambda \|\boldsymbol{s}\|_1, \tag{3}$$

where λ is a penalty parameter that can be tuned, to trade off the value of the ordinary least square error $\|\boldsymbol{y} - \boldsymbol{A\Psi s}\|_2^2$ for the number of the non-zero entries (degree of sparsity) in $\boldsymbol{s}$. Algorithmically, the aforementioned convex optimization problem in Eq. (3), known as *LASSO* problem, can be tackled by any generic second-order cone program (SOCP) solver. The original signal in the time domain can be reconstructed by computing $\widehat{\boldsymbol{x}}_L = \boldsymbol{\Psi}\widehat{\boldsymbol{s}}_L$.

Recent works have developed over this basic idea, in order to achieve higher compression rate and recovery accuracy. The authors of [69] use compressed sensing to design a continuous biomedical signal acquisition system. They further exploit the inherent group sparsity structure of many biomedical signals in order to group their components in a fusion center (Figure 4). Using this group sparsity improves the signal recovery accuracy.

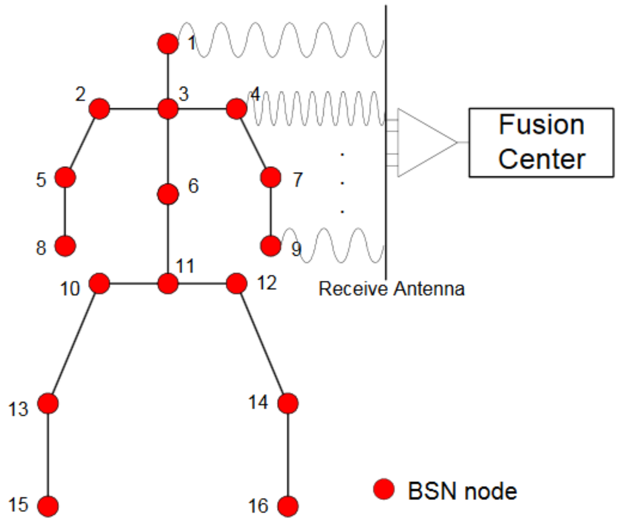

Figure 4: The biomedical signal acquisition system of [69]. The image is from [69].

In the work of [70], the compression rate and reconstruction accuracy of compressed sensing techniques are improved through the use of wavelet representations of the signal. Being applied for ECG signals, this method uses prior information about the wavelet coefficient structure and their dependencies across different scales and incorporates it into the reconstruction algorithm. Figure 5 depicts the reconstruction of an example input signal, using the method of [70].

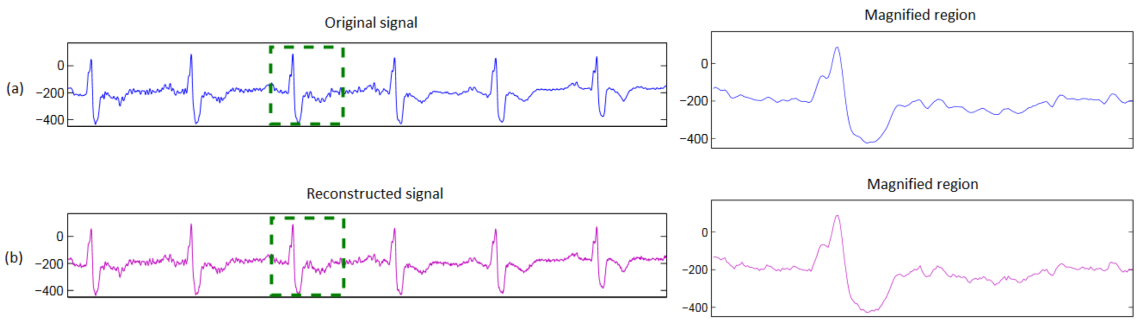

Figure 5: Reconstruction of an example signal using the method of [70]. (a) The original signal, to the left, and the magnification of the dashed area, to the right. (b) The reconstructed signal, to the left, and the magnification of the dashed area, to the right. The images are from [70].

The work of [71] has addressed the problem of compression of more complex signals, which do not exhibit sparsity structure, such as Electroencephalogram (EEG) signals. EEG signals are non-sparse both in the time domain and in transformed domains, such as the wavelet one. In such cases, the reconstruction quality is lower compared to sparse signals. The authors of [71] make use of Block Sparse Bayesian Learning (BSBL) [72] [73] in order to address this issue. BSBL assumes that the input signal can be organized into a concatenation of non-overlapping blocks, exploits the intra-block correlation in order to improve recovery performance (see Figure 6).

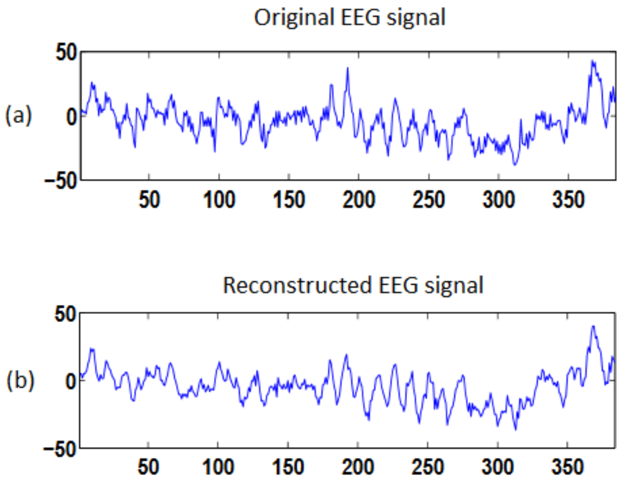

Figure 6: Reconstruction of an example EEG signal using the BSBL-based compressed sensing method of [71]. The images are from [71].

3.3.2 Signal analysis

After the sensor signals are recovered from their compressed representations, they can be analyzed, using time series analysis and knowledge discovery algorithms, such as those described below, in Section 4.2 . However, before they can be efficiently analyzed, these signals often need a pre-processing step, in order to remove any noise and extract basic signal properties, such as peaks and principal rates. This section reviews common techniques for noise removal, peak detection and rate extraction. After the signal has been processed using such techniques, it can be provided as input to more sophisticated algorithms of knowledge extraction.

3.3.2.1 Signal de-noising

Signals acquired from sensors such as those used in FrailSafe are usually corrupted by noise due to powerline interference, muscle movements, etc. This makes the application of signal de-noising techniques necessary, prior to the analysis of the signal and information extraction.

Noise usually adds high frequency components to the original signal, therefore a common technique for noise removal is the application of a low-pass filter to the noisy signal. The filter cuts the high-frequency components of the noise, allowing only the original signal to pass through. An example of this technique can be seen in Figure 7.

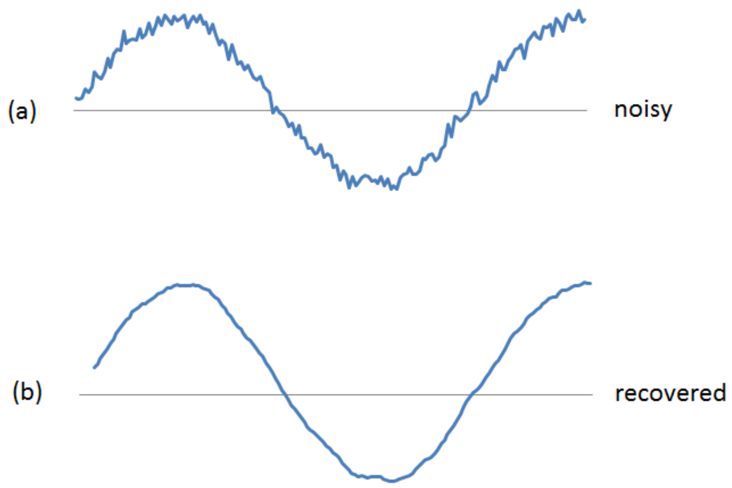

Figure 7: Signal de-noising using a low-pass filter. (a) The noisy signal. (b) The recovered signal, after the application of the low-pass filter.

However, smoothing the original signal with a low-pass filter can also lead to the removal of fine details of the original signal, which may be essential, especially in medical applications [74]. A different approach, which is able to capture fine details of the original signal, is the use of wavelets. The use of a low-pass filter is equivalent to transforming the noisy signal in the frequency domain and truncating the high frequencies above a specified threshold. The advantage of using wavelets is that the transformation does not consider only frequencies, but also the position of the various signal frequencies in time. The wavelet transform results in a set of coefficients at various scales. As seen in Figure 8, the large values of the high frequency coefficients occur in the noisy parts of the signal, thus removing them is an effective method for signal de-noising.

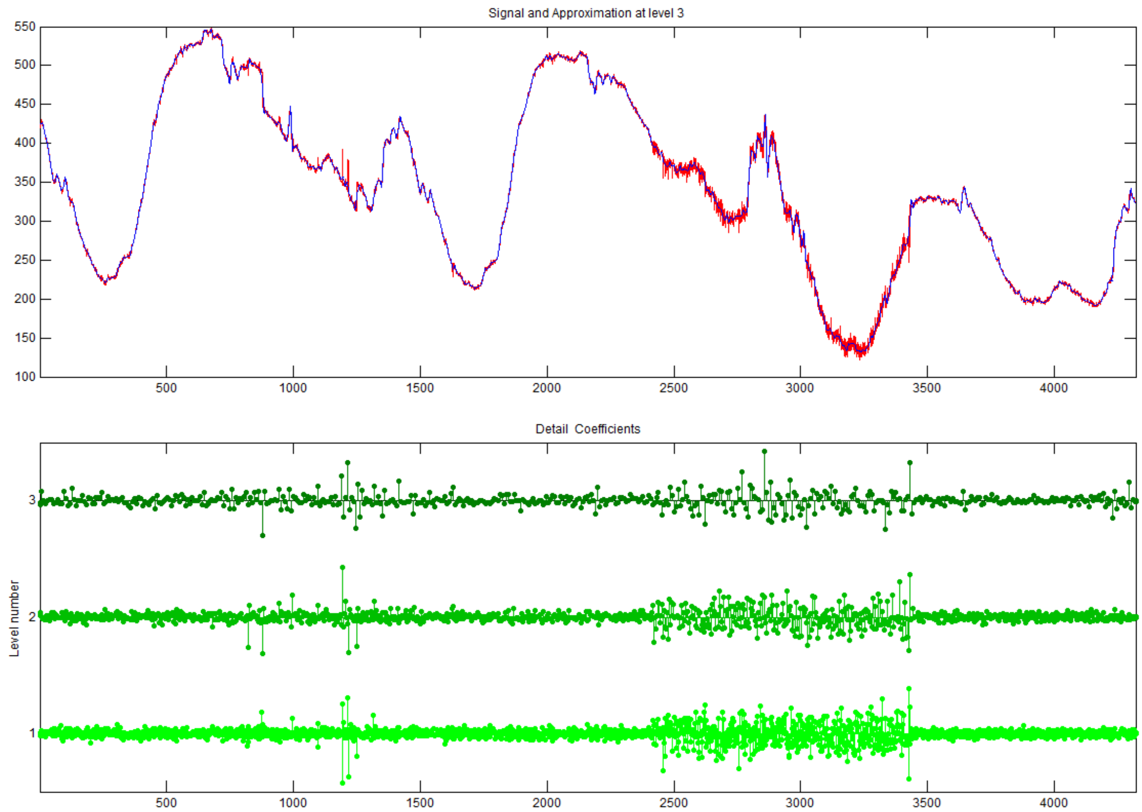

Figure 8: Example of wavelet-based signal denoising. The top plot shows the noisy signal (red), along with the de-noised approximation (blue). The bottom plot shows the amplitude of the high-frequency wavelet coefficients. It can be observed that the largest amplitudes occur at the noisy parts of the signal. The image is from [74].

Especially in ECG signals, research has been directed towards such methods for removing noise while preserving the fine details of the signal. The authors of [75] make use of the Nonlocal means (NLM) denoising method, used in image denoising, The estimation of a signal sample is computed as the weighted sum of other samples of the signal that are similar, independently of their position in the signal. This method has the advantage of utilizing the redundancies existing in the signal, since the ECG signal, similar to images, tends to have parts of similar form throughout the whole signal. This makes the estimation able to better preserve the peaks, rather than using a low-pass filtering technique. Figure 9 illustrates the application of the NLM method on a noisy input signal. The authors of [76] extend this method by considering blocks around each sample, in order to exploit the similarities in local neighbourhoods. Furthermore, the acquired similar blocks are collected into 2D matrices, which are de-noised using 2D Discrete Wavelet Transform de-noising (see Figure 10).

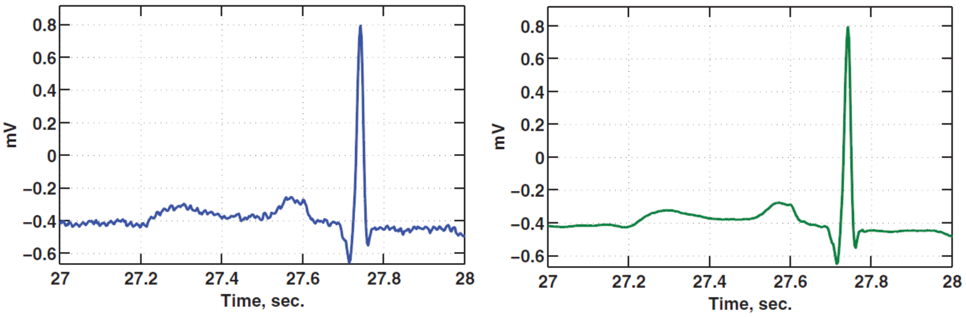

Figure 9: Example of ECG signal de-noising, with the NLM method of [75]. The left image shows the noisy input signal, while the right image depicts the de-noised signal. The image is from [75].

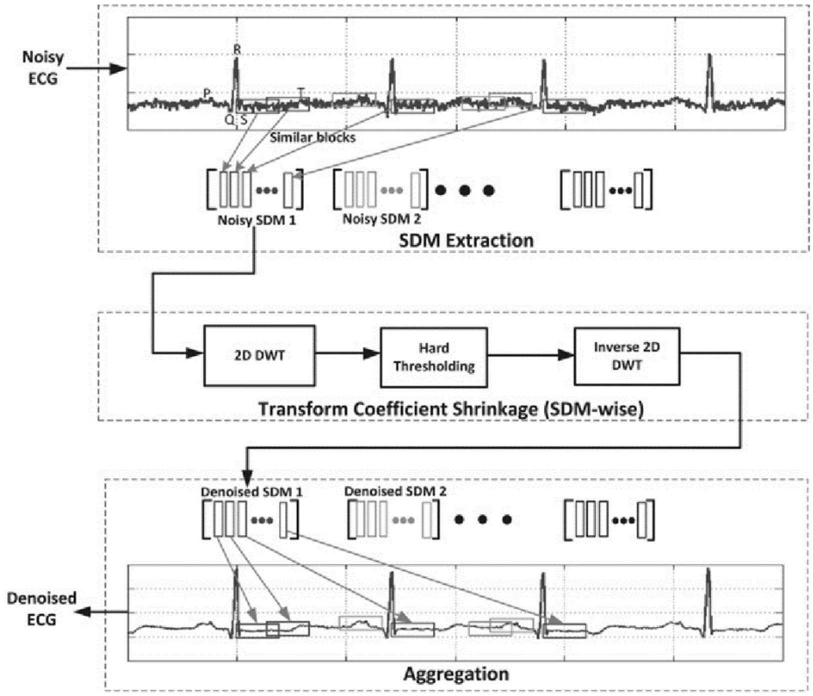

Figure 10: The ECG signal de-noising method of [76]. The image is from [76].

3.3.2.2 Peak detection

Detecting peaks in a signal is crucial in medical applications, since the peaks can be used to compute e.g. pulse rates, respiratory rates, peak amplitudes, etc. The simplest method for peak detection is the introduction of a threshold and the consideration of a peak as the time that the signal exceeds the threshold value. However, ambient noise, disturbances or signal amplitude variation during the signal acquisition process render peak detection a non-trivial task.

A first attempt at removing the influence of amplitude variation is the consideration of the signal derivative, instead of the absolute signal value, for peak detection. Irrespectively of the signal's amplitude, a peak usually occurs when the signal abruptly changes its amplitude from a low to a high value. Derivative-based peak detection considers the rate of change of the signal and records a peak at a zero-crossing point of the derivative, only after the latter exceeds a threshold value. In this manner, only abrupt signal changes are denoted as peaks. At the same time, the absolute amplitude of the signal does not greatly affect the position of the peak. Figure 11 illustrates an example of this method.

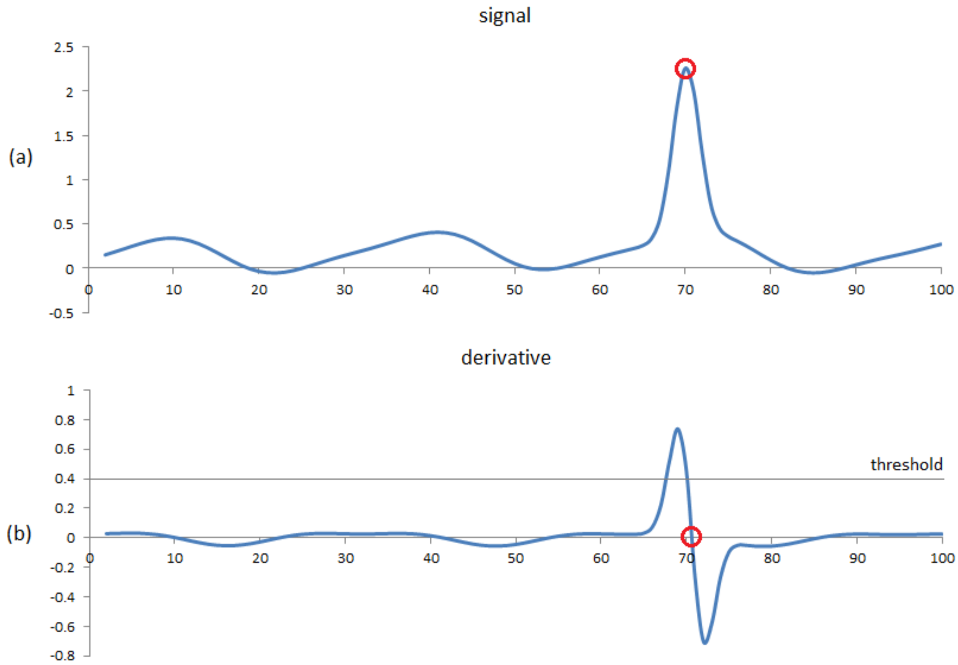

Figure 11: An example of derivative-based peak detection. (a) The input signal. (b) The derivative of the signal. The solid horizontal line denotes the threshold value. After the derivative crosses the threshold value, the next zero crossing denotes the original signal's peak.

Complex medical signals, such as ECG signals, are challenging for peak detection, due to the often non-stationary form of the peak, in addition to measurement noise. The authors of [77] have considered a multi-stage procedure, in order to accurately detect peaks in ECG signals. First, the signal is de-noised using a band-pass filter and intensified, using first-order differentiation. Then, a non-linear transformation is applied, in order to produce positive peaks, regardless of the polarity of the input signal. The Shannon energy envelope has been used as the non-linear transformation, since it achieves small difference in amplitude between successive peaks, as well as reducing the effect of low-value noise components. After this pre-processing, the actual peak detection is performed using the Hilbert transformation of the energy envelope, and correcting false negatives, caused due to the odd symmetry of the transformation, by subtracting the output of a moving average filter. The peaks are detected at the positive zero-crossing points (negative to positive transitions) of the corrected Hilbert transformation. Although the existence of peaks is correctly detected, the time instances of the peaks differ slightly from the times of the true peaks. The last step of the method is to correct the times of the peaks by searching the largest amplitude within a small area around the detected peak time, in the original signal. Figure 12 demonstrates the various stages of the method for an example signal.

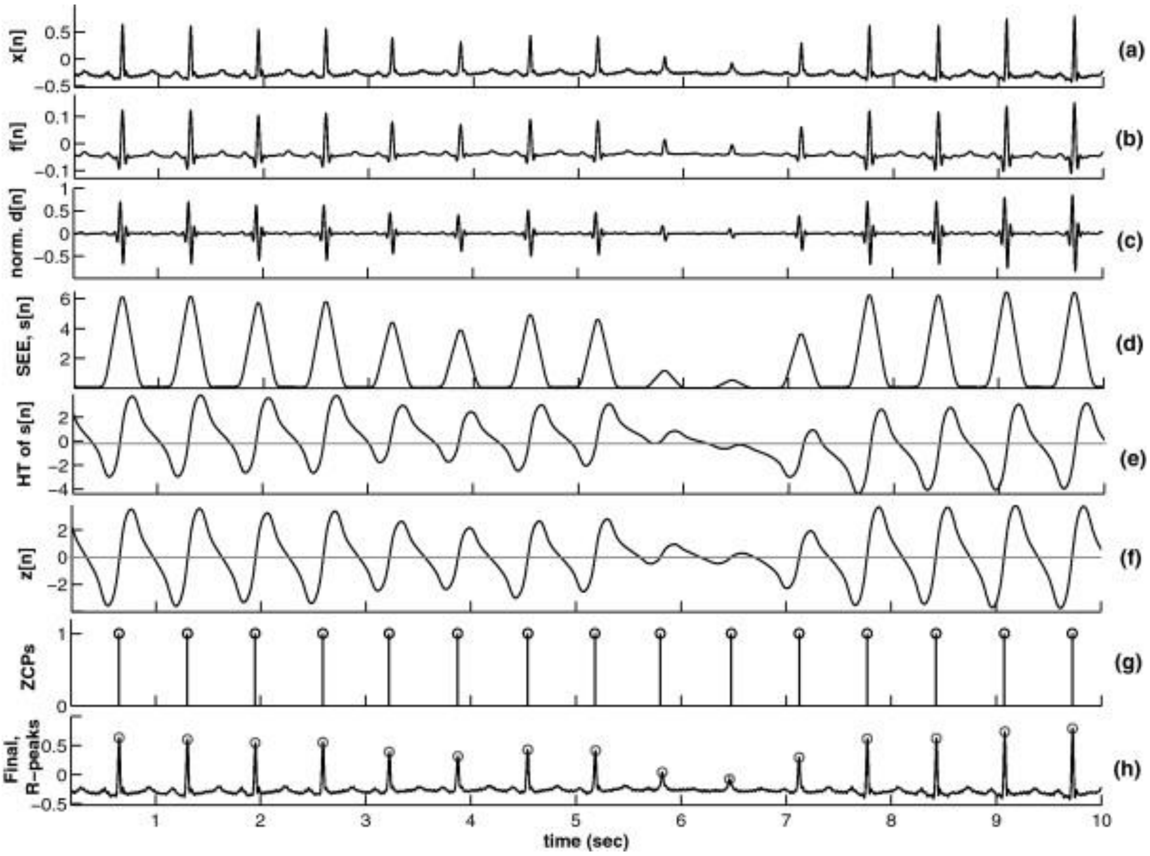

Figure 12: An example of the multi-stage peak detection method of [77]. (a) The input signal. (b) The output of the bandpass filter. (c) The output of the differentiation. (d) The Shannon energy envelope estimator. (e) The output of the Hilbert transformation. (f) The output of the correction using a moving average. (g) The output of positive zero-crossing point detector. (h) The final output of the peak detector, after the time correction. Image is from [77].

A different approach to peak detection is to use supervision information, with the use of proper peak features, in order to train a peak detector. The authors of [78] compare various peak detection models that follow the same underlying principles: First, candidate peaks are found in the signal, using very rough peak detection, such as finding regions where the signal has a large value between two small values. Then, a set of characteristic points on a candidate peak are considered, as depicted in Figure 13, namely the Peak Point (PP), the first and second valley points (VP1 and VP2), the first and second half points (HP1 and HP2), the first and second turning points (TP1 and TP2), and the peak point of the moving average curve of the signal (MAC(PP)). These points are used to define a set of peak-describing features, which will be used to train the peak detector. In total, the methods reviewed by [78] define the following features:

- *Valley-to-peak amplitude at the first half of the wave*
- *Valley-to-peak amplitude at the second half of the wave*
- *Turning point amplitude at the first half of the wave*
- *Turning point amplitude at the second half of the wave*
- *Moving average amplitude*
- *Peak width*
- *First half wave width*
- *Second half wave width*
- *Turning point width*

- *Half point width*
- *Peak slope at the first half wave*
- *Peak slope at the second half wave*
- *Turning point slope at the first half of the wave*
- *Turning point slope at the second half of the wave*

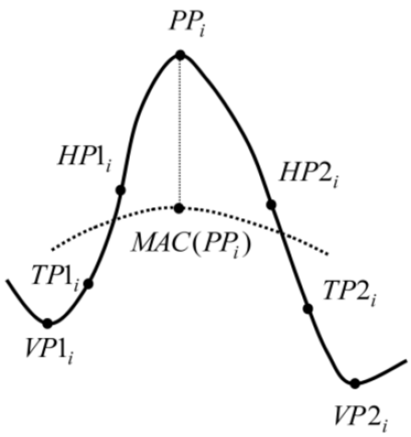

Figure 13: Characteristic points of a candidate peak, used for feature extraction in the methods reviewed by [78].

These features are extracted from peak and non-peak training candidate points, in order to train a rule-based classifier. The output of the classifier is a set of thresholds for the various features. If all the considered features of a test candidate point exceed the learned threshold values, the test point is classified as a peak point.

3.3.2.3 Rate extraction

Several types of medical or activity signals of importance in FrailSafe, such as heart and respiratory signals, or step signals, are periodic in nature. The principal rate appearing in these signals is an important characteristic of the patient's health condition. In order to extract the prominent rate from an input signal, two different approaches may be applied:

- *execution of a phase onset algorithm in the time domain*
- *use of a time frequency representation* (TFR)

In order to estimate the phase onset, the input signal is inverted and the corresponding local maxima are automatically detected. In case the input signal varies significantly with time, as e.g. an audio signal recording the patient's breath, it is best to pre-process it by considering an envelope function, which transforms it to a positive function in time representing some notion of energy of the signal. A common envelope function is the Shannon entropy. The Shannon entropy (SE) of a random signal with probability density function p is:

$$SE(p) = -\sum_{i=1}^{N} p_i log p_i,$$

where N is the number of possible signal values. The Shannon entropy of a signal can be computed within a small time window, which moves ahead with time, so that the whole signal is covered and SE is computed for each time instance. The pdf p can be estimated either by using the signal values histogram or by using the Parzen-window density estimation method with a Gaussian Kernel [79] [80]. Figure 14 shows an example of respiratory rate phase onset detection using the breath sounds acquired using a sound recorder, e.g. one contained in a smartphone. The solid red lines indicate the breath-phase onsets detected using the SE signal. Dashed blue lines indicate the phase onsets detected using only the information from the acquired breath sounds.

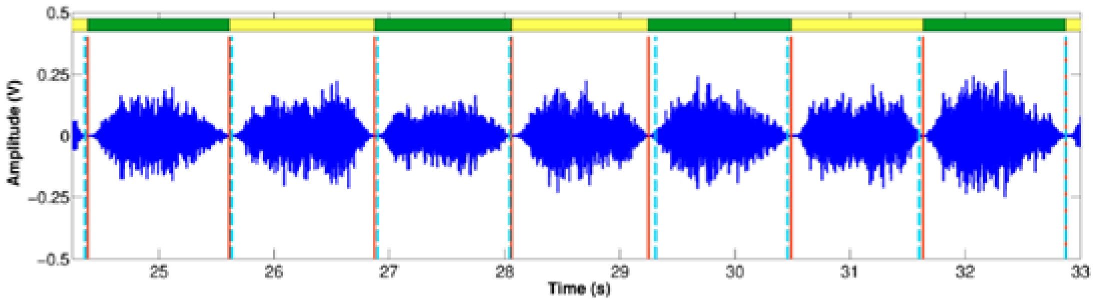

Figure 14: Example of the phase onset rate detection algorithm.

However, the TFR can lead to more accurate results and allows the determination of which frequencies of a signal under study are present at a certain time. This is useful when analyzing signals whose frequency content varies with time, as e.g. is the case for the respiratory rate. A widely-used TFR is the spectrogram (SP), given by the magnitude of the short time Fourier transform (STFT) [81] [82]. Figure 15 shows the spectrogram of a SE signal, where the main frequency content is located at twice the value of the breathing frequency, since SE has two lobes for each breathing cycle.

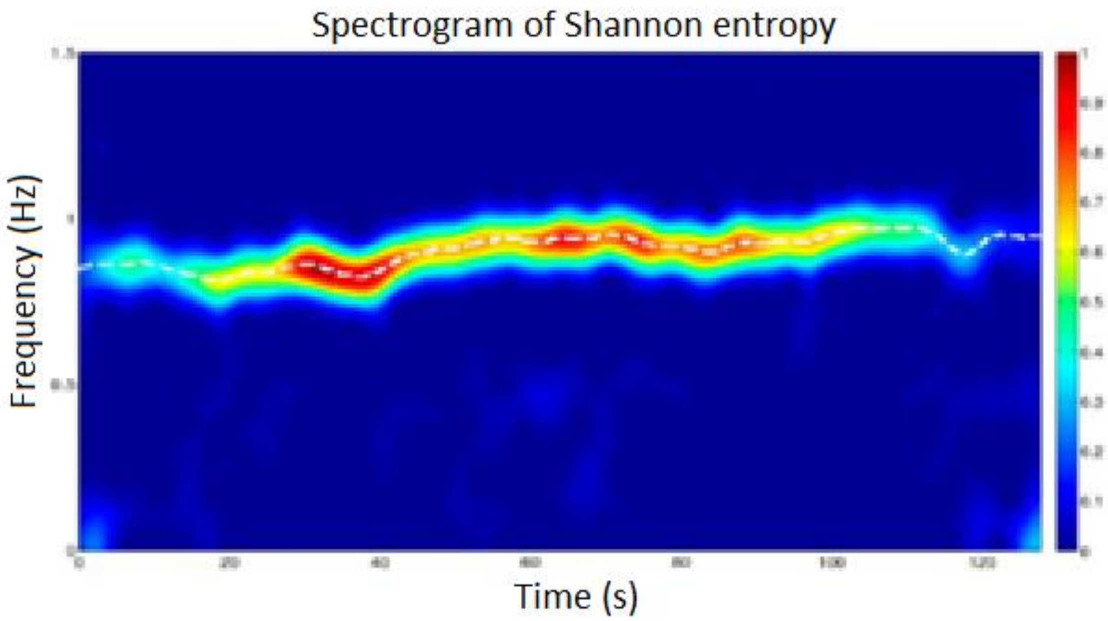

Figure 15: Example of a TFR by computing the spectrogram of an input signal.

4 PATIENT MODELING AND DATA MANAGEMENT & PROCESSING

Static and dynamic patient data management is an integral part of any medical monitoring system. The efficient storage, organization and manipulation of the main variables and parameters of the patient models, together with enhanced retrieval, mining and monitoring capabilities are considered as basic functionalities. First, Section 4.1 presents how virtual user modeling research, focusing on several disabilities, has attempted to address critical issues of human-computer interaction through a large number of analytic, usability-oriented approaches by providing patients and caregivers with interface and tools fitting to their specific needs. Second, Section 4.2 provides several state-of-the-art approaches that offer efficient storage, querying as well as spatiotemporal analysis and mining functionalities of mainly streaming multidimensional and multimodal time series data.

4.1 Patient model representation and existing EHR records

User modeling is the subdivision of human-computer-interaction (HCI) research field which describes the process of building up and modifying a conceptual understanding of the user [83]. The goal of user modeling 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 [84]. 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) [85]. 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. Throughout the years, extensive research has been conducted and introduced in the literature by exploiting the field of ontology design [86].

Though a wide variety of design patterns have been introduced, a mixture of them is commonly applied. These can be discriminated along the following four dimensions: (i) user type, (ii) gathering approach, (iii) time-dependency data and (iv) updating method. More specifically, the model representation may be tailored either to a *specific user* or to a *user group* designed to cover the majority of users with the maximum accuracy. The modeling system may acquire information (also known as *user profiling*) explicitly by means of a user-completed questionnaire or implicitly, by observing user actions and making inferences based on the stored knowledge. User model may depend on the time sensitivity of the acquired information since it may include from highly specific information (*short-term*) to more general information (*long-term*) data. Finally, user models can be divided by their update strategy to *static*, where the main data is gathered once and normally not changed again; and *dynamic*, which allow a more up-to-date representation of user's characteristics.

A significant effort has been performed the latest few years in the European Union (EU) to develop virtual user models, focusing on several user characteristics, in such a form that would enable their direct simulation, automated or semi-automated, in a variate of interactive scenario platforms. *VERITAS* [19] in collaboration with three other FP7 projects, namely *VICON*[20], *MyUI*[21], and *GUIDE*[22] have come up, following suggestions of the EC, to a formal Extensible Markup Language (XML) and Web Ontology Language (OWL) representation of patient models of people with disabilities, chronic

[19] *http://veritas-project.eu*

[20] *http://vicon-project.eu/*

[21] *http://myui.eu/*

[22] *http://guide-project.eu*

conditions and functional limitations, that is currently discussed for potential standardization in the W3C Model based User Interface body. Actually, the VERITAS project developed an open library of various categories of virtual user models, including cognitive, physical, psychological, behavioral and AR/VR models, covering a wide range of population groups and especially focusing on groups in risk of exclusion, e.g. older people, people with disability (vision, hearing, speech, motor), people with co-existent condition, etc (see Section 4.1.1). Relevant, the MyUI and GUIDE projects developed virtual user models that aim mainly to be accurate user profiles for interface adaptation and finally the *VAALID*[23] project developed user models of older people.

As the medical systems are continuously enhanced with modern information technologies, detailed clinical models are becoming a crucial component of healthcare [87] and they are holding the promise to encapsulate the majority of health factors in order to be used for the personalization of healthcare and therefore for the optimization of its results and efficiency. *Electronic Health Records* (EHR) [88] can be considered a specific case of patient models where the contained medical parameters are primary used for monitoring by healthcare personnel and sharing across different health care settings without any consideration for automated processing and analysis. EHR is an evolving concept defined as an explicit representation of a much wider spectrum of information of individual patients or populations including from general personal characteristics to a multitude of medical information (geometric, kinematic, physical, behavioral and cognitive), which are utilised for the personalised annotation of the raw measurements and the automated extraction of valuable conclusions related to the health condition of the patient or population [89]. Furthermore, personalised 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. However, it is often difficult to have a common format or even definition of patient model due to the wide range of users and applications. While numerous solution attempts have introduced many standards and specifications, such as *Edifact, HL7v2, DICOM, HL7v3, HL7 CDA, EN/ISO13606, ASTM CCR, SNOMED CT, ICDx, OMG Corbamed* and *HDTF (RLUS, EIS, CTS2)*, and more recently *HL7 FHIR* (including many implementation technologies, e.g. free/open *FreeMed, GnuMed, openMRS, Harvard SMART*; and of course commercial products and in-house systems, none of these are likely to solve the problem on their own. Merging of already existing public healthcare databases is a common software challenge (attempts have been far from successful since the costs of trying to integrate disparate standards as well as systems outweighed the benefits), but can be considered as a key benefit that can improve healthcare delivery [90]. Contrary to the aforementioned standards, *openEHR's* technical deliverable is a coherent, self-consistent platform and clinical models that work with it. It provides ways to import and export data based on other standards but always guarantees consistent semantics internally. openEHR[24] works closely with classic standards groups, including ISO 13606, HL7, OMG and CEN, and in fact provides one of the best ways to safely integrate many of the standards issued by these organisations.

The essential outcome of the openEHR approach is systems and tools for computing with health information at a semantic level, thus enabling true analytic functions like decision support, and research querying (see Section 4.1.2). There are some key benefits to openEHR's approach[25]. Firstly, it is now possible to build an EHR repository independently of content specifications. In other words, your EHR system doesn't need

[23] *www.vaalid-project.org/*

[24] *http://www.openehr.org/*

[25] *http://www.openehr.org/resources/white_paper_docs/openEHR_vendor_independent_platform.pdf*

to know a priori about any of the clinical data it will process, such as vital signs, diagnoses or orders. Models for data sets and forms are also developed separately, and user interfaces (UI) form components are generated from these definitions. This enables a new generation of EHR systems that routinely adapts to new requirements - because that's how the architecture is designed in the first place. Secondly, building software is now very different. Significant parts of the software are now generated by tools from the templates, reducing the amount of work to do, and greatly improving semantic traceability. Components and systems conforming to openEHR are 'open' in terms of data, models and APIs. They share the key openEHR innovation of adaptability, due to the archetypes being external to the software, and significant parts of the software being machine-derived from the archetypes. Strategically, the openEHR approach enables a platform-based e-health software market, in which vendors and developers of back-end and front-end solutions interface via standardised information models, content models, terminologies and service interfaces. This gives procurement stakeholders' new choices, enabling them to: avoid product and vendor lock-in; retain ownership of the data for secondary use; let their clinical experts be directly involved in solution development, via archetype authoring; and finally allows application developers to concentrate on their applications, and simply plug in to a reliable back-end.

In our case, systems for the older people and people with disabilities has to be adaptive (its behaviour can change in response to a person's actions and environment) and personalized (its behaviour can be tailored to the user's needs) [91]. According to these features, FrailSafe has to adapt, not only to the user's actions and environment, but also to their behaviour and frame of mind. A context-sensitive system should reconfigure dynamically to accommodate the needs of users, taking into account a wide range of users and context or behaviour situations. This user-centred functioning of these systems has to be supported by an adequate user model. The intelligence and interface of the system have to be aware of the user abilities and limitations to interact with the person properly. The user model must include information about the person's cognitive level, sensorial and physical disabilities. The immediate option could be achieved through a very meticulous model, fully parameterizing the person; however, this could be difficult to use in practice. Identifying and modeling all the impairments of each disabled patient to personalize medical operations is a challenging task because severely disabled patients can be affected by many different and unrelated conditions which are not taken into account by generic disability stereotypes [92]. Moreover, current EHR standards do not support the detailed specification of disabilities. However, starting from scratch without relying on any standard such as International Classification of Diseases (ICD)[26] and International Classification of Functioning, Disability and Health (ICF)[27] (see Section 4.1.3), makes it much more difficult to propose a patient user profile as well as having it adopted by clinicians [93].

Building and implementing Frailsafe's health informatics application system requires broad-level understanding of healthcare standards, coding systems, and standard frameworks. Hence for using, developing, and promoting any health informatics application, it is imperative to study and evaluate existing material on past and ongoing work in these areas. The following section provides fundamental insights of the user modeling functional requirements from various diverse domains including structural, data content and exchange standards as well as classification and services.

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[26] *http://www.who.int/classifications/icd/en/*

[27] *http://www.who.int/classifications/icf/en/*

4.1.1 VERITAS

VERITAS aims to develop, validate and assess an open framework for built-in accessibility support at all stages of ICT and non-ICT product development, including specification, design, development and testing based on the virtual user concept. The goal is to introduce simulation-based and VR testing at all stages of product design and development into the automotive, smart living spaces, workplace, infotainment and personal healthcare applications areas (see Figure 16). VERITAS aims to ensure that future products and services are being systematically designed for all people including those with *disabilities*, *functional limitations* as well as *older people* by capturing the personal preferences and interaction-related parameters of the people and mapping them to dynamic virtual user models. Delivering to product/software developers generic instructions - embedded in an empowering virtual reality platform, for exploring new concepts, designing new interfaces and testing interactive prototypes that will inherit universal accessibility features, including compatibility with established assistive technologies is VERITAS' ultimate goal. The main VERITAS innovation lies in the fact that, even if there have been some limited and isolated attempts to support accessibility testing of novel products and applications, there is a clear lack of a holistic framework that supports comprehensively virtual user modeling, simulation and testing at all development stages and realistic/immersive experience of the simulation.

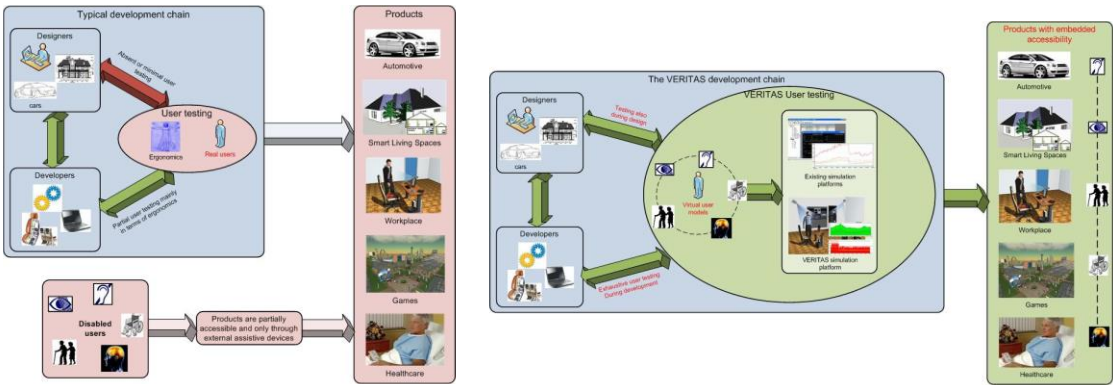

Figure 16: Typical development chain (left) before and (right) after VERITAS.

More specifically, VERITAS aims at creating new tools and methods that facilitate and streamline the process of creation, design, construction and seamless deployment of accessible technological solutions and services for persons with disabilities in various daily life environments. The user models are generated based on the analysis of user needs, existing models (physical, cognitive, behavioural and psychological), guidelines, standards, methodologies and existing practices but also based on a multisensorial platform that will sense the needs of real users with disabilities by measuring their behaviour in simulated environments.

The VERITAS user modelling methodology is being built based on four major building blocks following a top-down approach (see Figure 17):

1a. *Abstract User Models* refer to a high level description of potential users, initially formed by examining the current state-of-the-art, existing standards and guidelines related to several disabilities via ontologies and are broken down according to the disability category, i.e. cognitive user models, physical user models, behavioural and psychological user models.

1b. *Task Models* reflect to the actions that are systematically performed by the users in the context of an application scenario collection. They follow a hierarchical structure from high level tasks to low-level primitive tasks.

2. *Generic Virtual User Models* refer to a specific category of virtual users and can be comprised from one or more Abstract User Models. They also include description on how the specific disabilities affect the execution of specific tasks (primitive or not) that are described in the task models.
3. *Virtual User Models* are instances of the Generic Virtual User Models which one of one describe a specific virtual user with specific accessibility evaluation needs and requirements.

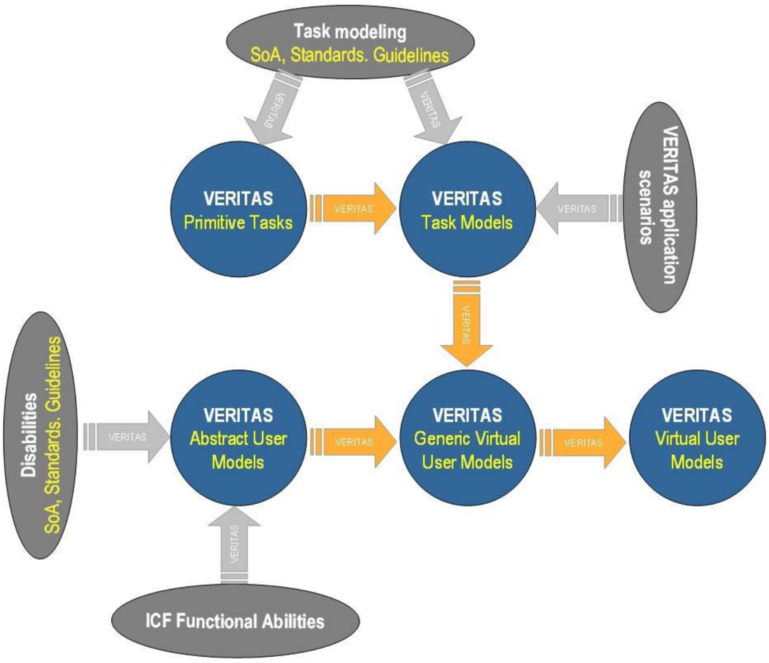

Figure 17: VERITAS User/Task Modeling Methodology.

4.1.2 OpenEHR

The openEHR approach is multi-level, single source modelling within a service-oriented software architecture, in which models built by domain experts are in their own layer (see Figure 18. (left)). It is delineated by an open set of standard specifications [94] that describes the management and storage, retrieval and exchange of health data, while ensuring universal interoperability among all forms of electronic data (more specifically EHRs). The abstract specifications consist of the *Reference Model* (RM), the *Service Model* (SM) and *Archetype Model* (AM). The first two correspond to the ISO RM/ODP[28] information and computational viewpoints respectively. The latter formalises the bridge between information models and knowledge resources.

[28] *https://en.wikipedia.org/wiki/RM-ODP*

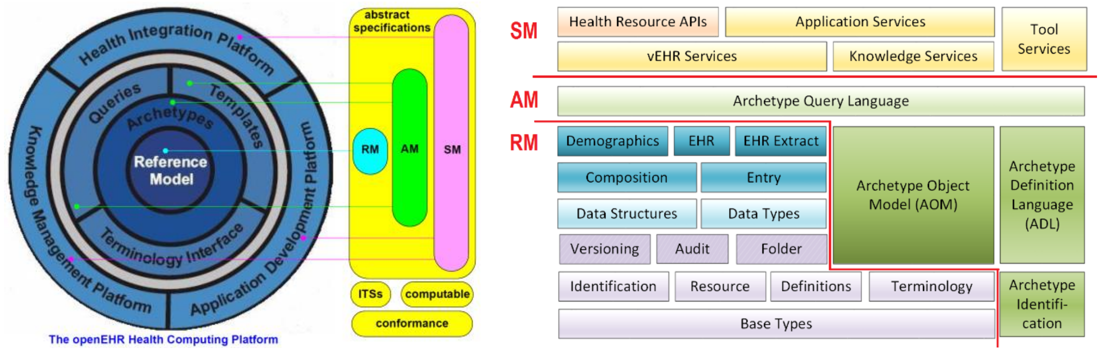

Figure 18: Detailed overview of the openEHR model layers (left) and corresponding packages (right).

More specifically, the heart of the openEHR framework is a very stable information *reference* model that defines the logical structures of EHR and demographic data. To remove the need for modelling the same data point more than once, the next model level consists of the *archetypes*; a library of data points/data groups that are independent of particular use. The international library of openEHR archetypes currently contains about 500 archetypes, or 6,500 data points. Another advantage is that these archetypes can be modelled by clinical professionals or health informatics experts, by using the archetype model specification and tools for their authoring and editing, without any technological knowledge of the final EHR systems. Archetypes also form the basis of semantic *querying*. Queries are expressed in a language which is a synthesis of SQL and W3C XPaths, extracted from the archetypes. At the next level, the data-points and data-groups are assembled into context-specific data sets or *templates*; e.g. it could be the data for a form, a particular message, or a document. All openEHR systems are built with templates, which contain the relevant bits of various archetypes. Templates preserve the paths of archetype elements they use, even within variable depth structures. Templates are usually developed by implementers local to the solution being built, but it is also possible to build a standard template for a country, e.g. a discharge summary. Archetypes and templates also act as a well-defined semantic gateway to *terminologies*, classifications and computerised clinical guidelines. Last but not least, the last model level, closest to the final user are template-generated artefacts define the exposed application program interfaces of major *services*, such as XSDs and UI forms.

One of the important design aims of openEHR is to provide a coherent, consistent and re-usable type system for scientific and health computing. Accordingly, the ‘core’ of the RM (bottom-most layers) provides identifiers, data types, data structures and various common design patterns that can be reused ubiquitously in the upper layers of the RM, and equally in the AM and SM packages. The Figure 18 (right) illustrates the relationships between the key packages. Note that dependencies only exist from higher packages to lower packages.

4.1.3 Medical Classification

Medical classification, or *medical coding*, is the process of transforming descriptions of medical diagnoses and procedures into universal medical code numbers. The diagnoses and procedures are usually taken from a variety of sources within the health care record, such as the transcription of the physician's notes, laboratory results, radiologic results, and other sources. These diagnosis and procedure codes are used by health care providers, government health programs, private health insurance companies, workers' compensation carriers, software developers, and others for a variety of applications in medicine, public health and medical informatics, including: statistical analysis of diseases and therapeutic actions; reimbursement (e.g., to process claims in medical billing based on diagnosis-related groups); knowledge-based and decision support systems; direct surveillance of epidemic or pandemic outbreaks.

Statistical classification brings together similar clinical concepts and groups them into categories. The number of categories is limited so that the classification does not become too big (compared to *Nomenclatures classification*). Another feature of statistical classification is the provision of residual categories for "other" and "unspecified" conditions that do not have a specific category in the particular classification. The World Health Organization (WHO) maintains several internationally endorsed statistical classifications designed to facilitate the comparison of health related data within and across populations and over time as well as the compilation of nationally consistent data[29]. These include three main (or reference) classifications on basic parameters of health prepared by the organization and approved by the World Health Assembly for international use, as well as a number of derived and related classifications providing additional details. Some of these international standards have been revised and adapted by various countries for national use. The ICD and ICF constitute the core classifications in the WHO family.

The ICD is the international "*standard diagnostic tool for epidemiology, health management and clinical purposes*", designed as a health care classification system, providing a system of diagnostic codes for classifying diseases, including nuanced classifications of a wide variety of signs, symptoms, abnormal findings, complaints, social circumstances, and external causes of injury or disease. This system is designed to map health conditions to corresponding generic categories together with specific variations, assigning for these a designated code, up to six characters long. Thus, major categories are designed to include a set of similar diseases. The ICD is currently used worldwide for morbidity and mortality statistics, reimbursement systems, and automated decision support in health care. This system is designed to promote international comparability in the collection, processing, classification, and presentation of these statistics. The ICD is part of a "family" of guides that can be used to complement each other, including also the ICF which focuses on the domains of functioning (disability) associated with health conditions, from both medical and social perspectives.

The ICF is structured around the following broad components: (i) physical: *body functions* and *structure*; (ii) mental**:** *activities* (related to tasks and actions by an individual) and *participation* (involvement in a life situation); (iii) social: *additional information on severity* and *environmental factors.* Functioning and disability are viewed as a complex interaction between the health condition of the individual and the contextual factors of the environment as well as personal factors. The classification treats these dimensions as interactive and dynamic rather than linear or static. So, all aspects of a person’s life (development, participation and environment) are incorporated into the ICF instead of solely focusing on his or her diagnosis. A diagnosis reveals little about one’s functional abilities. Diagnoses are important for defining the cause and prognosis, but identifying the limitations of function is often the information used to plan and implement interventions. Once a rehabilitation team is aware of the daily activities a client is required to participate in, the problem solving sequence set up by the ICF can be utilized.

4.1.4 Relevance to the FrailSafe Project

In FrailSafe we will model older people with a holistic approach by exploiting a solution that will keep together low-and high-level clinical, physiological, behavioral, social and environmental parameters. The identification and detailed conceptual definition of the

[29] *http://www.who.int/classifications/en/*

entities/concepts of interest for the personalized patient models (e.g. disease, symptom, diagnosis, risk factor, sensor input, treatment, action plans, interventions, etc.) will be analyzed in the very beginning of the project. The representation will take into account the patient’s health record, physiological parameters, co-morbidities and behavioural information of the patient’s daily living. For this purpose, we will adopt an approach that represent an evolving virtual entity based on existing rich and extensible representation formats (VERITAS, openEHR) in order to represent the ageing related diseases in finer detail, emphasizing on physiological, behavioral and social factors; thus build a structured machine readable patient representation format that will allow personalized adaptation of patient user interfacing, feedback and intervention strategies that will support the healthcare professionals in their decision process and will finally make dynamic data analysis and feature extraction processes more efficient.

4.2 Data management and knowledge discovery

In order to extract various information from given data, multiple and thorough steps have to be taken into account. One of the main aspects of the system is the storage used to support all internal functionalities of the mental extraction decision system ensuring security and meeting all applicable regulations and standards. State of the art techniques for storage usage prevent system failure by utilizing failsafe secondary storage systems that can take over as master in case current master stops working properly. Many large healthcare organizations are building out a similar strategy, as they migrate to the cloud in order to tie together the providers, hospitals, and insurance organizations into peer based hybrid clouds which will enable them to more efficiently and securely share digitized patient information and other critical records. Data mining of this information has enabled advancements in medicine and fundamentally changed the medical industry to facilitate better treatment outcomes.

4.2.1 Data Management

4.2.1.1 Type of data

Managing FrailSafe’s multimodal data is a task of great importance. The huge data files that contain the raw sensor data generated by the devices, the medical records of the older people, the annotations generated by the experts (both clinicians and researchers), and the files that contain the analysis results need to be stored effectively, aiming to fulfill the data access requirements that arise during offline analysis.

After contacting all partners and the vendors that produce the devices, a summary of the expected input data was made. This summary that is shown in the following table will be used as a guide towards the design of the database.

Device	Parameters	Input data
Smartex Wearable Wellness System (WWS)	Heart rate (HR) - sampled every 5 sec (from heart signal sampled at 250 Hz)	ECG: integers, sampled at 250Hz, saved on microSD, uploaded offline. HR: integers, 1 datum every 5 sec, saved on microSD, BT transmitted
	Respiration Rate (RR) - sampled every 15 sec (from piezoresistive sensor sampled at 25 Hz)	Respiration: integers, sampled at 25Hz, saved on microSD, uploaded offline. BR: integers, 1 datum every 15 sec, saved on microSD, BT transmitted
	IMUs - sampled at 100 Hz	To be decided number of IMUs, sampling rate, what to be transmitted

		and what to be saved and uploaded offline, probably in any case quaternions
	Steps per minute	Integer, 1 datum per 15 sec
Dynamometer	Strength evaluation	Collect value every 2 sec and transmit it through BT
Beacons	Indoor activities	Indoor location: one integer + 2 floating point numbers (the ID of the room in which the person is + the x, y person coordinates in the facility). Each set of measurements is taken by the mobile phone every 15 sec (programmable). Stored in microSD, uploaded offline. Indoor activity index: one integer (Katz Index of Independence in Activities of Daily Living) Patterns of activity extracted from WWBS data
GPS	Outdoor activities	GPS localization data (floating point x and y coordinates), provided at programmable time intervals, collected by the mobile phone. Outdoor activity index: one integer (Lawton-Brody Instrumental Activities of Daily Living scale (IADL))
Blood pressure monitor	Systolic Blood Pressure/Diastolic Blood Pressure/ Heart Rate	Persons with risk of social exclusion
Impedance scale	Body Weight/Body Mass Index	Floating point numbers for the body weight and the body mass index
Mobilograph	Systolic Blood Pressure/Diastolic Blood Pressure/ Heart Rate/ Aortic Systolic Blood Pressure / Pulse Wave Velocity	Floating point numbers for the parameters
AR Game	Others (Cognitive state / behaviour / physiological state)	Cognitive state: One integer (cognitive state index) + complete game statistics, collected by the tablet each time the user completes a cognitive game. The data are stored on the microSD card of the tablet and uploaded offline.
Clinical questionnaires	Nutrition, Co-Morbidities	Multiple answer questionnaires
Self-filled questionnaires	Social interaction	Multiple Choice answers + Free Text fields for Text Analysis

Table 9: List of system parameters and data that will be collected

4.2.1.2 Database Management Systems

Formally, a database refers to a set of related data and the way it is organized. Access to these data is usually provided by a database management system (DBMS) consisting of an integrated set of computer software that allows users to interact with one or more databases and provides access to all of the data contained in the database (although restrictions may exist that limit access to particular data). The DBMS provides various functions that allow entry, storage and retrieval of large quantities of information and provides ways to manage how that information is organized.

Depending on the model used to store and process the data, the DBMS can be divided into two categories: the relational and the NoSQL.

The Relational Database Management Systems (RDBMS) is based on the relational model which was introduced already in 1970s. Using the relational model the information is stored in tables in a highly structured way, ie for storing information about a patient a new row is created in a table and each column contains specific information about the patient (age, nutrition, co-morbidities etc). Relations between tables are possible using references (e.g. the patient's ID number). However, RDBMS is now considered to be a declining database technology. While the precise organization of the data keeps the warehouse very "neat", the need for the data to be well-structured actually becomes a substantial burden at extremely large volumes, resulting in performance declines as size gets bigger. Thus, RDBMS is generally not thought of as a scalable solution to meet the needs of 'big' data.

NoSQL (commonly referred to as "Not Only SQL") on the other hand represents a completely different framework of databases that allow high-performance, and agile processing of information at massive scale. In other words, it is a database infrastructure that is designed to be adaptive to the heavy demands of big data. The efficiency of NoSQL can be achieved because unlike relational databases that are highly structured, NoSQL databases are unstructured in nature, trading off stringent consistency requirements for speed and agility. NoSQL adopts the concept of distributed databases, where unstructured data may be stored across multiple processing nodes, and often across multiple servers. This distributed architecture allows NoSQL databases to be horizontally scalable; as data continues to explode, adding more resources will sustain the high performance. The NoSQL distributed database infrastructure has been the solution to handling some of the biggest data warehouses on the planet – i.e. the likes of Google, Amazon, and the CIA.

4.2.1.3 FrailSafe DBMS

Based on the nature of the data of the FrailSafe project, a NoSQL database was decided that will be more appropriate. Among the numerous NoSQL solutions the HBase was chosen. The motivation behind this choice is that HBase is part of the Hadoop ecosystem, which provides high scalability in data analysis and knowledge discovery algorithms as well.

HBase is an ongoing, top level Apache project and an integral part of the Hadoop ecosystem. Its primary characteristics are that it is open source, distributed, and non-relational. According to the CAP theorem categorization, HBase is a CP database [95] [96]. Also, in the taxonomy of the emerging NoSQL movement it is a key-value database, namely that its primary data structure, at least conceptually, is the associative array. As such, design principles for HBase differ from those of the relational world [97] [96]. HBase shares the same data model with Google BigTable [95]. In HBase tables comprise of rows and columns, with data rows having a sortable key and an arbitrary number of columns. Tables are stored sparsely, so that rows in the same table can have widely varying columns, if so deemed by the underlying application. HBase is tuned for sparse data stored in large rows and, moreover, HBase tables can be used as input or output of MapReduce jobs over Hadoop.

Delving deeper, HBase relies on Bloom filters in order to index the sparse data [98] [99] [100]. A critical requirement is that rows should be sorted according to the key value. Therefore, rows with keys which are close, lexicographically or otherwise depending on the key nature, are very likely to be physically stored to the same machine [101] [102]. Therefore, choosing a row key convention is of paramount importance. For example, in a table whose keys are domain names it makes the most sense to list these names in reverse order notation so that rows about a subdomain will be near the parent domain row [97].

Connections to the relational world are provided by Apache project Phoenix, which allows the formulation of SQL queries and the use of OLTP analytics over Hadoop for low latency applications. Thus, existing SQL and JDBC APIs with full ACID transaction capabilities can be used over an HBase backbone [98] [97].

Applications relevant to the project include RDF storage for a specified electronic health record ontology [103] and visualization over Hadoop and HBase for a number of biosignals [104].

4.2.2 Data Analysis and Knowledge Discovery

4.2.2.1 Pre-processing Techniques for Text Mining

The essential part of the patient modelling process is the pre-process of the patient data along with the analysis and classification process in order to extract the mental state of the patient. Concerning the data pre-processing step, it is a procedure based on the User Profiling Model (T4.3) and the Linguistic Corpus (T4.4). Primary goal will be the creation of the dataset for the next step, the classification procedure. The result will be the patient mental model used to classify future input.

The current state of the art techniques of data pre-filtering for text classification are composed of grammatical and syntactical analysis of text along with the use of word removal techniques (for instance stopwords). Furthermore, the data pre-processing procedure involves feature selection and extraction in order for the final dataset to be composed. Feature selection and extraction is a vital part of the overall process with serious impact in the performance and accuracy of the model and is characterized as a highly empirical process and strictly related to the domain of application. After the dataset has been composed, a classification procedure will be designed and implemented based on state of the art techniques [105]. Currently, literature for text classification the best performing algorithms that are proposed are ensemble classifiers using mostly the simple models of Bayesians, support vector machines (SVMs) and Neural Networks. To achieve the best possible performance for the dataset, a model with the mixture of those will be implemented emphasizing in the best possible parameters optimization through trial and error and accuracy evaluation. To deliver the output of the mental model, a software package will be developed. State of the art methodology for remote services will be implemented in order for the decision making model to work without any disruption through a single API point of access. Finally, all necessary security measures, with the use of encrypted transmission and password protected access will be handled properly.

4.2.2.2 Data Fusion

During the past years, clinical monitoring of physiological parameters by wearable or implantable sensors is a research area with high interest [106, 107, 108]. New health care monitoring systems arise with the aim of addressing the issues of managing and monitoring elderly people and persons with special abilities [109, 110]. Many issues have to be taken into account while considering this kind of systems, such as power issues, security of private information and system bulkiness [111]. These issues are expected to be addressed by technology's advancements in microelectronics, low-energy IC design, wireless sensor networks and big data analytics techniques.

Prognosis [107] is a physiological data fusion model for a multisensory health care monitoring system. Based on a fuzzy regular language for the generation of the prognoses of the health conditions of each patient, it is designed so as to describe the current health state and context of the corresponding patient. Moreover, authors in [112] developed a portable and real-time monitoring system; in this system, a seizure detection algorithm in embedded systems for online monitoring EEGs and detecting seizure events, experimented on animals is implemented. In [111] a middleware is presented targeted on smart-phone like health care applications focusing on the efficient management of sensor data. *MyHeart* project [113] aimed at fighting cardiovascular diseases (CVD) by prevention and early diagnosis. The developed system included an ECG as well as an activity sensor and was able to classify human activity by adopting the use of smart clothing. In addition, *Human++* [114, 115] has developed a body area network consisting of three sensor nodes and a base station. Each sensor is collecting and processing multichannel data from ECG, EEG and EMG, while the base station functions as a data collector in star topology, regulating the information flow.

In recent years, much more attention has been paid to the constraints imposed due to the real time processing of the huge amount of data in health care monitoring applications. In [116], a flexible framework that performs real-time analysis of physiological data in order to monitor the subject in her daily activities is proposed. Real time processing systems should fulfil a number of requirements. Particularly, low latency is essential in real time applications, as well as data fusion for being able to mine heterogeneous data sources.

In [117, 118], authors make use of the tri-axial accelerometer sensors embedded in mobile phones in order to support geriatricians in frailty detection. The data collected from the accelerometer is then combined with the clinical indicators (from tests and medical instruments) and then analysed in the smartphone in order to prevent falls, injuries and predict future pathologies.

The work of [119] is focused on the differences between frail and non-frail elderly persons while performing ADL functions. They collect accelerometer data from the subjects' smartphones and perform a statistical analysis. Another work that focused on ADL functions of frail and non-frail elders was [120], where sit-to-stand and stand-to-sit transitions were examined. Using data from a set of accelerometers and gyroscopes, they analysed the time needed to perform these transitions and propose a model to classify the elderly persons. Similarly, in [121] the participants were classified as frail or non-frail using inertial sensor data collected while they were performing the Timed Up and Go (TUG) test. Then on a later study [122] they combined data from inertial and pressure sensors in order to quantify the balance and mobility of older adults using TUG, Five Times Sit to Stand (FTSS) and quiet standing balance.

4.2.2.3 Time series analysis

One of the fundamental problems in time series analysis is dimensionality reduction i.e. the reduction of its data points. Naive approaches such as sampling [123] have the drawback of distorting the shape of the reduced time series especially when the sampling rate is too low. Such a drawback is partly tackled by methods using the mean value to represent each frame of the time series after its segmentation into non-overlapping windows of fixed size. This method proposed by Keogh et al. [124] is called *piecewise aggregate approximation* (PAA). Later, Keogh et al. extended PAA to *adaptive piecewise approximation* (APCA) in order to allow different lengths for the successive frames [125]. Another common technique for dimensionality reduction converts the numeric time series to symbolic form by discretizing the time series into segments and then converting each segment into a symbol [126, 127, 128, 129]. Lin et al. [130, 131] propose a method called symbolic aggregate approximation (SAA) to convert the result from PAA to symbol string. Megalooikonomou et al. [132] propose to represent each segment by a code word from a codebook of key-sequences. This work has extended to multi-resolution consideration [133].

Another common family of approaches transform the time series data to another domain including *discrete Fourier transform* (DFT) and *discrete wavelet transform* (DWT) which express the time series as linear combination of basic functions. In addition, a large amount of relevant works in the literature include feature extraction and feature selection. The first one creates artificial features for the representation of the data, aiming in size reduction and improved processing time, while the other selects a subset of the data (features). Furthermore, *principal component analysis* (PCA) is a transformation that converts possibly correlated features to an orthogonal basis set of principal components that consists of linearly uncorrelated features. The linear combinations of the principal components can represent the data with the highest variance in a feature subspace and thus is considered as optimal. PCA sorts the eigenvalues of the covariance matrix of the feature vectors in descending order and retains the eigenvectors that corresponds to the largest ones since they capture a high percentage of the total variance (e.g. 99%). The selected eigenvectors form the transformation matrix and result in feature vectors with reduced dimensionality. The resulting feature vectors either the original or the reduced can be used as samples for traditional classification or clustering data mining tasks.

Time series analysis and data mining tasks usually require a similarity measure or distance metric. The similarity/dissimilarity between two time series is usually measured by evaluating the Euclidean distance on the transformed representation. Euclidean distance is not always being the suitable distance function in specified domains [133]. Besides Euclidean-based distance measures, other distance measures can easily be found in the literature. One of the most popular similarity measures is called the dynamic time warping (DTW) [134]. Focusing on similar problems as DTW, the Longest Common Subsequence (LCSS) model [135] is proposed. The LCSS is a variation of the edit distance and the basic idea is to match two sequences by allowing them to stretch, without rearranging the sequence of the elements, but allowing some elements to be unmatched. One of the important advantages of an LCSS over DTW is the consideration on the outliers.

4.2.2.4 Fall detection

Falls are a common cause of injury among elderly people. According to the World Health Organization, 28-35% of people aged 65 and over fall at least once a year with serious consequences, such as heavy injuries and even death. Additionally, the moments after a fall are very crucial. Many people experience what is called the “long lie,” a long period of immobility after a fall that can have serious complications in one’s health. Unless measures are taken, the number of injuries and the costs associated with fall-related trauma will double in the near future [136]. Fall detection is therefore rendered an extremely important aspect of healthcare.

The most challenging aspect of fall detection is the distinction between falls and ADLs such as sitting, standing or walking since falls typically occur when performing daily activities. In particular, ADLs with acceleration are often confused with falls. Misinterpreting a fall as an ADL can have serious effects in the subject’s health [137]. As a result, a fall detection system should be able to accurately distinguish exactly when a fall occurs. This requires the fall to be detected in real time. Another challenge is to make the system as less invasive as possible, with low false-alarm rates. Subjects using the system should feel comfortable and their everyday life should not be affected. Accurate, reliable and real-time fall detection systems are therefore essential.

Significant research has been conducted in this field and various fall detection systems have been developed in the past years. Noury et al. [138] and Yu et al. [139] have investigated the principles of fall detection and early works on the subject as well. More recent reviews of works on fall detection can be found in [140, 141]. Fall detection approaches are divided into two main categories: vision based and wearable device based.

Several context aware systems that use devices like cameras or infrared sensors to detect falls within an environment have been developed. Rougier et al. [142] used human shape deformation to track the person's silhouette in recordings taken from four cameras. Falls and ADLs were classified with 98% accuracy. In [143], a human 3D bounding box was created and the Kinect infrared sensor was used to accurately detect falls without any prior knowledge of the environment. Olivieri et al. [144] used motion templates taken from a camera to recognize certain ADLs and detect falls, achieving 99% recognition rate. However, these approaches have certain limitations. The system can only monitor activities within the environment and thus outdoor activities are excluded, restricting the mobility of the user. Other people moving within the environment might also "confuse" the system and trigger false alarms in some cases.

As a result, the use of wearable sensors has been preferred by many researchers. With the advances in *micro electro mechanical* (MEMS) technology, sensors such as accelerometers, gyroscopes and magnetometers have been integrated in small motion sensor units. Small devices that contain the above sensors can be used to collect movement data and detect falls. They are compact, light and have low power consumption. They can be placed in the subject's pockets or be easily attached in different body parts without making the subject uncomfortable, thus, making the analysis of outdoor activities possible. Different body parts have been proposed for the sensor placement for both improved accuracy and minimum intrusion to subject's everyday life. Yang and Hsu [145] have examined the fundamentals of such sensors as well as optimal sensor placement.

In fall detection studies, typically a simple thresholding technique is used. A fall is detected when the negative acceleration is suddenly increased due to the change in orientation from upright to lying position [146]. In [147], the results of certain threshold-based methods that consider fall impact, velocity and posture have been assessed and tested on elderly subjects achieving 94.6% sensitivity. Thresholding methods sometimes tend to miss "soft falls" meaning falls that might not exceed the threshold. Also certain ADLs with high acceleration might exceed the threshold and get misclassified as falls.

Machine learning techniques have been used to achieve more reliable results. The main classification problem is to distinguish between falls and ADLs. Every recorded movement has its own pattern. By extracting features from the signal, these patterns can be classified by different classification methods. Before raw data are given to different classification algorithms, they must be pre-processed using a windowing technique. Such a technique divides the sensor signal into smaller time segments (i.e., windows) and a classification algorithm is applied separately on each window, producing a classification result. After pre-processing, features from the time or frequency domain are extracted to feed trained classifiers such as neural or Bayesian networks, SVMs, decision trees, k nearest neighbours (K-NN), etc. Kaldegari et al. [148] used statistical features such as maximum, minimum, mean, range, variance and standard deviation extracted from a waist-worn tri-axial accelerometer to investigate the performance of various classifiers on fall detection. The multilayer perceptron yielded the best sensitivity (90.15%). Özdemir and Barshan [149] added frequency-domain features such as autocorrelation coefficients and DFT coefficients extracted from data acquired by sensors placed in different body parts. Six classifiers were used to assign a fall or ADL class label to the concatenated from all sensors feature vectors. All methods achieved higher than 97.47% and 93.44% sensitivity and specificity, respectively. Yuwono et al. [150] obtained data from a single waist-worn tri-axial accelerometer and extracted features using a clustering method (Particle Swarm Optimization). Then they proceeded to classify the data achieving above 98.6% sensitivity, in detecting falls.

Regarding the location where the sensors should be placed, the waist has been considered as the optimal choice since it is close to the body's center of gravity [151]. Wrists, head and other areas have also been used [151, 137]. In particular, Özdemir and Barshan [149] acquired data from sensors placed in six body parts including ankle, thigh, wrist, waist, chest, and head. In order to proceed with classification, the features extracted from each location are concatenated to a single feature vector leading to a high-dimensional feature space. However, fall detection is usually performed for real time purposes which require a lighter processing that can be achieved either through dimensionality reduction or selection of a single sensor unit located at the optimal position.

4.2.2.5 Human motion Identification

Human motion monitoring is a must in surveillance of older people, since the related information is crucial for understanding the physical status and the behaviour of the older people. Older people suffering from frailty are often required to fulfil a program of activity which follows a training schedule that is integrated within their daily activities [152]. Therefore, the detection of activities such as walking or walking-upstairs becomes quite useful to provide valuable information to the caregiver about the patient's behaviour. Under conditions of daily living, human-activity recognition could be performed using objective and reliable techniques.

Monitoring the activities of daily living requires non-intrusive technology. The main devices an older person can be instrumented through are classified into two main categories based on the used technology: vision-based and wearable. In computer vision, complex sensors such as cameras that continuously record the movement of the elderly have been used to submit the acquired data to specific image algorithms that recognize human activities. In general, tracking and activity recognition using computer vision-based techniques perform quite well in a laboratory conditions or at well-controlled environments. However, their accuracy is lower in real-home settings, due to the high-level activities that take place in the natural environments, as well as the variable lighting or clutter [153]. Furthermore, computer vision methods require a pre-built infrastructure, which instead of the time and cost of installation, introduce limitations for the space of application since it is hard to be used outdoors. As a result, wearable devices such as body-attached accelerometers and gyroscopes are commonly used as an alternative in order to assess variable daily living activities. The human motion detection problem using wearable sensors is an emerging area of research due to their low-power requirements, small size, non-intrusiveness and ability to provide data regarding human motion. The acquired data can be processed using signal processing and pattern recognition methods, in order to obtain nearly accurate recognition of human motion.

Data acquired from wearable sensors have been used to evaluate several human-activity recognition methods proposed in the literature. Acceleration signals have been used to analyze and classify different kinds of activity [153, 154] or applied for recognizing a wide set of daily physical activities [18]. Feature selection techniques have also been investigated [155]. The reclassification step introduced by Bernecker et al [156] has been demonstrated to increase motion recognition accuracy. The results achieved by the on-board processing technique for the real-time classification system proposed by Karantonis et al. [157] demonstrate the feasibility of implementing an accelerometer-based, real-time movement classifier using embedded intelligence. Khan et al. [153] proposed a system that uses a hierarchical-recognition scheme, i.e. the state recognition at the lower level using statistical features and the activity recognition at the upper level using the augmented feature vector followed by linear discriminated analysis. Considering the machine learning algorithms for human motion identification that are found in the literature, the most widely used are artificial neural network [157, 158, 159], naive-Bayes [160] and support vector machines [155, 161, 162, 163].

4.2.3 Visualization tools for frailty-related knowledge discovery

Information visualization concerns the use of interactive computer graphics in order to get insight into large amounts of abstract data, such as multivariate, hierarchical, healthcare and network data [164]. Conventional visualization techniques, such as bar-charts, pie-charts, and line-charts, are useful for the depiction of information of a higher level, but fail to depict large and complex data sets in detail. Therefore, and in order to enable the easy extraction of patterns, trends and outliers, a variety of novel visualization methods are continuously being developed for specific applications [165] [166] [167] [168] [169].

Visual analytics is the process of using visualization techniques, data analysis methods, as well as interaction with the human operator, in order to perform fast and insightful data exploration and decision making [170]. Visual analytics employs analytics techniques such as feature extraction, dimensionality reduction, clustering, prediction and anomaly detection in order to provide the viewer with informative visualizations. In addition, rich interaction techniques are utilized, in order to allow the operator to explore the data, by selecting, configuring, abstracting, filtering and connecting them [171].

Their ability to provide insight into large amounts of complex data makes visual analytics techniques especially useful for healthcare and biomedical applications. This has resulted in numerous existing methods and tools which utilize various visualization types and user interaction levels [172] [173]. Recent works have employed visual properties such as color and position [174] [175] or animation [176], in order to visually encode patient information, group patients with similar characteristics together and discriminate between different events. Visual queries have also been utilized in combination with pattern mining and interactive visualization, in order to explore large datasets more efficiently. Visual analytics has significant applications in genomic analysis [177], where visualization of genome sequences and their correlations allows the investigation of virus outbreaks [178] and exploration of similarities and mutations in the genome [179].

Visual analytics techniques will be used in FrailSafe as a means of knowledge extraction involving human operators in the loop. Moreover, their interactive nature allows them to provide personalized views of the data, targeting specific individual users. In the next sub-sections, recent methods, applications and tools for the interactive visualization of health-related data are presented in more detail.

4.2.3.1 Big data and visual analytics in health care

The study of [180] presents the visualization approaches used in the health care environment and takes the first steps toward the formulation of a universal methodology for the design of such environments. Even though the study focuses on the visualization approaches that support healthcare personnel in general and specifically medical researchers, the visualization approaches presented can be used for presentation of frailty data to both doctors and patients themselves. The time-oriented visualization approach of Figure 19 can be adopted for the presentation of not only the patient’s medical history but also for the presentation of the measurements of the sensors that will be integrated with the FrailSafe system. The statistically oriented view of Figure 20 is also a useful starting point for the development of analytics tools that will be implemented by the final system, aiming to support scientific researchers to understand and use the collected data, doctors to use the patients history and optimize the suggested treatments, hospital administrators to understand the inefficiencies in their organization structures and more importantly patients to improve their health through the understanding of the current state of their condition and the effects of their treatments for its improvements.

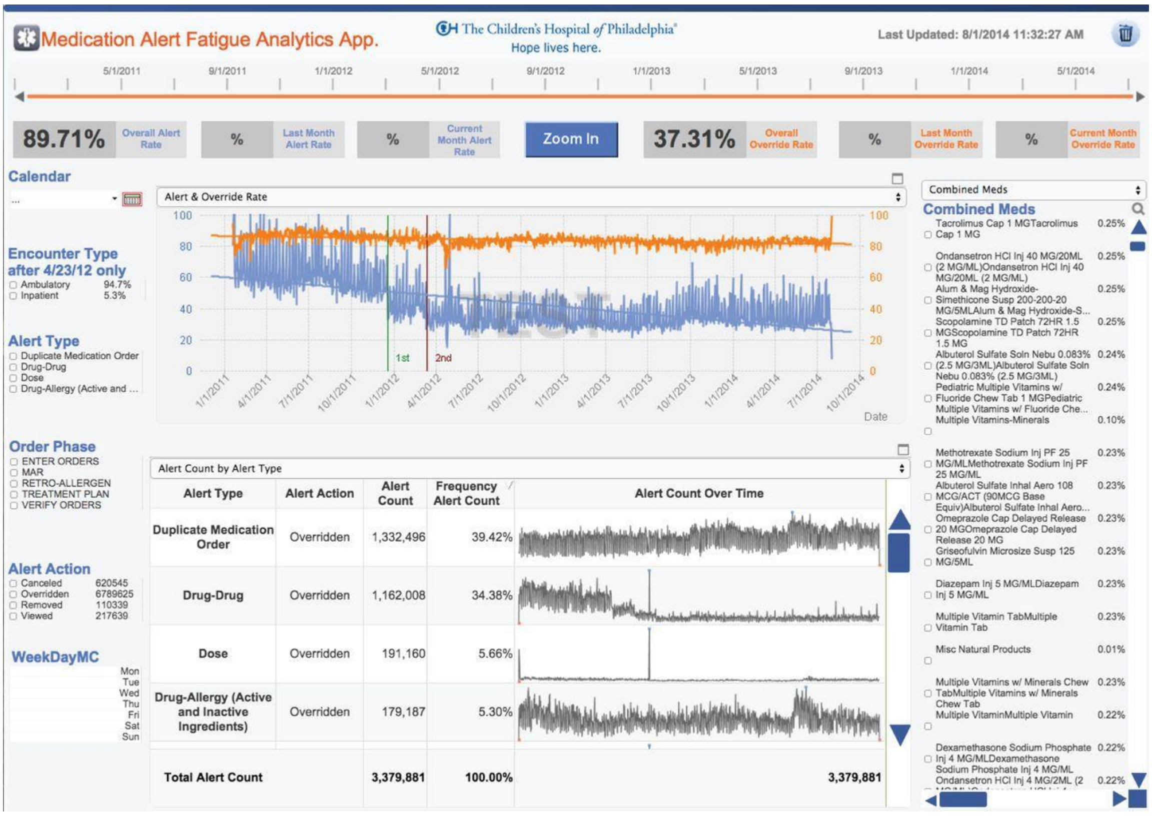

Figure 19: Screenshot of The Children's Hospital of Philadelphia Perioperative Blood Transfusion visual analytics dashboard (tools used to enable the user to explore historic blood transfusion data).

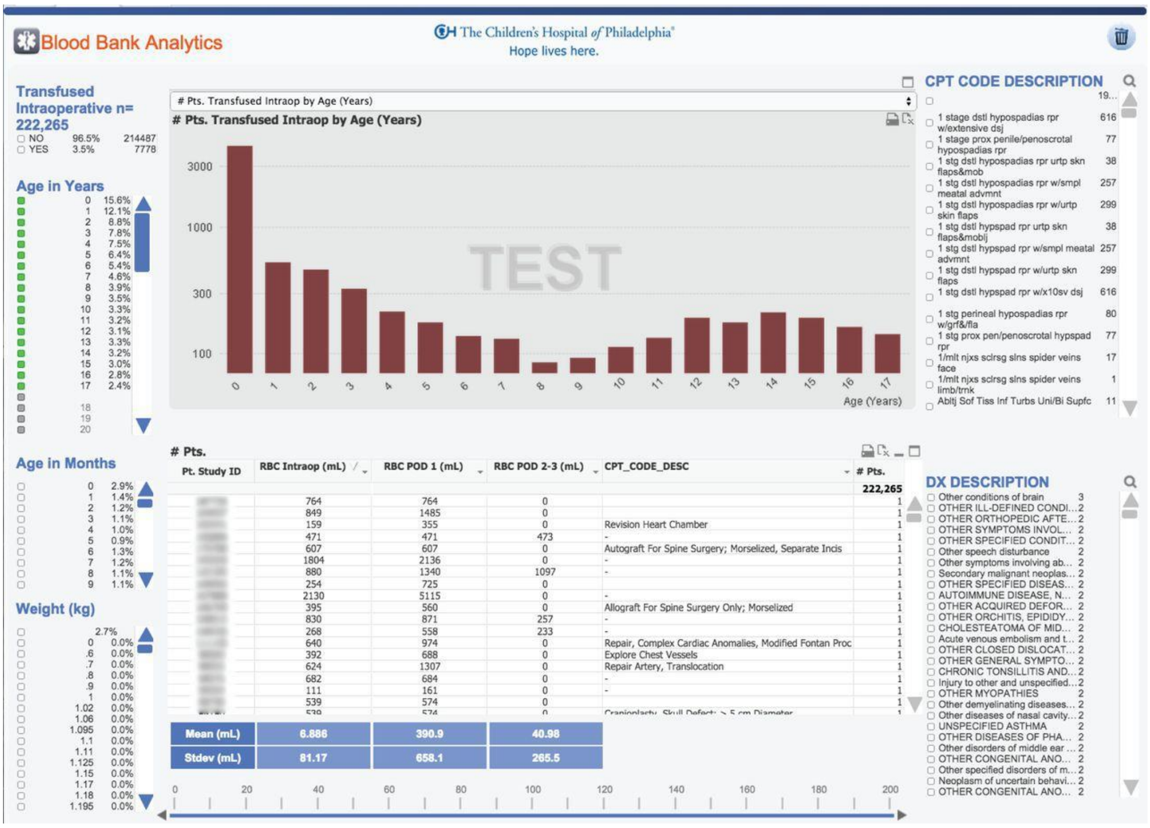

Figure 20: Screenshot of The Children's Hospital of Philadelphia Medication Alert Fatigue visual analytics dashboard (tools used to enable the user to explore electronic health record medication alert data).

4.2.3.2 Visualization of medicine prescription behavior

The current environment for the visualization of medicine prescription behavior has been thoroughly described in recent bibliography [181] [182], outlining the importance of such approaches for the efficient management of healthcare towards cost effectiveness, but also as a means for the protection of patients and the optimization of their treatment. The frailty metrics that will be defined during the FrailSafe project, as well as any treatment indicators and prescriptions will be, among others, time-dependent. Therefore, the visualization of frailty metrics should always involve their presentation as a function of time also in relation to the effects on the patient's condition. Even though the above approach focuses mainly on the supervision of medication prescriptions from a management and administration point of view, it can offer useful ideas for the supervision of frailty metrics and treatment adherence by patients and also allow patients to understand their treatment approach and schedule their visits to their doctor and pharmacy (see Figure 21 and Figure 22).

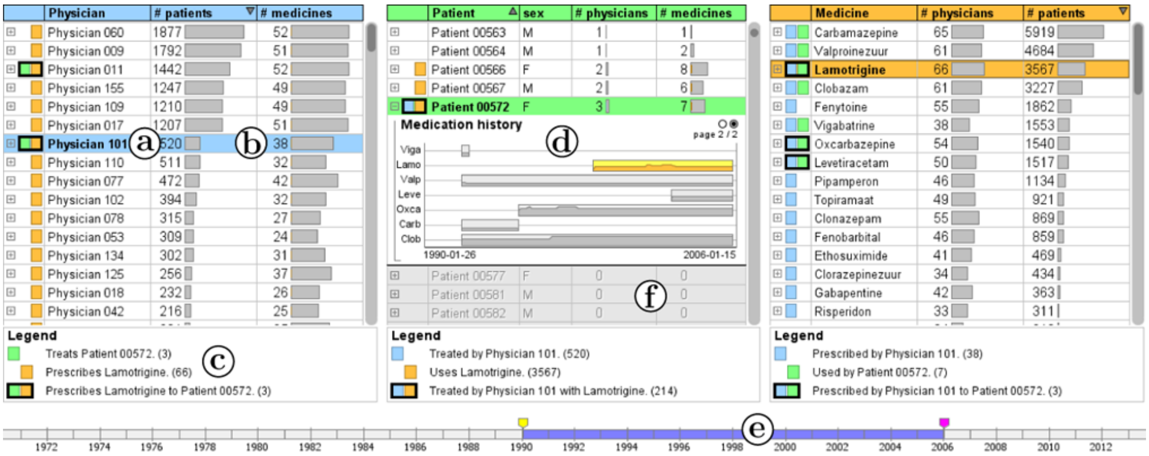

Figure 21: Screenshot of the 3TV describing physicians, patients, and medicines. (a) A selected physician is highlighted with a blue color; (b) Additional columns show distribution characteristics such as the number of patients treated by a physician; (c) A legend explains in natural language how the RRGs have to be interpreted, and shows between brackets how many of these exist in the corresponding table; (d) Row extensions can be used to obtain detailed information about a specific item, in this case the patient's medication history; (e) The selection on the timeline indicates the interval from which the data is taken; (f) Greyed out rows show physicians, patient, or medicines that have no prescriptions in the selected time window.

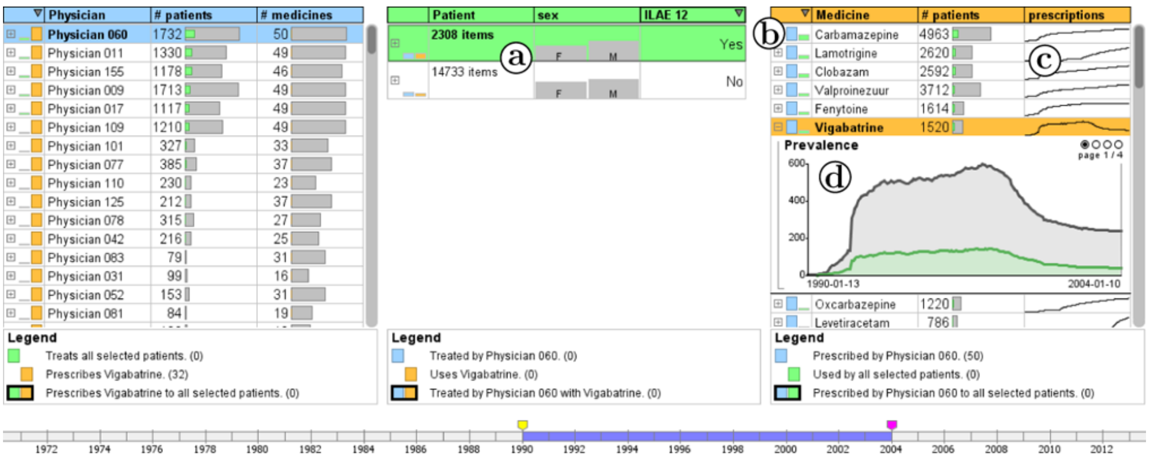

Figure 22: Screenshot of the 3TV with a different configuration. (a) Patients are grouped by the column that indicates whether they have a symptomatic localization-related syndrome (classified as ILAE 12), this results in two groups; (b) By sorting on the RRG column, we find out that Carbamazepine is the most commonly prescribed medicine for patients with this syndrome; (c) Sparklines give a global indication of how the number of prescriptions associated with each row develops over time; (d) An extension showing a medicine's prevalence (the number of patients using it) over time, the green graph represents the selected patients. In case of Vigabatrin we spot a sudden decrease of patients just before the year 2000, due to a discovery that this medicine can cause blindness. Other views on medicines can be selected by pressing the buttons in the top right corner of the extension.

4.2.3.3 Visual analytics to enhance personalized healthcare delivery

The visualization approach presented in this section aims to aggregate the complex environment of healthcare parameters and electronic health records in a common framework that will allow the fast and efficient supervision by doctors [183] [184]. It is therefore no surprise that the visualization approaches included in this platform can provide a very useful perspective in the presentation of frailty related information and in the framework of the FrailSafe project. First and foremost, the timeline of the patient's condition is enhanced with the continuous presentation of the extracted metrics and predicted values which are separated using different colors and an adapted time scale. Furthermore, the current approach includes the visualization of the different treatments as a function of time, helping practitioners understand the relation of therapies with the measured health outcomes for the specific patient (see Figure 23). Furthermore, the recommendation pane including very useful information such as the percentage of patients that saw an improvement when following this approach is a very useful tool for doctors but can also help patients understand their condition and be more engaged when following their doctor's suggestions (see Figure 24).

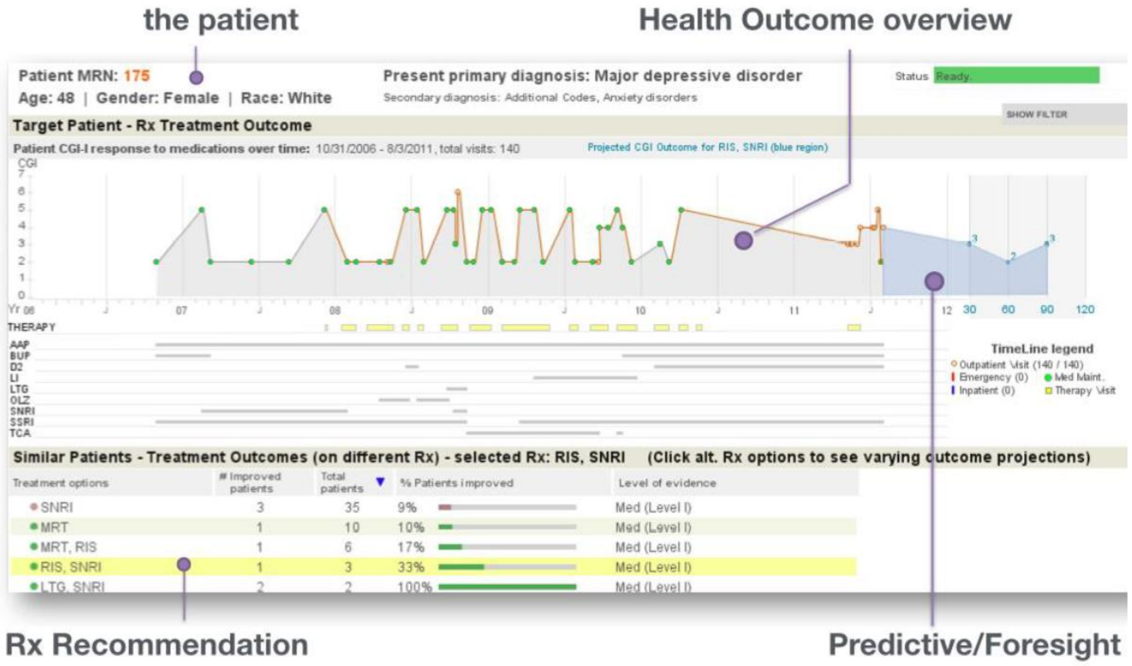

Figure 23: Dashboard-style visual User Interface with integrated and interactive data views to impact health delivery.

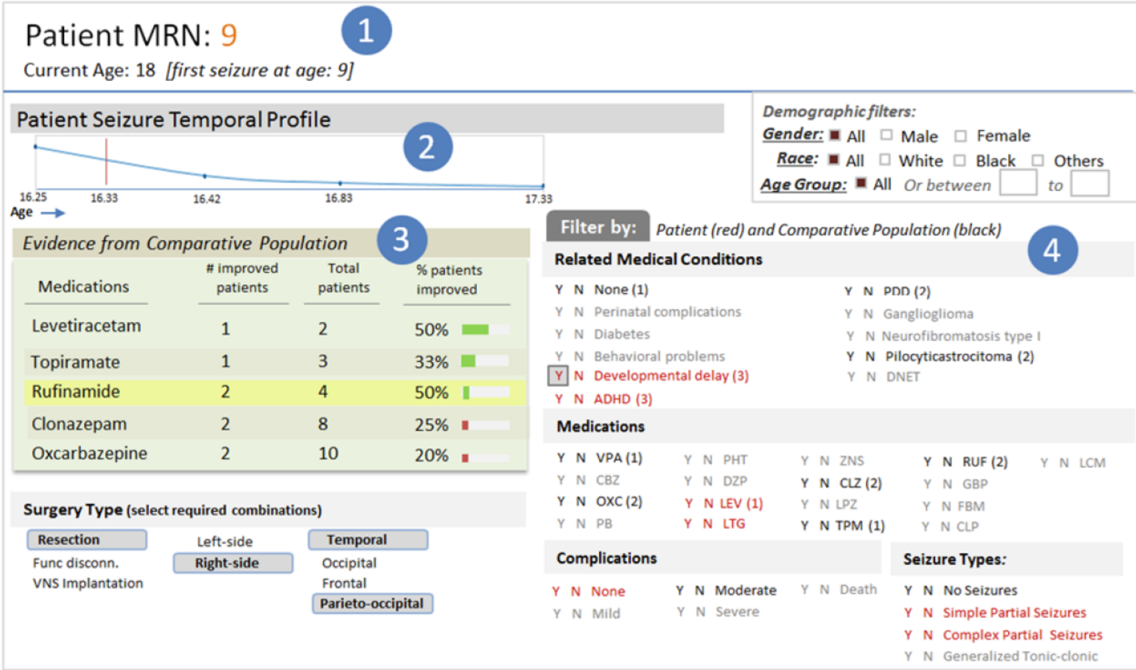

Figure 24: View showing comparative population data for use in decision support for an individual patient. Different data views are labeled. 1: Demographics for an individual patient; 2: Seizure history for an individual patient; label 3: Treatment evidence aggregated from the comparative population; 4: Data attribute level filters with yes/no (Y/N) toggles for variable selection.

4.2.3.4 Big Data and health analytics: Interactive Visualization

Two recent publications [185] [186] have provided a comprehensive review of some alternative interactive visualization approaches with special focus on *EventFlow* as it is presented in Figure 25. Despite the fact that frailty is not the targeted application of EventFlow, its visualization structure can be very useful for the definition of respective FrailSafe tools in order to support doctors to supervise efficiently their patients and medical researchers to manage clinical trials and also study their results.

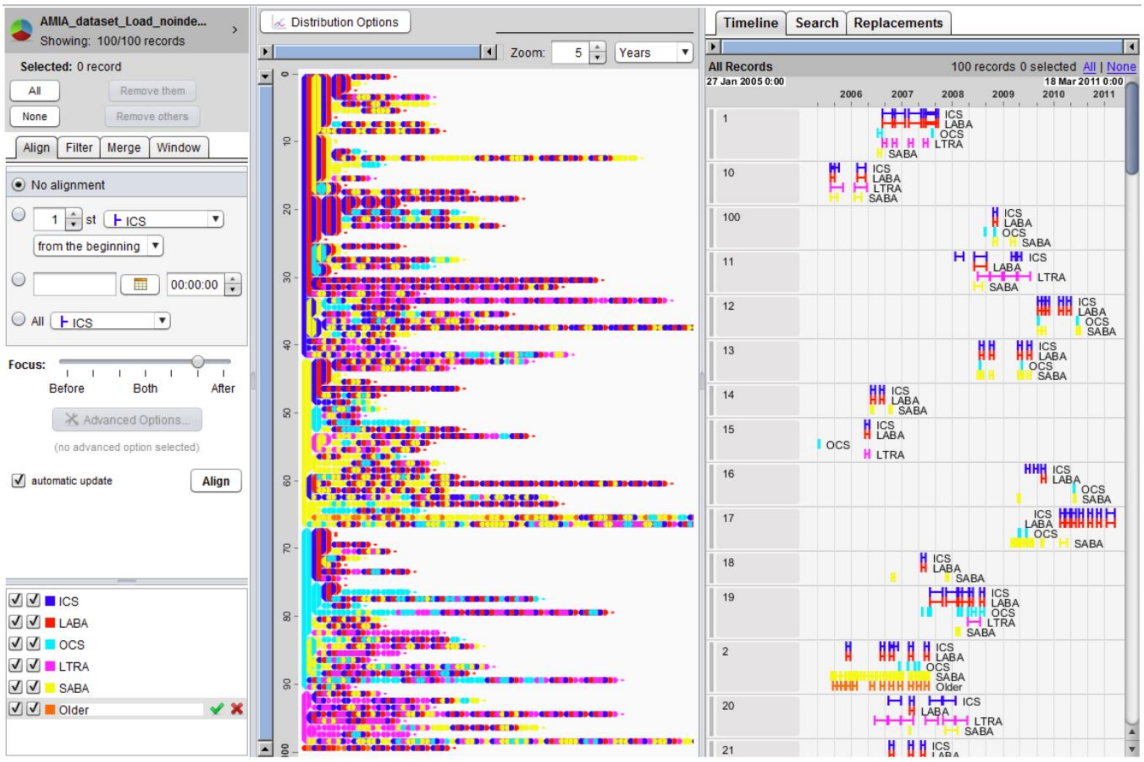

Figure 25: EventFlow overview of 100 patients' prescription records. (Different prescriptions are indicated with different colours).

4.2.3.5 PatientsLikeMe

Among the visualization platforms reviewed in this study, it is important to mention the case of *PatientsLikeMe*[30] (see Figure 26). This platform can provide with valuable information for the design of the Virtual Community Platform as it will be developed under the FrailSafe project. The polling bars as used by the PatientsLikeMe platform are a useful tool for the engagement of patients and can also help them understand their disease, find people with similar difficulties and discuss their treatments.

[30] *https://www.patientslikeme.com/*

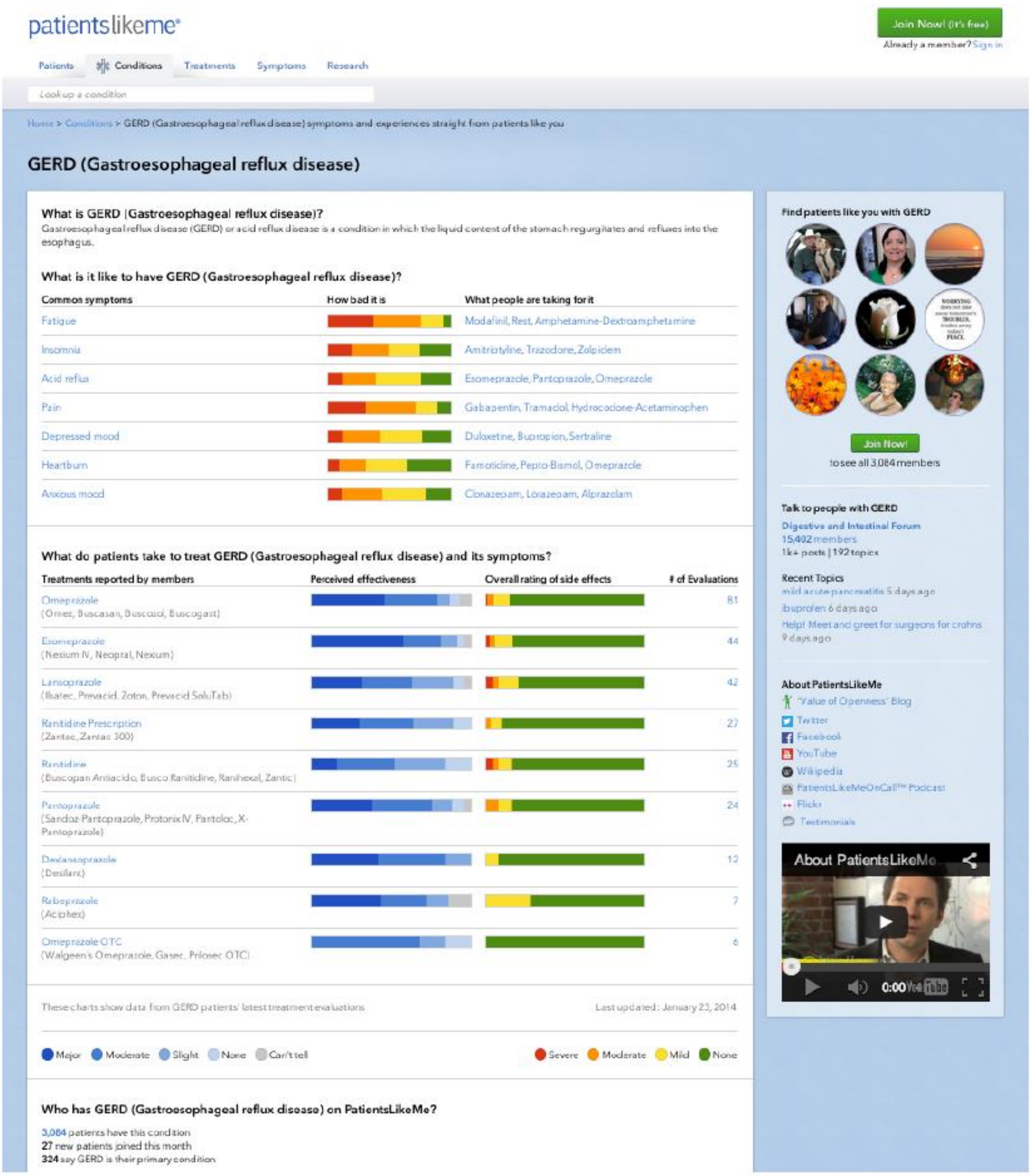

Figure 26: A PatientsLikeMe example visualization interface.

4.2.3.6 Information visualization for healthcare informatics

In this section, the concept of the *Five Ws* in the area of medical information visualization is introduced, namely who, when, what, where, and why. The proposed system seeks to improve the usability of information captured in the EHR and show via multiple examples the time and effort needed to access and analyze the medical patient information can be lowered on the basis of the above described framework of Five Ws [187] [188].

Both the visualization approaches of Figure 27, namely the radial and sequential views, may prove very useful for the representation of frailty conditions. Firstly the radial view can be used in order to visualize the relations between measured parameters and identified risk factors, whereas the sequential presentation holds the promise to further simplify the presentation of the evolution of frailty as a function of time. Even though the above system is developed to the holistic presentation of the patients' health status, it can offer valuable ideas for the multi-parametric depiction of frailty and especially the combination of physiological, environmental and behavioral parameters as they will be assessed and studied under the framework of FrailSafe.

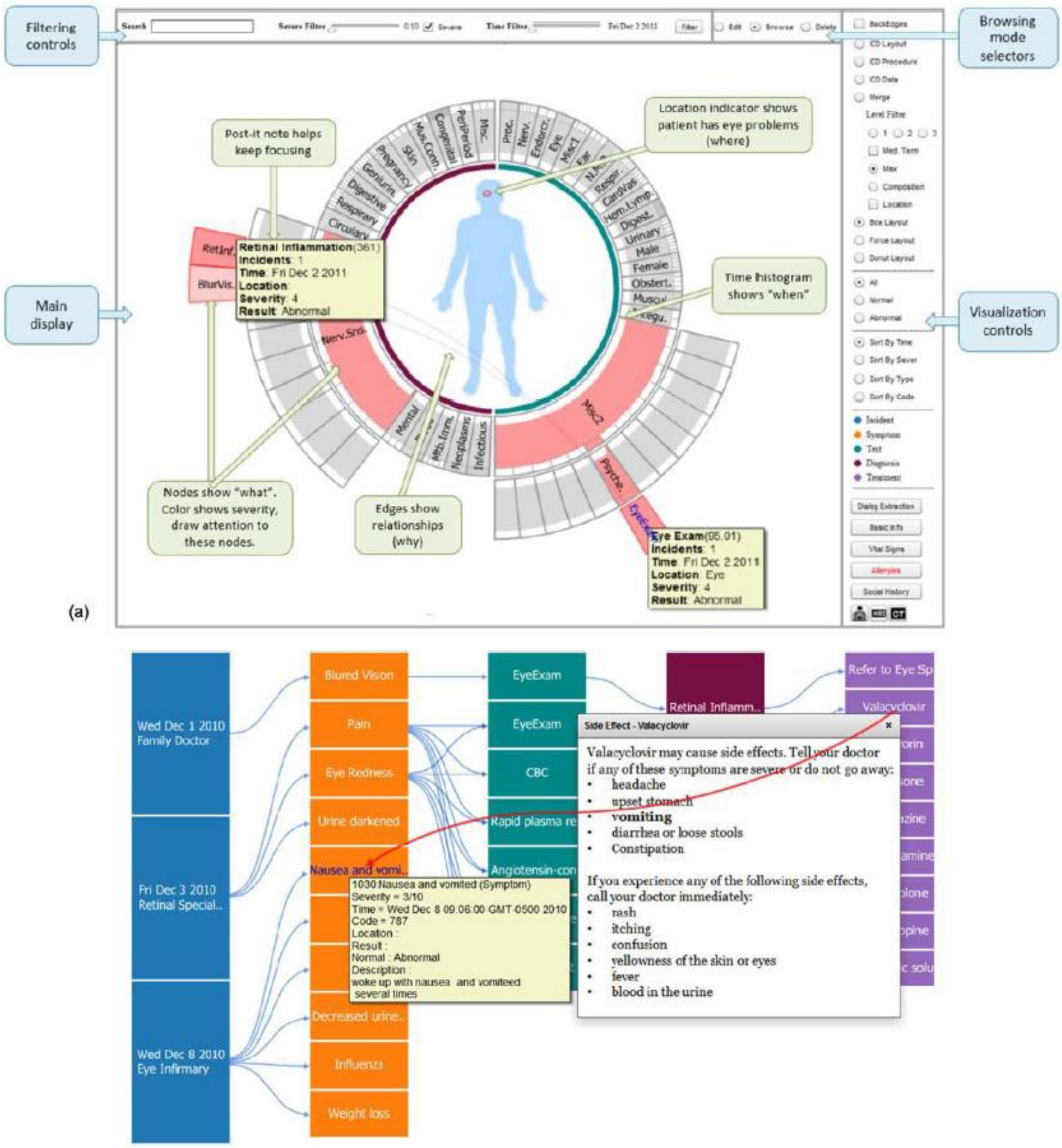

Figure 27: The radial and sequential views of the proposed system of health informatics visualization.

4.2.3.7 Mutlifacet visual analytics for healthcare

In this section, three visualization approaches of health-related data are presented, oriented towards the clustering of patients' data [189]. In addition to the commonly used visualization approach of clustering with node-connection diagrams (see Figure 28), the *SolarMap* and *DICON* displays are presented, which are two innovative enhancements for the presentation of clustering results based on their separation parameters. In the first case (see Figure 29) the parameters of clustering are presented in a circle around the clustering diagram together with their connections with each node. Furthermore, the DICON approach (see Figure 30) visualizes these parameters chromatically for every clustered node and assists the user to easily understand the fundamental basis of the clustering in terms of the differentiating parameters. All the above approaches can provide significant help for the design of similar functionalities for the FrailSafe system.

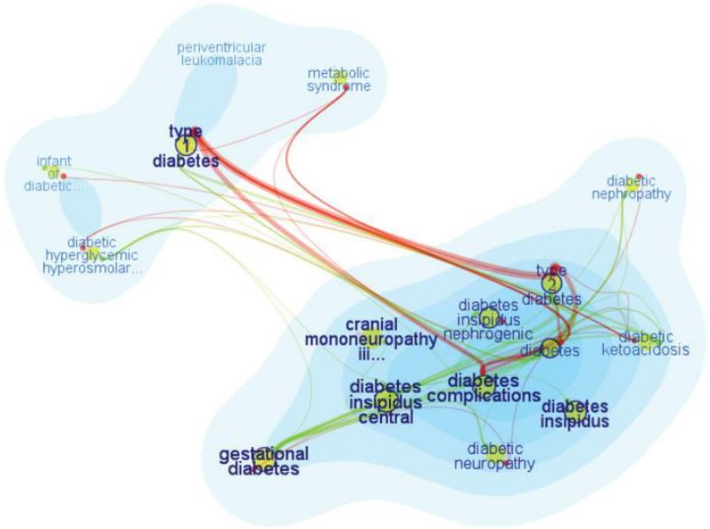

Figure 28: FacetAtlas visualization showing two clusters corresponding to type 1 and type 2 diabetes.

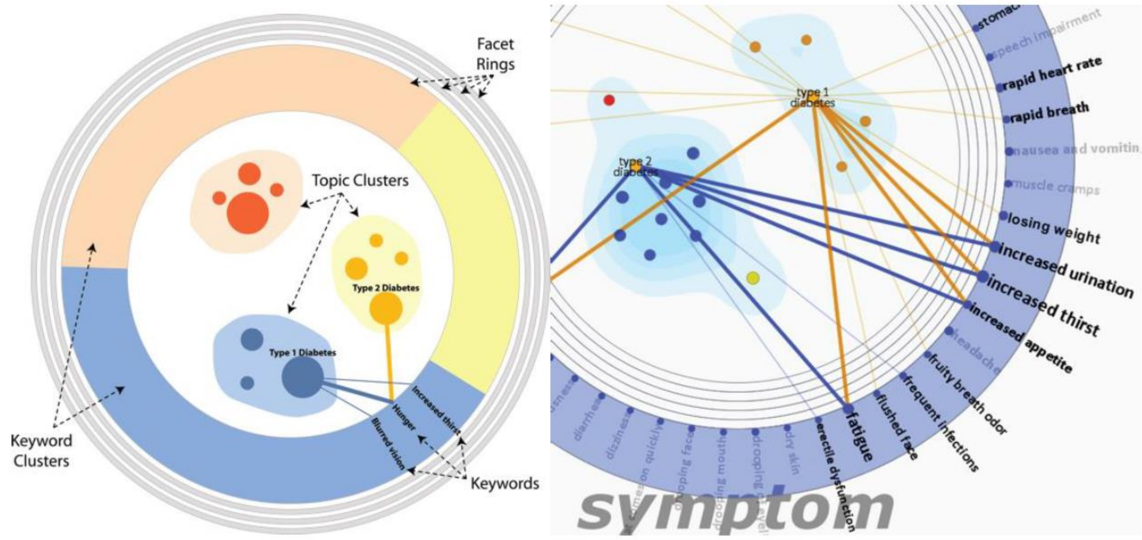

Figure 29: Visual Encoding of SolarMap.

Figure 30: DICON displaying 50 distinct five-dimensional patient clusters. The visual design of the icons makes it easy to determine which cohorts of patients are similar to one anotherVisual encoding for the DICON visualization technique. (a) Each individual entity is described by a feature vector. (b) The individual features are encoded using color-coded cells, which are packed together to form an icon for the entity. (c) Multiple icons can be grouped to form a cluster icon, which is shown in (d).

4.2.3.8 IHME data visualizations

The *Institute for Health Metrics and Evaluation* (IHME) [190] provides a set of visualization tools for the exploration and comparison of worldwide collected health data. The visualized data cover a wide range of communicable, maternal, neonatal and nutritional diseases, non-communicable diseases and injuries. The visualized information includes the number of cases for each health issue in different countries, years, people ages, sexes, etc. Visualization tools include line plots, pie diagrams, heatmaps, stacked plots, arrow diagrams, tree-maps and geographical maps. The user is able to interact with the various visualizations, both to retrieve information and to modify the parameters, such as the country displayed or the age range. The user is also able to simultaneously view different visualizations of the same data, or two diagrams of the same type, in order to compare between two values of a specified parameter. Such visualization and interaction concepts can prove valuable for the design of the FrailSafe visualization tools. Figure 31 and Figure 32 illustrate example visualizations using the IHME tools.

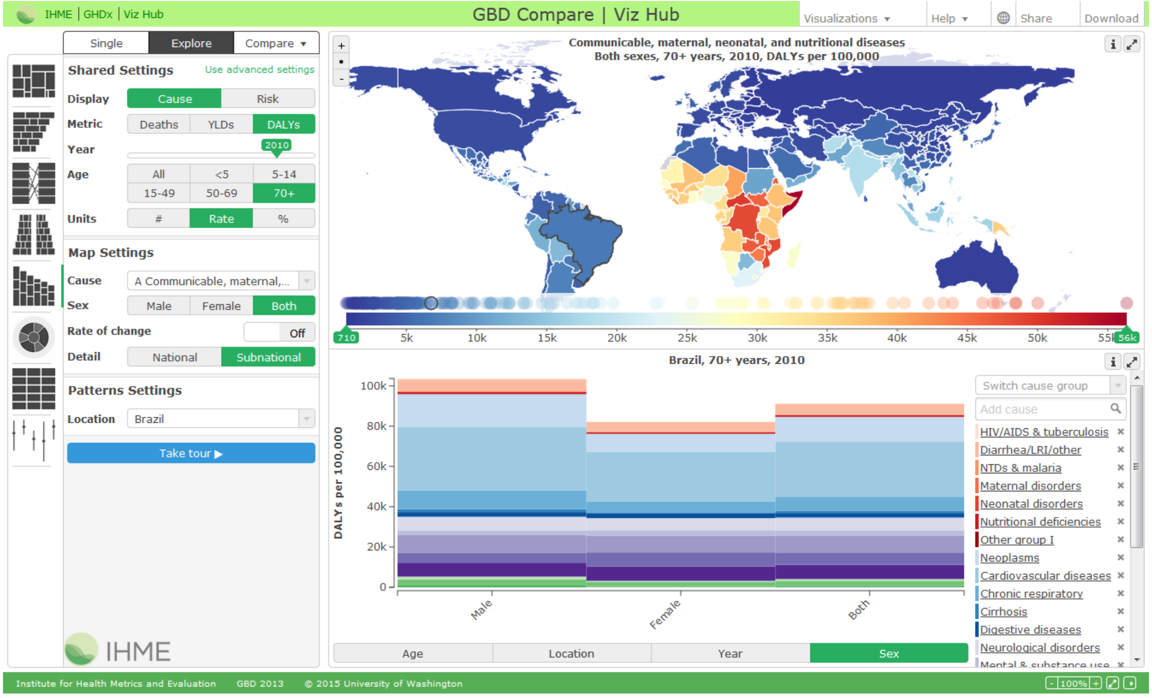

Figure 31: Multiple views visualization in the IHME visualization tools.

Figure 32: Comparison view of the IHME visualization tools.

4.2.3.9 GRACE

Geriatric Research in Ambulatory and Cognitive Excellence (GRACE) [191] is a visual analytics application specifically designed for the exploration of geriatric data. GRACE focuses on the facilitation of comparisons between multiple views of the available data. It supports two types of data: spatial ones, including *magnetic resonance imaging* (MRI) brain volumes, and non-spatial ones, including information such as age, gender and walking speed. As a pre-visualization step, GRACE employs data analytics techniques in order to discover connections and correlations between spatial and non-spatial geriatric data. GRACE is based on an interactive linked view design that allows the visual comparison of the multiple types of data and the generation of hypotheses regarding them (see Figure 33).

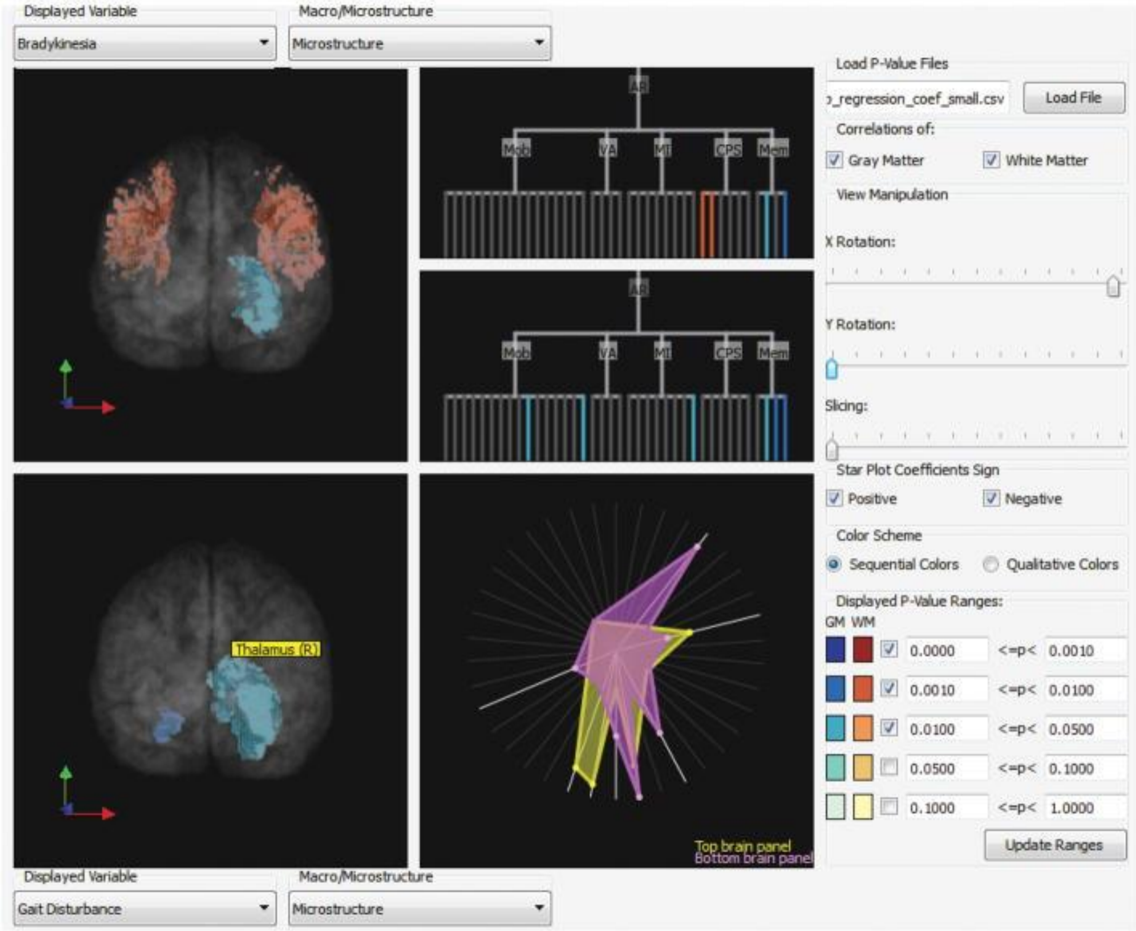

Figure 33: Screenshot of the GRACE visual analytics tool, depicting the multiple linked view design, showing spatial MRI data as well as non-spatial geriatric information.

4.2.3.10 Visual Analytics Platform

The Visual Analytics Platform (VAP) is an interactive tool developed by CERTH for the exploration of generic data of diverse types. It was originally developed for the purposes of visualizing and exploring data from mobile networks, under the name of *Mobile network Visual Analytics* (MoVA) [192], in the context of the EU project NEMESYS [193]. Since the end of the project, it has evolved into an application supporting any type of data, and has been used to visualize healthcare and biomedical data. The Visual Analytics Platform consists of four main functionalities:

- *Custom feature generation*
- *K-partite graphs visualization*
- *Multi-objective visualization*
- *Hypothesis formulation and validation*

VAP supports comma-separated value (CSV) files as its raw input, so that each line represents a record consisting of several attributes, as its columns. As a first step towards data visualization, VAP provides the operator with means to generate custom features from the raw data, by selecting specific columns of the raw data, combining them and extracting higher-level information from them, such as histograms. The operator can create more than one features, so that they can be used in combination in the subsequent visualizations.

The first of the two main visualization methods provided by VAP is the k-partite graphs visualization method (Figure 34), a method presented in [194] [195]. In this type of visualization, the features selected in the previous step are visualized as a planar k-partite graph, so that each vertex represents a value appearing in the selected columns and the edges connect values appearing in the same record in the input file. Force-directed placement methods are used to draw the graph on the two-dimensional screen. The k-partite graphs visualization allows the operator to quickly see which attributes, or sets of attributes, appear most often, by observing the amount of edges connecting the vertices to each other. The most common patters in the data tend to form clusters of vertices, thus providing useful insight to the operator. Properties of the vertices, such as the number of edges connected to them or the specific column of the raw file that they belong to, are also mapped to visual properties of the graph vertices, such as their size and color.

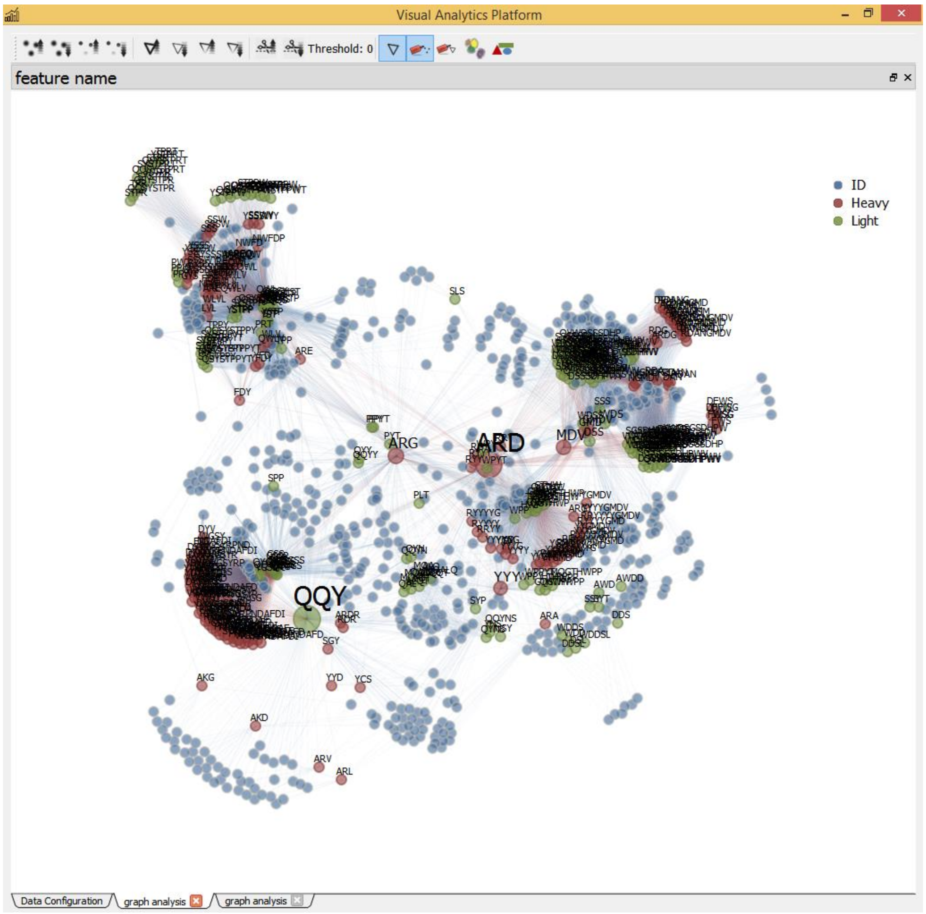

Figure 34: Example of the k-partite visualization method of VAP.

The other main visualization method of VAP is the multi-objective visualization method (Figure 35), which utilizes the method presented in [196] [197]. In multi-objective visualization, a set of entities is visualized as a set of points, so that points that are close to each other correspond to entities with similar characteristics. Which characteristics will be used as the entities or for the definition of the similarity are selected by the operator. In multi-objective optimization, each entity is described by a set of feature vectors, generated during the first step. Each feature vector type is used to define similarities among the entities, which are used to form similarity graphs among them. The multiple types of similarity are combined, in a multi-objective optimization manner, in order to provide a total graph that encodes the similarities among the entities. Similar to the k-partite method, the graph is drawn using force-directed methods. The final graph visualization is such that entities that are similar with respect to all feature types are placed close to each other, often forming clusters. The operator can select trade-offs among the feature types, in order to put more focus on one or another.

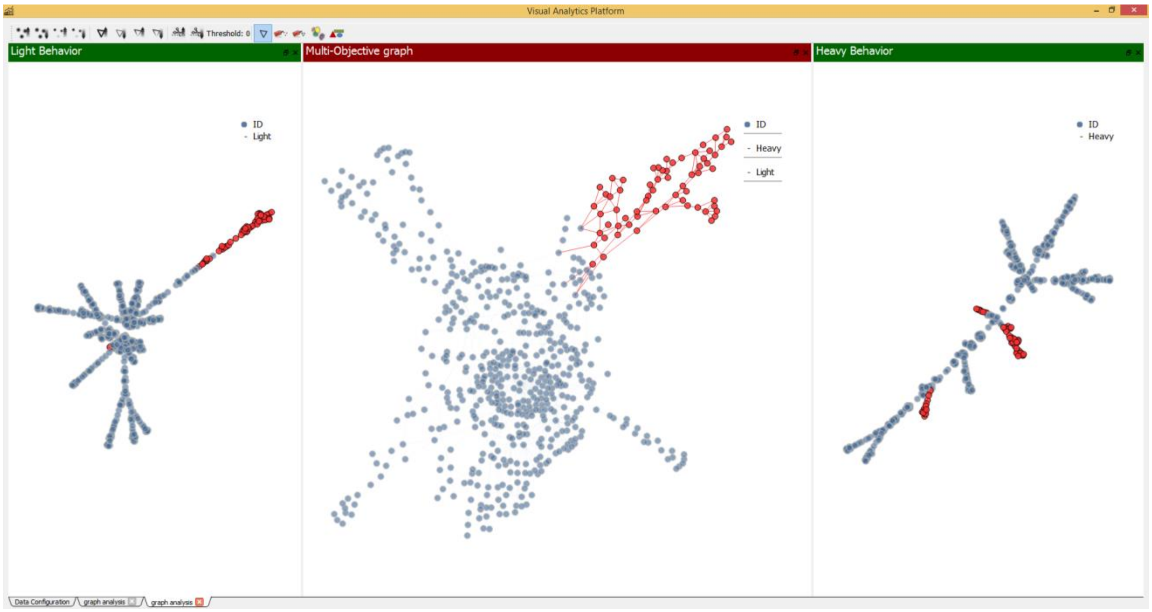

Figure 35: Example of the multi-objective visualization method of VAP.

The above main visualization tools are supported by interaction mechanisms, such as panning, zooming and brushing across several views of the same dataset. They are also supported by a hypothesis formulation and validation module. Using this functionality, the operator can formulate hypotheses regarding the data, such as selecting a set of them and suggesting that they belong to the same class, and the system automatically validates the hypothesis using in-built data analytics algorithms.

5 VIRTUAL AND AUGMENTED REALITY GAMES FOR FRAIL PEOPLE

5.1 Existing rehabilitation programs

Physical rehabilitation software tools have been in the market for short time. Before the release of the *Wii console* in the market, the use of body motion sensors was mostly restricted to the industrial market and for research. *Wiimotes* introduced the use of optical tracking, inertial sensors and pressure sensors are used on the Wii balance platform. The Wii console released in 2006 has been used profusely in rehabilitation therapy. Some of the standard games included with the console, such as *WiiSports* or *WiiFit*, already allow for some exercises relatively close to many of the required movements depending on the concrete rehabilitation area (see Figure 36). Microsoft and Sony have also included sensors in their pads, and in their games. But *Kinect* technology is probably one of the great steps to body motion tracking for the domestic market.

Figure 36: WiiSports example of use in rehabilitation.

Project/App	Sensing Device	Target Group
Nacodeal	Tablet + AR device	Older people
Dance! Not fall	Mobile devices	Older people with fall risk
Rewire	Kinect + Wii balance board	Persons with balance problems
Activa	Wii motes	Older people with Parkinson
Verve	Tablet + Immersive screen	Persons with risk of social exclusion
Exergaming	Kinect	Older people with balance problems
ElderGames	Custom large touch screen	Older people

Table 10: Summarization of serious games for older people.

On the other hand, *serious games, mental training*, and even *psychological treatment software tools*, for older people or not, have been researched and have reached the market before but without the use of natural interfaces. Here is a list with the most interesting rehabilitation games, based on 3D graphics and Virtual Reality (see Table 10: Summarization of serious games for older people.Table 10).

- *NACODEAL*[31] *- NAtural COmmunication DEvice For Assisted Living* [198] aims to improve the quality of life in older people as well as reinforcing the industrial fabric in Europe through the use of information and communication technologies. The project intends to provide new solutions to the difficulties arisen among older people when dealing with new technologies in their daily tasks or in the attempt to keep them involved in today's society by making use of them. A novel device gives older people with memory disorders the opportunity of enjoying an independent life, and at the same time through its interface gives them access to the digital world. In addition, the device is intended to project in the rooms where the user is (see Figure 37), the different instructions that can be of help with tasks using AR technologies.

Figure 37: Example of use of Nacodeal projection.

- *DDF*[32] *- Dance! Don't Fall* is an Android application that monitors the user's risk of falling while actively reducing it through fun exercise (see Figure 38). After the user performs choreographed moves, DDF gives feedback on their dancing performance and evaluates the risk of falling**.**

[31] www.nacodeal.eu

[32] http://dancedontfall.projects.fraunhofer.pt

Figure 38: Configuration interface of DDF on the smartphone.

The user wears the mobile phone on the lower back to track the dance steps (see Figure 39). The dance feedback has four dimensions, namely: accuracy, timing, stability and grooviness. For every dance, each dimension can be LOW, OK or HIGH. The fall risk evaluation is based on the quality of the locomotion and on additional clinical questionnaires that are suggested when a problem appears to exist. The application has three modes: 'Learn', 'Perform' and 'Compete'. The 'Learn' mode teaches users the dance steps and outlines the dance choreography. In 'Perform', users can dance along with the music by themselves. Finally, using 'Compete' users can challenge their friends in a group dance contest.

Figure 39: Game session on a big screen.

- *Activa*[33] is a project, developed by the Toy Research Institute (AIJU), which combines leisure activities with new technologies, enabling to improve both physical condition and social skills of Parkinson patients. Under this initiative, users employ the Wii console controls as an interaction tool what enables them to exercise the upper limbs, muscle tone and motor skills (see Figure 40). The

[33] http://activa.aiju.info

games have been developed to play collectively but also individually, fostering the socialization and communication between users.

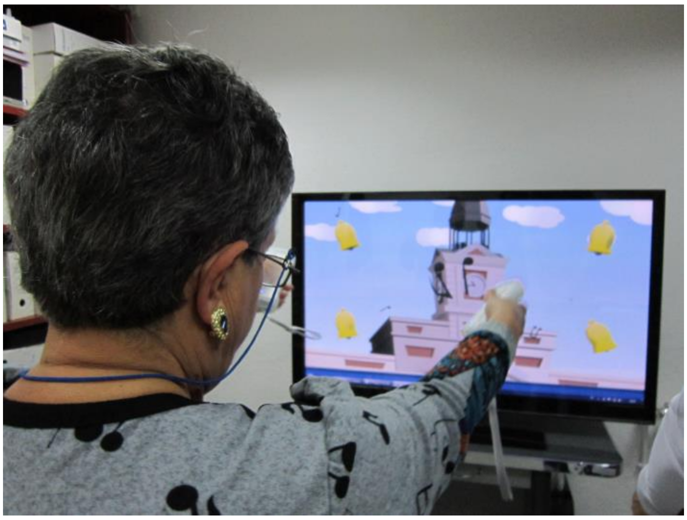

Figure 40: Game session on one of the Activa games.

- *Neumimic*[34] is a revolutionary and low cost physical therapy software program. It uses a Microsoft Kinect motion sensor to provide patients with accurate step-by-step instruction for at-home exercises with the purpose of assisting people affected by stroke during the rehabilitation process. The result is a sort of fancy videogame to allow therapists to set parameters for rehab therapy and allow the patients to follow through on them. Patients can improve their range of motion by seeing it tracked on a computer screen. One color on the screen indicates what therapists want the patient to work on during treatment. The other color shows a patient's progress to get closer to the other color on the screen and to improve the range of motion (see Figure 41).

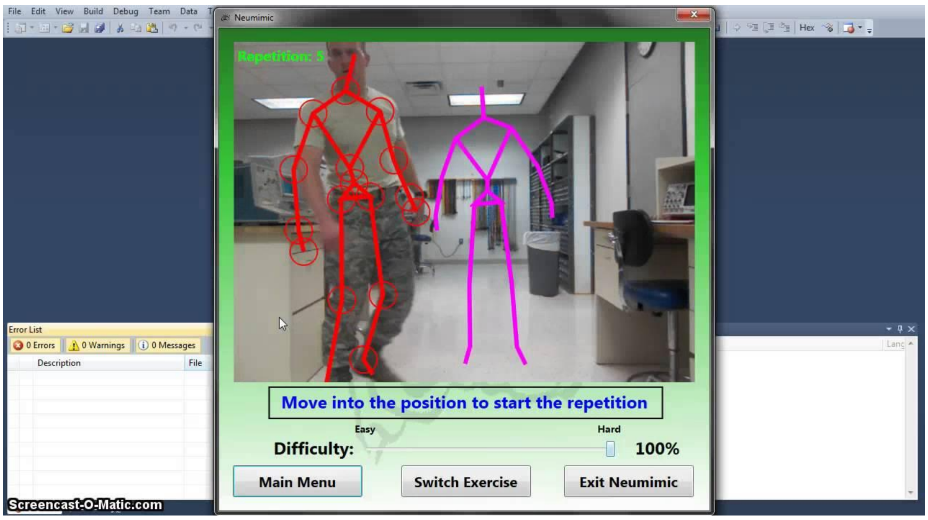

Figure 41: Rehabilitation session on Neumimic.

[34] http://startupcompete.co/startup-idea/business/neumimic/20828

- *Exergaming*[35] is a serious game in which the older people have to maintain their balance while shifting their weight from the left leg to the right leg in front of a Kinect (see Figure 42). The Kinect detects the movement of the player, and when executed correctly, the ice skater will start to move in-game. Along the way the players will have to dodge ice holes and duck for bridges to make the game more exciting. The results of the players will be saved and sent to their physical therapists or doctor. This way the attending physician can track progress. The game tries to save a lot of travelling back and forth to the hospital, doctor and/or physical therapist.

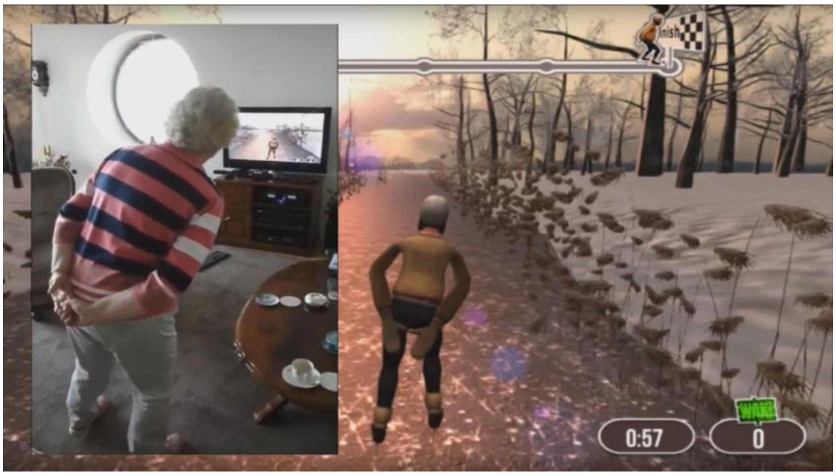

Figure 42: Exergaming game session.

- *VERVE*[36] is a research project, leaded by the Nice University Hospital that aims to support the treatment of people who are at risk of social exclusion, either because of fear, apathy and anxieties associated with ageing, or because of a neurological disorder by using a combination of new and existing scientific methods and computer technologies (see Figure 43). They are further hoping to help older people at risk of falling, persons with Parkinson's disease, Alzheimer's disease and memory problems, as well as those with phobias.

[35] www.8d-games.nl/exergame-ouderen

[36] www.innovation-alzheimer.fr/projets-en/verve-en

Figure 43: Verve's tablet game (left) and session on a large stereoscopic screen (right).

- *Rewire*[37] *- Rehabilitative Wayout In Responsive home Environments* [199] develops, integrates and field tests an innovative virtual reality based rehabilitation platform system based on a multi-level rehabilitation platform. The project pursues to create a Personalized Health System that can be deployed massively at the patients' homes, enable home-based effective rehabilitation to improve disabilities and functions. Is aimed at patients, discharged from hospital, who need to continue rehabilitation. The idea is to provide them the possibility of continuing the rehabilitation at home under remote monitoring by the hospital. The platform is constituted of three components:
  i. Patient station is deployed at patient's home. It guides the patient through the rehabilitation program by a set of mini-games shown on the TV screen (see Figure 44). Patient's motion is tracked by video based systems (hands-free paradigm) and the level of challenge is tuned to patient's current lifestyle measured with miniaturized with adequate dressed devices.
  ii. Hospital station is used at hospitals by the clinical staff to define the rehabilitation treatment by scheduling a program of exercises personalized to each patient, and monitoring the patient's progression through the analysis of the motion data sent back by the patient station.
  iii. Networking station collects valuable data related to rehabilitation while the patient is both in the hospital and at home.

[37] *https://sites.google.com/site/projectrewire*

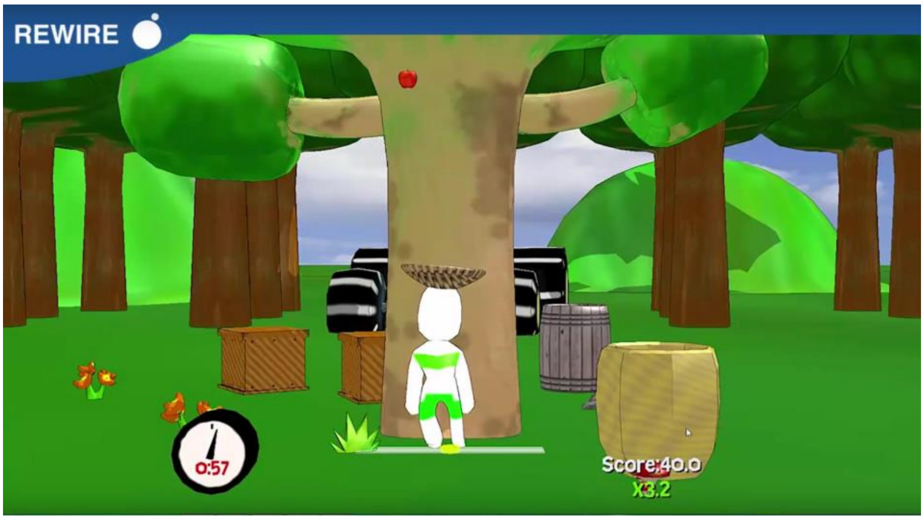

Figure 44: Rewire game session for balance improvement.

- *ElderGames*[38] [200] focus on the design and development of an application that explores how new and emerging advances in ICT can be adapted, applied and combined with play/leisure activities to improve the health (see Figure 45), welfare and quality of life for Europe's growing older adult population and, at the same time, provides those experts specializing in older people care and supervision, such as physiotherapists, physiologists, gym teachers, sociologists, etc., with an innovative application which they can use to monitor and to improve the quality of the care they deliver. ElderGames project intends to promote, through the creation of an easy-to-use IST platform, the communication between older people and their families across Europe by means of implementing an alternative and augmentative communication system able to overcome geographical and linguistic barriers.

Figure 45: ElderGames gaming session using the custom large touch screen.

[38] http://eldergames.brainstorm.es

5.2 User friendly interfaces and interactive environments

Both user interfaces and interactive environments need to be specially designed when they are intended for older people, both in terms of readability and ease of use. There are plenty of apps for smart devices which adapt their operative system interfaces, with bigger buttons, high contrast colors, or simplified interfaces (see Figure 46).

Figure 46: Android OS interface adapted for older people.

Without loss of generality, some popular examples are: *Necta Luancher*[39], *Seniors Phone*[40], *Fontrillo*[41], *Big Launcher*[42]. But once an application is running, mostly if it is based on a graphical user interface (GUI) library or on a game engine, these operative system adapting apps will not be of any use. Therefore FrailSafe developments will need to take into account the following premises:

Parameter	Usability Criteria
Buttons size	Buttons size has to main effects when displayed on touch screens. First, for older people, their visibility and the readability of their texts or images will inform better. But most important is the ease to click on them. The perspective when looking to a touch screen, makes difficult to point the finger exactly there the user wants to click. This problem is increased on older people and appropriate buttons size here solves the problem entirely.
Contrast	High-contrast interfaces help greatly readability. No complicated images should be shown on the screen's background. A dark background with a white text overlay will be better for older people with slower eye accommodation. On the other hand, a white background with black text will look better in direct sunlight. Yellow or white text over blue background has proven to be easy to read and comfortable after long sessions on the screen. User interfaces in FrailSafe will be checked for this.
Focus ease.	It has been observed in older people some difficulties when trying to focus fast

[39] http://launcher.necta.us/

[40] http://seniorsphone.mobi/

[41] http://www.fontrillo.com/

[42] http://biglauncher.com/es/

	moving objects. Thus, interface animations should be slow enough for them to perceive them properly. If not designed properly, the older people could reject the interface or simply not understand how their interaction takes place neither the feedback provided by the application.
Visual acuity (light interface)	This is another of the older people issues to be taken into account. Excessive accumulation of images on screen will difficult the user concentration. Age affects the eye capability to detect small details.
Font size and interface clarity.	All titles and labels should be large and easy to read. All items and navigation elements should be visible all the times; slide-out menus should be avoided. Icons shown on the interface should have text labels. Older people need to be very confident about what a button will do before they click on it. Users generally do not understand the meanings of icons when they are not accompanied by text. Text labels should be short, easily understandable and must not be abbreviated. They should be written in a recognizable language; for example, “today”, or “yesterday” will be clearer than a numeric date value. Only a limited number of items should be located in the menu (up to 7–8 items). Longer lists of items should be split into groups.
Quick and easy interface.	Basic navigation buttons, physical or virtual, should be visible at all times and the navigation model should be consistent across the entire interface. The structure of screens should be shallow; each complicated screen should have a descriptive label with meaningful instructions clearly displayed.
Audio feedback	Audio feedback confirms actions, allows for a clear feeling of interaction, and makes it faster and easy to navigate on the interface. Still sound should be short, loud, clear, non-obtrusive. Hearing can also get worse with age; older ears generally cannot detect very high and very low frequency sounds. All notifications should be louder, at least 10 dB above the background noise; 90 dB is the recommended sound value for seniors with age-related hearing loss (70 dB is the normal value for younger people).
Haptic feedback	Older people retain the ability to use fingertip contact for augmentation of body sway feedback despite reductions in their tactile sensitivity. In fact, older adults tend to show even greater efficacy of touch feedback for sway reduction than younger adults possibly due to greater sensory loss in distal parts of the lower extremities. Some benefits of the haptic feedback are: 1. *Private information*: haptic feedback is silent, non-visual, and individually communicated (not broadcast). 2. *Warning or alerts*: haptic feedback can be distinctive and unanticipated, helping users to re-focus their attention. 3. *Confirmations*: haptic feedback can provide intuitive verification of an action.

Interactive environments designed for older people also require to take into account very similar criteria.

Parameter	Usability Criteria

Visual acuity (simple scenarios)	In order to increase the immersion and the easy comprehension of the different elements present in a virtual environment, it should not be overloaded with models or complex textures. Objects need to be clearly defined, and interactive objects should be clearly defined.
Lighting and flares	Light affects perception of pictures, scenes and texts. It is observed that older people are more affected by glare. Fast changes in scenario illumination need to be taken into account and minimized, as they could affect gameplay.
Focus ease and visual accommodation	It has been observed on older people difficulty to perceive objects changing distance to the observer in a fast way. On virtual scenarios it will be desirable to analyse how the user will walk them and how the object will behave in order to avoid these rapid changes in position and distance on screen.
Depth perception	Depth perception is also reduced on older people. This situation needs to be taken into account, virtual elements should be placed clearly at different distances to guarantee that they will not become a problem regarding gameplay and usability.
Audio speech	Those instructions implying exhaustive explanations on activities to be carried out in the game, should be presented as text but also speech. Also audio speech could help understanding better different situations during the game.
Audio feedback	The aforementioned criteria for user interfaces applies in interactive environments.
Haptic feedback	The aforementioned criteria for user interfaces applies in interactive environments.

6 PERSONAL GUIDANCE SYSTEM

6.1 Modern personalised health support tools for frail persons

Modern information and communications technology, including the Internet and mobile phones, have become indispensable tools in most, if not all, sectors of modern society, including healthcare and providing a new method for using and manage health resources. Particularly, in the last decades there has been a growing interest in employing Information and Communication Technologies (ICT) to evaluate patients' functional impairments, as well as to help and support frail older people to be able to continue living at home, despite acute illnesses or a decline in functional ability, enabling them to maintain a good quality of life. ICT devices enable the patients' performances and actions to be captured in real time and real life situations and to be accurately evaluated. This is particularly important for domains such as cognition, motricity, eating and activities of daily living. As highlighted by the European Commission, the research must focus on the personalised health services and supportive eHealth infrastructure dedicated to chronic disease management for ageing and frail population [201]. Hereafter an overview of the current research and innovation activities and ongoing projects funded by the European Union that fit well with the context of FrailSafe project, is offered:

- ***ALFRED***[43] ***- Personal Interactive Assistant for Independent Living and Active Ageing*** [202], aims at developing a mobile, personalized assistant that helps older people stay independent, coordinate with their caregivers and foster their social contacts. The project is characterised by the use of innovative technologies such as advanced speech interaction in order to talk directly to the system. ALFRED will be user friendly and will provide context-sensitive services related to social inclusion, care, physical exercise and cognitive games.
- ***DOREMI***[44] ***- Decrease of cOgnitive decline, malnutRition and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion*** [203], focuses on three main health aspects related to frailty in older people: unhealthy nutrition, sedentariness and cognitive decline. Based on these health aspects, DOREMI environment is made up of a context-aware and smart system able to learn and reason about older people, their intentions, preferences and aims. Then, the system is able to provide feedback and propose solutions to improve frail older person lifestyle thanks to the specialist that will be able to select and assign a personalised lifestyle protocol that will be associated to a set of game typologies such as cognitive games, social games or exergames. Consequently, the old person will be able to select the game scenario which best corresponds to personal preferences and habits and the system, thanks to the loop monitor – learn, will understand how the old person evolves according to the compliance of the assigned protocol.
- ***MIRACULOUS-LIFE***[45] ***- Miraculous-Life for Independent Elderly Living*** [204], deals with the design development and evaluation of an innovative user-centric technological solution, the *Virtual Support Partner* (VSP), in order to support the older people (65+) in daily activity and safety needs. The main characteristics of the project is an avatar interface: an electronic and digital

[43] http://alfred.eu/

[44] http://www.doremi-fp7.eu/

[45] http://www.miraculous-life.eu/

person that older people can connect with. A crucial asset of the VSP will be its capacity for behavioural and emotional understanding. Thanks to its Avatar-based interface, the VSP is able fuse facial expressions, intonation, gestures and other contextual information of the user's environment to provide empathic responses and services. MIRACULOUS-LIFE provides ICT services to support daily activities stimulating and motivating older people to stay active prolonging their independence and improving their wellbeing.

- ***MobiGuide***[46] ***- Guiding patients anytime*** *everywhere* [205] has developed a Decision Support System (DSS) which access to the patient's' historical clinical data, analyses the data and alerts the patient about actions that should be taken. Furthermore, the system also makes recommendations regarding lifestyle changes or contacting caregivers.
- ***PERSSILAA***[47] ***- PERsonalised ICT Supported Service for Independent Living and Active Ageing*** [206], is a multimodal service model focusing on nutrition, physical and cognitive function. It is supported by an interoperable ICT service infrastructure, utilising intelligent decision support systems and gamification in order to support the users to maintain and/or improve the function mentioned above through three modules: healthy nutrition, physical exercise and cognitive function.
- ***FILANTROPOS - Fostering independent living in the aging population through proactive paging*** [207], is a self-funded on-going project, aiming at fostering independence and autonomy in older people without or with early clinical signs of frailty symptoms such as dementia, by improving their working memory and prospective memory capacity through the adoption of assistive smartphone technology. From a technological point of view, the project aims at leveraging the recent developments in mobile and context-aware computing to be able to provide "smart" suggestions to individuals by automatically analysing their environment and recognizing locations and time frames that are well suited to the completion of user's tasks.

It is interesting to note that the strongest relations and the closest synergies between the above mentioned projects and FrailSafe project come from *DOREMI* and *ALFRED* projects. Thanks to their outcomes, especially the ones related to multidisciplinary research areas (i.e., Sensors Network, serious games, activity recognition, advanced speech interaction technologies, etc.), and similarities in the adoption of cutting edge technologies and users' target, FrailSafe can be seen as their natural completion. Also *FILANTROPOS* seems to have relation with FrailSafe project; it can be seen as a tool able to monitor the patient's working memory in order to verify if frailty symptoms appear.

6.2 Mobile and cloud based interfaces, allowing the follow up of patient's clinical status

With the development of technologies such as mobile computing, wireless sensor networks, and Web server cloud computing, the required medical care and medical consultation can be provided easily and remotely. Particularly, cloud computing and associated services are changing the way in which we manage information and access

[46] http://www.mobiguide-project.eu/

[47] https://perssilaa.com/

data and eHealth services are keen about novel technologies, especially those that involve mobile devices. Furthermore, mobile networks are considered critical for solving future global health challenges [208] while the global market penetration of the mobile phones makes the mobile healthcare system (mHealth) a matured idea now, as Figure 47 shows, highlighting the evolution from eHealth to mHealth. Nowadays the integration of mobile interfaces and cloud infrastructure are transforming the healthcare environment proving new opportunities for their integration into the existing and well-known eHealth services enabling both remote healthcare monitoring and data collection.

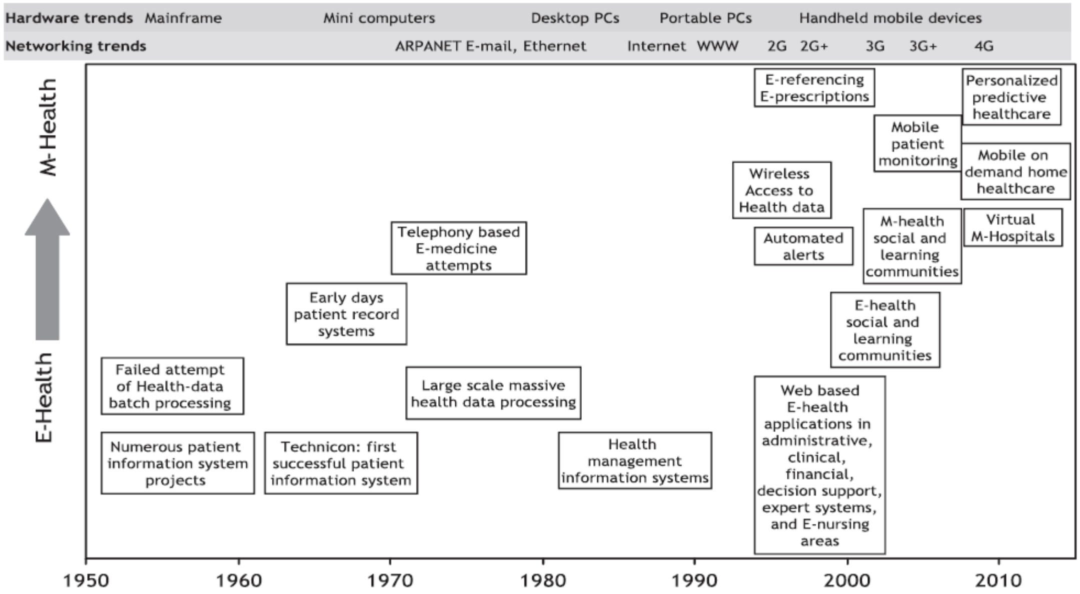

Figure 47: Evolution from eHealth to mHealth [209].

The scientific and commercial literature report on a number of cloud-based mHealth applications demonstrating they are largely available in various clinical contexts from wellness to chronic disease management, follow up clinical status and disease with high complexity care needs proving that:

- mobile devices are replacing paper medical charts
- clouds are enabling secure access to medical records
- mobile cloud collaboration tools are improving information sharing among medical professionals and patients

Hundreds of applications have already been developed to address specific health needs; particularly, *mobile health apps* can help to monitor health conditions, track medication schedules, locate a hospital or doctor, stick to a healthier lifestyle, and get access to various types of health information[48]. Particularly, mHealth applications have been grouped as: *chronic disease management*; *management and access of health personal data*; and *sports and wellness support*.

In the FrailSafe context, chronic disease management as well as management and access of health personal data are the two groups of main interest. To this end, we report on the current advances in the area of:

1. chronic disease management,

[48] http://www.myphr.com/Resources/mobile_PHRs.aspx

2. management and access of health personal data.

6.2.1 Chronic disease management applications

Patients with chronic disease are personally responsible for their own day-to-day care, and are often the first to monitor the severity of their symptoms and the efficacy of related treatment. ICT in the management of chronic diseases includes telemedicine, telehealth (nowadays, eHealth and mHealth) and home telecare. Hereafter the most significant projects and solutions that seem to be compliant with the sensitive requirements that must fulfil in the design and development of this kind of applications:

- ***Zappa*** [210] presents an extensible, scalable, highly interoperable and customizable open mobile platform designed to develop several remote mobile monitoring mHealth systems.
- ***DECIPHER*** [49] ***- Distributed European Community Individual Patient Healthcare Electronic Record*** [211] creates a mobile health care solution enabling secure cross-border access to existing patient, with chronic long-term conditions, to healthcare portals.
- ***MoCAsH - Mobile Cloud for Assistive Healthcare*** [212], is an infrastructure for assistive healthcare that embraces important concepts of mobile sensing, active sensor records, and collaborative planning by deploying intelligent mobile agents, context-aware middleware, and collaborative protocol for efficient resource sharing and planning. Data collected by the sensors such as body temperature, pulse, motion and time, are analysed and processed by an intelligent context-aware middleware.
- ***StatDoctors***[50] is a telemedicine service that offers mobile "*eVisits*" to doctors through mobile device technology. It provides an overview of what their service entails through an interface that is easy to navigate through.
- ***Doctor on Demand***[51] and ***Ringadoc***[52] are two of many mobile applications that allow patients to speak to a physician via phone or video chat. Note that although video-chatting functions do not allow doctors to physically provide their services in person, telemedicine has also shifted towards the video-chatting technology on mobile devices to offer quick services.
- ***Entra's MyHealthPoint***[53] is a suite of mobile and cloud based technology solutions and services for remote patient monitoring, telehealth and health data exchange. MyHealthPoint collects real time patient data (blood glucose, blood pressure, ECG, weight, activity, temperature, etc.) and uploading them to the cloud-based MyHealthPoint platform, stored in a secure and encrypted cloud-based database compliant with the HIPAA protocols for data aggregation, reporting and analysis.
- ***mHealth Alert***[54] is a chronic care management platform (HIPAA compliant) to control the health status of a patient in real time and take action

[49] http://www.decipherpcp.eu/

[50] http://statdoctors.com/

[51] http://www.doctorondemand.com/

[52] https://www.ringadoc.com/

[53] http://entrahealth.com/

[54] http://www.mhealthalert.com/chronic_care.html

accordingly. Particularly, mHealth Alert collects, analyses and consolidates biometric data from multiple telemedicine devices assigned to each patient (pulse oximeter, spirometer, blood pressure monitor, weight scale) and delivers alerts and notifications to physicians or professional caregivers' mobile devices or PCs for immediate and responsive care improving patient engagement and therapy adherence.

6.2.2 Management and access of health personal data

Demand for patient access to personal health records is growing faster. The model for this record is a repository of all clinically relevant health information kept securely and viewed privately by patients and their health care providers. However, this type of record doesn't seem to have beneficial effects for the primary stakeholder, the patient, but only for the relationship among patient and medical doctor (physician).

Hereafter, the applications that the State of the Art suggests as the most interesting, useful and easy to use from the patient point of view:

- ***MyHyppocrates***[55], a cloud-based platform that allows sharing of data between patients and doctors easily and securely, assuring a better use of health data to improve patients' medical treatment, and connection with third-parties' health devices such as monitoring tools or diagnosis instruments. It also provides a follow-up patient's app that allows for a better follow-up of patients suffering from chronical diseases or in convalescence. The patient can fully access to their data and share them with doctors and he/she can add data for self-monitoring.
- ***eHealthMonitor***[56] [213] provides a platform that generates a Personal eHealth Knowledge Space (PeKS) as an aggregation of all knowledge sources (e.g., EHR) relevant for the provision of individualized personal eHealth services.
- ***PatientsLikeMe***[57] is an online community built to support information exchange between patients. The platform provides customized disease-specific outcome and visualization tools to help patients understand and share information about accessing personal health information and sharing it within patient-to-patient dialogues.

6.3 Existing cross-platform infrastructures with physiological and behavioral sensors

The Medical Dictionary Online[58] defines patient monitoring *"…as the continuous or frequent periodic measurement of physiological processes such as blood pressure, heart rate or respiration rate of a patient*". Nowadays, there exists a variety of terms for the use of ICT in patient monitoring: *telemonitoring*, *remote patient monitoring*, *wireless patient monitoring* and *mobile patient monitoring*. Wireless network technologies so as sensors, are essential for the mobile patient monitoring. An interesting example of monitoring platform is the Personal Health Monitor (PHM) system; it has been designed for patient who have a suspected cardiovascular disease and need to be monitored around the clock. The PHM system proposes use of off-the-shelf sensor systems,

[55] http://myhippocrates.eu

[56] http://www.ehealthmonitor.eu/

[57] https://www.patientslikeme.com/

[58] http://www.online-medical-dictionary.org/

which incorporate a built-in sensor front end. This approach allows a PHM system user to use their own mobile phone running Microsoft Windows and to buy or rent the required sensors as illustrated in Figure 48.

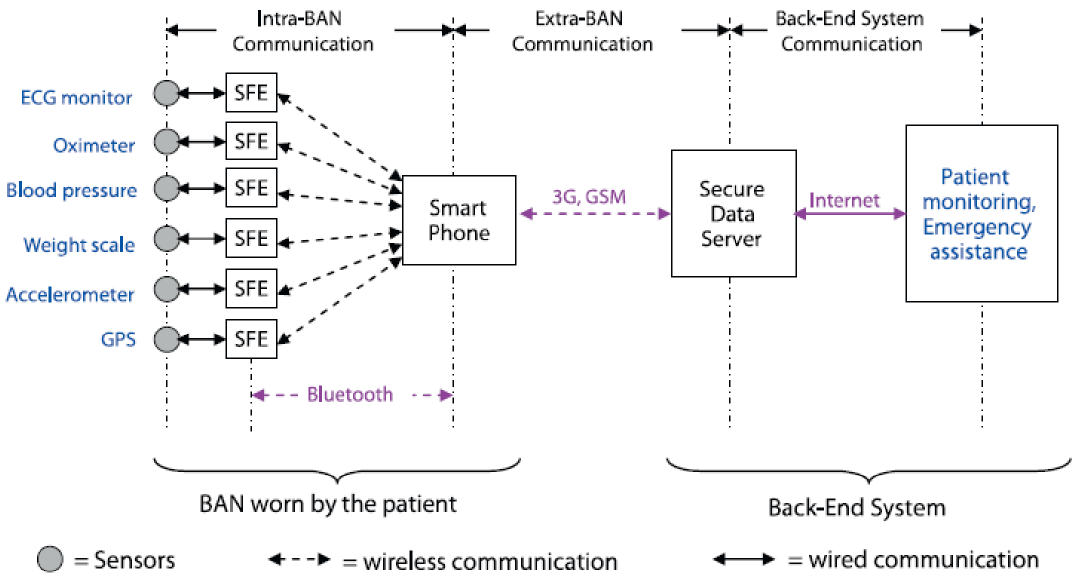

Figure 48: PHM Architecture Overview [209].

The currently key enabling technologies for patient monitoring in terms of physiological and behavioural parameters are sensor technology, particularly wearable technology, associated with communication technology and data analysis techniques (see Section 3). Applications of sensors systems (i.e., wearable, ambient sensors, etc.) deal with health and wellness, safety, home rehabilitation, assessment of treatment efficacy, and early detection of disorders. Furthermore, the integration of wearable and ambient sensors could provide ICT platforms able to provide physiological monitoring, to help in both diagnosis and ongoing treatment of a vast number of individuals with chronic diseases, home-based motion sensing, to assist frail persons in daily activities maximizing their independence and social/community participation. Hereafter, some research projects and products are synthetically described.

- ***inCASA***[59] ***- Integrated Network for Completely Assisted Senior citizen's Autonomy*** [214] aims at help and protect independent older people, prolonging the time they can live well in their own home by increasing their autonomy and self-confidence. It reuses pre-existing solutions/services for human/environment monitoring, integrated in order to collect and analyse data in order to profile user habits and implement customized intelligent multilevel alerts/communication services.
- ***AMON - Advanced care & alert portable tele-medical MONitor*** [215] developed and validated a wearable personal health system that will monitor and evaluate human vital signs using advanced bio-sensors. The system gathers and analyses the vital information and further transmits the data to a remote telemedicine centre, for further analysis and emergency care using

[59] http://www.incasa-project.eu/

GSM/UMTS cellular infrastructure. The Wrist-mounted Monitoring Device includes sensors such as heart rate, heart rhythm, 2-lead ECG, blood pressure, O2 blood saturation, skin perspiration and body temperature.

- ***wHealth*** [216] is a platform for the monitoring of various physiological, physical and behavioural parameters, enabling effective communication between patients and clinicians.
- ***Hi Health***[60] is an ecosystem where health and care patient data are gathered from wirelessly connected sensors and biometric devices. Three services characterize the platform: 1) *Telecare* provides services for the safety and wellbeing of patients; 2) *Telehealth* provides constant monitoring of a user's condition enabling better and more focused treatment of the patient's health; 3) *Remote Diagnostics* connected to the Remote Diagnostic cloud platform, in order to perform health check making the results of the test immediately available to doctors via the internet, allowing the remote examination and diagnosis.
- ***Cisco Open Platform for Safety and Security***[61] provides a system to prevent, prepare for, respond to, and recover from incidents through: quantitative sensors, qualitative sensors, human identification (biometrics), object identification, actuators, real-time analytics, sensor fusion, correlation, and baselining, legacy integration, common operational picture.
- ***EMERGE Emergency Monitoring and Prevention***[62] main goals are: immediate detection of an emergency, early recognition of a problem, its nature and its sensitivity, and emergency prevention by early detection of changes in behavioural pattern. Health parameters (pulse rate and skin temperature) are acquired using sensors integrated into a wrist wearable device, while location tracking information are acquired by RFID carpets, Ultra Wide Band (UWB) sensors, ultrasonic and infrared presence sensors.

Hereafter a list of interesting products and projects leading applied sensor infrastructures (wearable, smart phone, and ambient assisted living based sensors) and aiming at general health monitoring of people in the home and community settings, is proposed:

- ***Medisana*** (***VitaDock Online developed by Kaasa***[63]), is a cloud based solution, connecting health devices by Medisana, to maintain and exchange vital data of individuals in a safe and secure fashion. Currently, the platform is used by 120.000 registered users residing within Germany, the Netherlands, France, Italy and other European countries. From the functionality point of view VitaDoc by Medisana allows to save, view, analyse and export the personal vital data like blood pressure, blood glucose, body temperature, weight and activity;

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[60] http://www.roadtosmartlife.it/ada/images/stampa/RTSL-SanterReply-HomeCare-Assistance.pdf

[61] http://www.cisco.com/c/dam/en_us/solutions/industries/docs/gov/COPSSSensingandActuation_wp.pdf

[62] http://cordis.europa.eu/project/rcn/80505_en.html

[63] https://cloud.vitadock.com/

- ***iStopFalls***[64], which main objective is to develop and implement an ICT-based technologies which can be easily integrated in daily life activities of older people living at home, allowing continuous exercise training, reliable fall risk assessment, and appropriate feed-back mechanisms, based on discreet measuring technologies and adaptive assistance functions;
- ***iCARER***[65]**,** is a platform able to provide an environment where the older adult's activities of daily living are unobtrusively monitored, in order to supervise their performance and detect possible problems, using personal and environment sensors. Particularly, the sensors employed in the monitoring environment (motion sensors, room occupancy, bed sensors, electrical appliance usage sensors, etc.) are distributed in the older adult's home and transparently register the actions that she/he performs. Data from these sensors together with the results of questionnaires can then be analysed to identify tasks that generate stress or activities that are potentially problematic.

64 http://www.istoppfalls.eu/cms/front_content.php

65 http://www.icarer-project.eu/

7 CONCLUSIONS

In this deliverable, we have provided the baseline definitions and representations as well as we have reported on the current advances, solutions and methodologies in the specific areas related to this project. FrailSafe will contribute significantly in a multitude of scientific and technological facets pushing the boundaries of current care delivery systems for older people by developing innovation techniques beyond state-of-the-art for each of the aforementioned fields by providing real time monitoring of physiological, behavioral and social parameters; ensuring adherence to pharmacological treatments; and finally offering innovative therapies based on AR games for maintaining/enhancing their cognitive and motor functionalities. Without loss of generality, such research and technology contributions will also be applicable for generic next-generation remote healthcare methodologies.

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