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Author(s):	Oberdan Parodi, Maria-Aurora Morales, Jonica Campolo, Franca Giugni, Federico Vozzi (CNR-IFC); Enrico Calcina, Sabrina Vincenti, Gianfranco Angelo Bedin (SI4LIFE); Rachael Dutton (Accord); Rowland Sandys (Extra)
Contributor(s):	Michela Rial (CNR-IFC), Francisco Lupiáñez-Villanueva (UOC); Antonio Ascolese (IMA)
Reviewer(s):	Mark Scase (DMU)

*Dissemination Level:
PU=Public
PP=Restricted to other program participants (including Commission Services)
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CO=Confidential, only for members of the consortium (including Commission Services).

**Nature of Deliverables:
R=Report
P=Prototype
D=Demonstrator
O=Other

Abstract

The deliverable D2.1 "Target users and scenarios of use" is focused on a literature analysis of the three impairments in elderly people, under evaluation in DOREMI project: Malnutrition, Sedentariness and Cognitive Decline. These are described respect to effects and/or relation with a series of co-morbidities as cardiovascular impairments, metabolic alterations (type 2 diabetes and metabolic syndrome), osteoporosis and cancer. Furthermore, the major parameters for evaluation of the impairments are reported, according to the literature analysis. These parameters, together with Inclusion/Exclusion criteria, will be the base for the DOREMI user selection. Finally, a section is dedicated to useful inputs for WP5 game environment development.

Keywords

Ageing, Malnutrition, Sedentariness, Cognitive Decline, Cardiovascular disease, Metabolic alteration, Cancer, Osteoporosis, Functional Scales, Social interaction, Gamification.

LIST OF BENEFICIARIES

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1	Consiglio Nazionale Delle Ricerche	CNR	IT	1	36
6	The Extracare Charitable Trust	Extra	UK	1	36
10	SI4LIFE – Scienza e impresa insieme per migliorare la qualità della vita scrl	SI4LIFE	IT	1	36
11	Accord Housing Association Ltd	Accord	UK	1	36

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0.9	DMU	Final revision of the document and suggestions	22/04/2014
1.0	CNR-IFC	Final refinement, submission	24/04/2014

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1. ABBREVIATIONS

AD = Alzheimer Disease

BBS = Berg Balance Scale

BIA = Bio Impedance Analysis

BMI = Body Mass Index

BP = Blood Pressure

CAD = Coronary Artery Disease

CO = Cardiac Output

CPM = Count Per Minute

CVD = Cardio Vascular Disease

EPIC = European Prospective Investigation into Cancer and Nutrition

EUNAAPA = European Network for Action on Aging and Physical Activity

FPG = Fasting Plasma Glucose

HDL = High Density Lipoprotein

HF = Heart Failure

HR = Heart Rate

IL = Interleukin

IU = International Unit

LDL = Low Density Lipoprotein

LV = Left Ventricular

MCI = Mild Cognitive Impairment

MUFA = Monounsaturated Fatty Acids

NCD = Non-Communicable diseases

NT-proBNP = N-terminal pro-hormone of Brain Natriuretic Peptide

PA = Physical Activity

SFA = Saturated Fatty Acid

TNF-alpha = Tumour Necrosis Factor alpha

UDH = Unhealthy Dietary Habits

WHO = World Health Organization

2. EXECUTIVE SUMMARY

The deliverable D2.1 titled “Target users and scenarios of use” describes the three impairments, Malnutrition, Sedentariness and Cognitive decline in elderly, under analysis in DOREMI project, and their relation with a series of diseases that can make worse the health condition of elderly population.

Initially, a literature analysis focused on the three impairments, is described. For all of these their effects and/or relations with cardiovascular impairments, metabolic alterations (type 2 diabetes and metabolic syndrome), osteoporosis and cancer are taken in account. Literature shows how these main areas of interest have a heavy influence in the development diseases. Furthermore, a literature analysis was conducted to evaluate the most recent an important published studies addressing the need of a well targeted user definition for the preparation of the Active Ageing Lifestyle protocol, carried out in Task 2.2.

In the second section, the deliverable is centred on the set of parameters and scales useful for evaluation of each impairment level in elderly people. The target user needs will be identified in terms of mobility characteristics in house and outdoor, the most common daily and leisure activities, the habits in the living ambient, the choices of housing features to meet the particular needs of elderly population with respect to the differing health and physical characteristics. The described parameters are included in Inclusion criteria that, together with Exclusion criteria (paragraph 7.2), are fundamental for the selection of users for DOREMI protocol treatment. A scenario of use is also presented.

Finally, a paragraph is dedicated to the inputs definition necessary for games environment development, forecasted activity of WP5, necessary to facilitate the easy personalization of the game scenarios according to different end user categories.

3. INTRODUCTION

All countries in Europe are experiencing an ageing of their populations, with a decrease in the number of people of working age per retiree. By 2050, an estimated 35% of the European population will be over the age of 60, compared to 20% in 2005, especially among those above 80 years. Health trends among the elderly are mixed: severe disability is declining in some countries but increasing in others, while mild disability and chronic disease are generally increasing. As a consequence, long-term care costs are certain to increase with the ageing of the population unless appropriate measures are implemented in time. Population ageing will not inevitably lead to significantly higher health care expenditure if appropriate measures are implemented and elderly people empowered to follow them. Effective measures should reduce the risk factors linked to functional decline and chronic diseases, provide personalized training and educational formats able to communicate strategies for getting *elderly people* a continuum part of the today's life, in order to maintain their active contribution to development activities in the respect of dignity and safety due to their ageing. A fundamental role in preservation of a healthy state is represented by the promotion of an active lifestyle in elderly, focused on physical activity, balanced nutrition and cognitive exercise: this approach, aging on well-being, can reduce and postpone the natural psychological decline in older people.

Prospects for healthy ageing are characterized at first by "a proper nutrition"; evidence-based strategies have been proposed to improve quality of dietary habits, through appropriate protocols which consider needs linked to specific cultures, environmental and lifestyle habits. This approach must be considered not only in the way of promoting a daily *food-based guideline*, but also in the way of empowering knowledge on components of foods, about which little is known. As a matter of fact, a correct knowledge of food's components, rather than prescriptions of multivitamin and mineral supplementation, can result in lowering major health diseases affecting elderly people, either in primary or secondary prevention.

Furthermore, no human age can have more benefits than elderly from fighting sedentariness with regular exercise.

Research and trials provide specific recommendations on living an active daily life, physically correct, that include exercises that empower endurance and flexibility, strengthen muscles, and improve balance. These long term recommendations prevent all typically age-associated diseases including hypertension, cardiovascular diseases, diabetes (NIDDM), mainly if joined to a healthy nutrition.

Concerning the age-associated loss of body protein and decreased bone density, strength training and muscle mass reinforcement play a role in active prevention, when specific and calibrated programs, targeted to specific conditions of each elderly person, are adopted.

No human age can have more difficulties than elderly in making regular physical activities outdoor: it will be of primary importance to reduce sedentariness at home, empowering people of an active daily life even in their own houses.

Increasing interest in problems regarding sedentariness and malnutrition as risk factors for chronic diseases has been seen, and the two impairments have been linked to **cognitive decline**. **Unhealthy dietary and sedentary habits** influence cognitive decline, which in turn has a relevant impact on the independence and the autonomy of elderly people, playing a primary role in progressive further removal of a well balanced diet and regular physical activity. As a matter of fact, older adults may have more difficulties in following correct lifestyles, as well as memorizing new concepts and changing their habits, with consequent generalized decline. Measures and lifestyle protocols able to synergistically act against these three impairments can prevent or delay a systemic deterioration of health and quality of life, restoring the previously lost well-being.

Lifestyle interventions addressing the three impairments may become **effective therapies** in elderly people, leading to increase participation and engagement in everyday life, with the vision of reducing contemporary physical, nutritional and cognitive decline.

4. REVIEW AND LITERATURE ANALYSIS

The preparation of the Active Ageing Lifestyle protocols will start from the review and analysis of the most important studies addressing the need of elderly people at risk of malnutrition, sedentariness and cognitive decline, the main conditions affecting the quality of life of elderly people.

Whereas literatures provides an unique concept of sedentary life and cognitive decline, according to the WHO (World Health Organization), malnutrition means “badly nourished” and this concept is a broad term which refers to both **under-nutrition (sub-nutrition)** and **over-nutrition,** resulting in an abnormal body mass index (BMI). In both conditions it is unhealthy dietary habit that usually causes lack of “metabolically useful” food, or limited consumption of foods that provide inadequate amount of specific needs, e.g. proteins, dietary fibres, micronutrients or, conversely, an excessive intake of food or unhealthy food that results metabolically unsustainable [1].

Epidemiological studies show us that both these **Unhealthy Dietary Habits (UDH)** can influence cognitive decline: the unbalanced intake of food, vitamins, lipids, minerals, antioxidants, micro and macro nutrients can increase the risk of this major impairment in the quality of life in the elderly, being crucially involved in the correct brain functioning [2-7].

Ageing arrives with health and functional changes joined to a decline in many body functions: a radical change in structure, a change of percentages in composition of our body masses, and age-associated loss of body protein (the specific muscle mass) - sarcopenia - a direct cause of a decrease in muscle strength [8-10].

Fighting a sedentary lifestyle seems to be the obvious answer, and not only for the improvement of this last factor in HRQL (Health Related Quality of Life). Specific literature, examining young and middle-aged subjects, demonstrated that important body fat parameters and aerobic capacity were not related to age but to the *total number of hours the subjects were exercising per week*: these results are very important in the determination of body fat accumulation too [11,12].

Increasing physical activity is a crucial strategy for improving both health and quality of life of the elderly in which **malnutrition**, **cognitive decline** and **sedentariness** result as dependent variable conditions [13-15].

Nowadays, the recent literature is unanimously affirming that dehydration - the adverse consequence of inadequate water intake in the dietary habits of the elderly - is to be controlled: as a matter of fact is strictly proved how a dehydration level can increase several damages involved in the cognitive function enough to make this parameter a reliable predictor of progressive decline. As far as the dehydration concept is concerned, it is physiologically linked to the decline in lean body mass, accompanied by a decrease of water in the elderly body: it becomes of primary importance increasing the percentage of lean body mass [16].

In simple words, older adults are at risk of dehydration due to reduced fluid intake and increased fluid loss and with ageing there is a reduction in renal concentrating capacity in response to the lack of water that contributes to the blunted capacity of the elderly to defend themselves against dehydration [17,18].

As far as the analysis of recent literature is concerned, **malnutrition**, **cognitive decline** and **sedentariness** are the three major impairments affecting the quality of life of elderly people. When at least two are present, these able to generate a wicked synergy among them.

The DOREMI project targets these three conditions affecting the quality of life of elderly people (Figure 1).

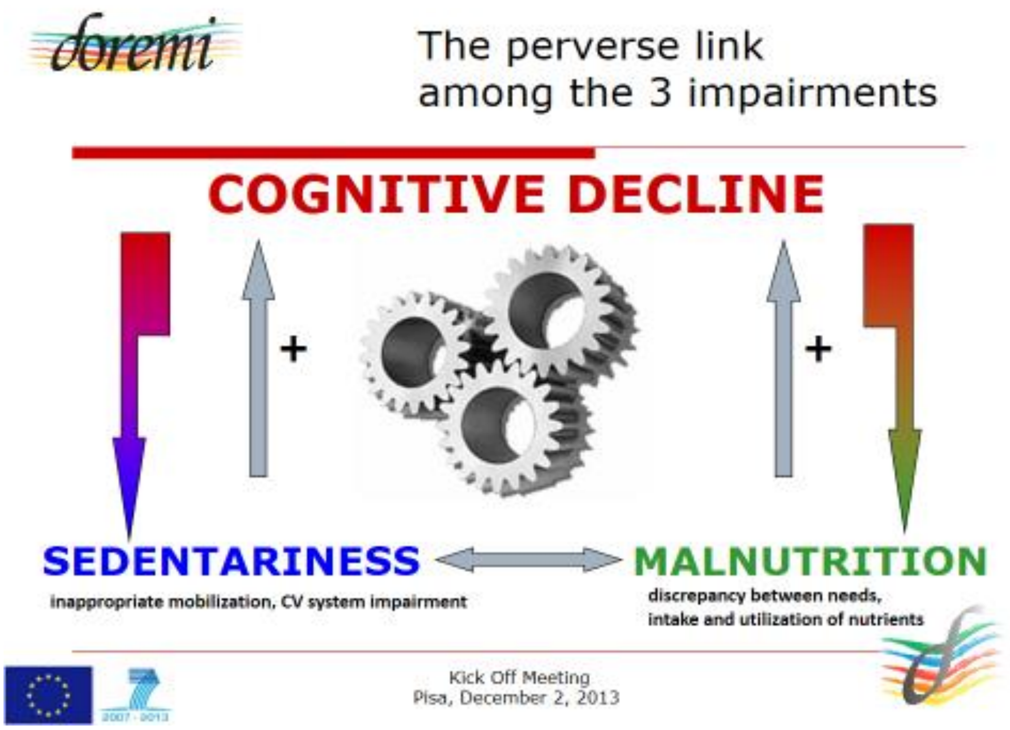


Figure 1. The three impairments of DOREMI study and their relation.

The project will develop a systemic solution for the elderly, able to prolong the functional and cognitive capacity by empowering, stimulating and unobtrusively monitoring daily activities. It promotes health by a constructive interaction between mind, body and social engagement. During a pilot study, food intake measurements and personalized metabolic control, exergames for social interaction stimulation and cognitive training programs will be proposed to an elderly population. The project combines multidisciplinary research areas in serious games, social networking, Wireless Sensor Network, activity recognition and contextualization and behavioural pattern analysis. The effectiveness and impacts, on both users and healthcare system, will be proofed in with a set of pilots set up in Italy and the UK, involving both elderly users and care providers.

4.1 UDH-Malnutrition

Malnutrition, due to the discrepancy between needs, intake and utilization of nutrients represents the primary cause responsible in a deterioration of the health of the elderly, and constitutes a major risk factor for many chronic-degenerative diseases. As far as the concept of malnutrition is concerned, we talk of **sub-nutrition** when a person does not *consume enough* food or *consume unbalanced* food.

On the other side, we talk of **over-nutrition** when people *eat more calories than they need*, and in Europe as in all developed countries, is not rare to find people reaching elderly age already overweight. Nowadays it is frequent to find the two aspects together, that is over-nourished people (obese people) with sub-nutrition aspects due to the wrong intake of basic correct nutrients. This factor in the elderly increases morbidity and a reduction in quality of life [19].

As Dr. Harlem Brundtland, Director General WHO said at the World Economic Forum 2000 *"Nutrition is a key element in any strategy to reduce the global burden of disease. Hunger, malnutrition, obesity and unsafe food all cause disease, and better nutrition will translate into large improvements in health among all of us, irrespective of our wealth and home country."*

Intervention trials have shown that reduction of blood pressure by 6 mmHg reduces the risk of stroke by 40% and of heart attack by 15%, and that a 10% reduction in blood cholesterol concentration will reduce the risk of coronary heart disease by 30%. The elderly are particularly vulnerable to malnutrition, attempts to provide them with adequate nutrition encounter many practical problems. First, their nutritional requirements are not well defined. Since both lean body mass and basal metabolic rate decline with age, an older person's energy requirement per kilogram of body weight is also reduced. The process of ageing also affects other nutrient needs. For example, while requirements for some nutrients may be reduced, some data suggest that requirements for other essential nutrients may in fact rise in later life. There is an increasing demand worldwide for WHO guidelines which competent national authorities can use to address the nutritional needs of their growing elderly populations [20,21]. Many of the diseases suffered by older persons (cardiovascular diseases, sarcopenia, metabolic alterations, neurological diseases) are the result of dietary factors, some of which have been operating since infancy. These factors are then compounded by changes that naturally occur with the ageing process [22]. Degenerative diseases such as cardiovascular and cerebrovascular disease, diabetes, osteoporosis and cancer, which are among the most common diseases affecting older persons, are all diet-affected [23]. As with younger people, drug therapy should be considered only after serious attempts have been made to modify diet.

Dietary changes seem to affect risk factor levels throughout life and may have an even greater impact in older people [24,25].

One of the reasons for the increase of attention to the problem of malnutrition is that, contrary to previous thinking, is not uniquely the concern of poor counties: deficiencies of macro and micronutrients represents a public health problem in some industrialized countries, reaching particular segments of the "at risk groups" population such as the elderly who live alone, often having an unbalanced diet.

The importance of correct nutrition in the elderly life starts in the prevention of age-related diseases such atherosclerosis, type 2 diabetes, neuro-degenerative disorders linked to cognitive decline, and ends with the reduction of medical and social costs crossing through the main concept of the quality of life [26].

Based on the statement that a correct diet is an important factor in preventing age-related diseases in those over 65 years old, at the moment the **NU-AGE project** develops dietary concepts addressing specific needs of this target of population for a healthy ageing in Europe, including the study of a new food pyramid to meet the nutritional needs of the elderly (Figure 2).

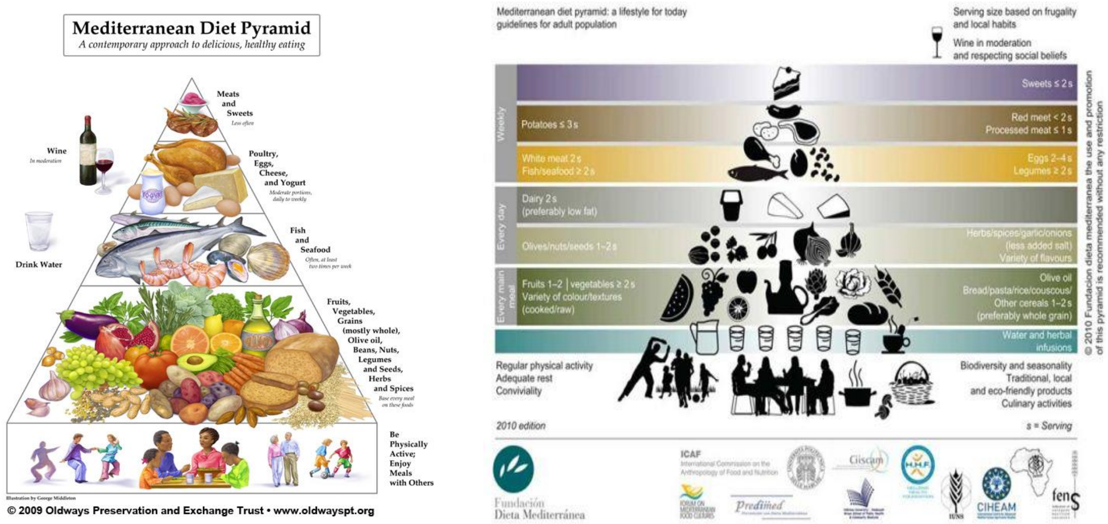


Figure 2. The food pyramid.

The NU-AGE project, www.nu-age.eu [27], funded by the European Commission, conducts studies with the aim of creating functional foods for healthier diets in Europe's ageing population. This one-year trial involves 1,250 volunteers in five EU countries, split into a group that receives dietary advice and a control group that receives no dietary advice and will be completed in late 2014. The results, which include targeted nutritional recommendations, will feed into scientific evidence on the effect of a whole diet on preventing age-related decline. The NU-AGE project results provide guidance to over 65s in order to optimize the diet and help to prevent age-related diseases. The trial results will provide strong insights for a correct dietary management in DOREMI's pilot study (D6.4). However so far, the ICT based models and tools, designed to promote and assess the effectiveness of these corrections through appropriate diet regime as well as the coherence of applications and its performance inside the elderly ambient living, have not been exploited in NU-AGE project, while models and tools will be the core of DOREMI tasks on correct nutrition in elderly.

Nowadays, as far as the malnutrition concept is concerned, the acquisition of the body composition is not just knowing the weight: it also means understanding the values of its components (lean mass, skeletal muscle mass, water, fat mass), and monitoring how the components can change over time. One geriatric syndrome, sarcopenia, is a downward spiral that may lead to decreased strength and functionality [28] and is strictly associated to the progressive decline in skeletal muscle. Several European organizations working in nutrition and geriatric medicine *(European Society of Clinical Nutrition and Metabolism [ESPEN], the International Academy of Nutrition and Aging [IANA] and the International Association of Gerontology and Geriatrics—European Region [IAGG-ER])* created a joint European Working Group on Sarcopenia in Older People (EWGSOP).

The final EWGSOP paper has described techniques for measuring variables of sarcopenia.

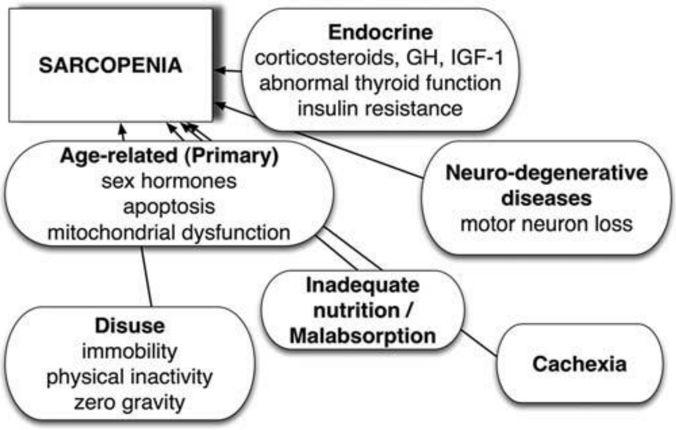


Figure 3. Mechanism of sarcopenia.

The parameters to be measured in sarcopenia are the amount of muscle and its function and the challenge is to determine how best to measure them accurately (Figure 3) [29]. It is also important to recognize change by repeating the same measures over time in the same individuals in order to improve the role of nutrition (amounts of macronutrients, proteins and amino acids, micronutrients, e.g. vitamin D) and to play important roles in protecting and building lean body mass with the correct intake of dietary supplements in the final goal of *identifying dietary strategies,* lifestyle changes that can prevent or delay the onset of sarcopenia. *Norman et al.* conducted a study that investigated the association between **Bio-Impedance Analysis BIA**, a complementary way to estimate the volume of fat and lean body mass and muscle function. The study investigated the association between resistance and reactance normalized for height (R/H and Xc/H) and hand grip strength, an assessment of muscle function [30].

Based on the statement that the human body consists of about two-thirds water, divided into compartments extracellular (outside the cells) and intracellular (inside the cell), a well-balanced state of hydration is the first condition for a correct metabolic functioning. For the assessment of hydration status, it is not only important to know how much of the total body is water, but the distribution between the intracellular and extracellular water, which determines the state of normal hydration, excessive hydration (fluid retention) or dehydration. The test itself is inexpensive, easy to use, readily reproducible and BIA measurement techniques, used under standard conditions, have been studied for >10 years, and have been found to correlate well with Magnetic Resonance Imaging predictors [31].

Why is body composition important to our health? A normal balance of body fat to lean body mass is associated with good health and longevity. Excess fat in relation to lean body mass, a condition known as altered body composition, can greatly increase your risk of cardiovascular disease, diabetes, and more. BIA enables early detection of an improper balance in your body composition, which allows for earlier intervention and prevention. BIA also provides the measurement of fluid and body mass that can be a critical assessment tool for our current state of health.

BIA serves to measure the progress while we are working to improve our health. Improving BIA measurement, or maintaining a healthy BIA values, can help to keep our body functioning properly for healthy ageing and reduce risk of illness. By using BIA information, a personalized dietary plan, nutritional supplements, and exercise can be recommended to support optimal health and well-being.

4.1.1 Effects of UDH on cardiovascular impairments

Malnutrition is the state produced by the intake of too few macronutrients, too many macronutrients or excessive amounts of inappropriate substances such as alcohol. One of the most commonly used definitions identifies malnutrition as “a state of nutrition in which a deficiency, or excess, of energy, protein and micronutrients causes measurable adverse effects on tissue/body form (body shape, size and composition) and function, and clinical outcome” [32]. The under-nutrition reflects an inadequate food intake and consumption which is associated, in older subjects, with a reduction in body fat and body weight. These reductions can lead to a variety of health-related consequences, including a decline in functional status, impaired muscle function, decreased bone mass, micronutrient deficiencies, reduced cognitive functions, increased hospital admission and even premature death [33,34]. Moreover, under-nutrition can adversely affect the well-being of older persons, worsening of existing cardiovascular problems [35].

Recent literature suggests that involuntary weight loss in older persons is comprised of three primary syndromes: starvation, sarcopenia and cachexia [32,36] and that the weight loss may be the result of any two or three of those syndromes in combination.

Starvation is generally accepted to occur as a result of protein-energy and vitamins deficiency [36,37]. Sarcopenia is a progressive loss of muscle mass, not attributable to the presence of pro-inflammatory mediators (Figure 3) [38-40], which is associated with increased frailty, loss of strength, reduced physical function and diminished capacity for exercise, as a result of decreased muscle mass and alterations to muscle structure. Sarcopenia is also combined with accumulation of intra-abdominal fat mass. Cachexia is mediated by pro-inflammatory cytokines and is defined as a complex metabolic syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass [41].

Inadequate intake of protein and energy results in proportional loss of skeletal and myocardial muscle, diminished strength and exercise capacity [42]. Maximal oxygen consumption declines with age at a rate of 3–8% per decade beginning at age 30. A decrease in myocardial mass is associated to impairment in generation of cardiac output [43]. Under-nutrition is associated with a longer hospital stay and increased both long term mortality and in hospital mortality for elderly patients with different cardiac and non cardiac diseases [44]. In long-term hospitalized patients, malnutrition is associated with increased all-cause and cardiovascular mortality [45]. Vitamin D deficiency is associated with cardiovascular diseases (CVD) such as coronary artery disease, hypertension and heart failure.

The nutritional status of elderly patients with systolic heart failure, in particular, adversely affects quality of life and is related to blood values of the peptide NT-proBNP [46]. Therefore, a multidisciplinary collaboration between cardiologists, geriatricians and metabolism and nutrition experts is warranted in older subjects to reduce morbidity and mortality.

Overweight or obesity are well established and independent risk factors for coronary artery disease and mortality in the general population. Although alterations of coronary circulation (micro and macro) can alter the heart structurally, excess amounts of adipose tissue alter the heart morphologically by causing secondary increases in circulating volume [47]. Obese subjects have a higher cardiac output and a lower total peripheral resistance than do lean individuals.

The prevalence of obesity increases with age, peaks at about 60–65 years, and tends to drop slightly over 65 years, partly because of premature mortality. In the USA, the prevalence of severe obesity (BMI≥40 kg/m2) is 3.3% among older men and 8.8% among older women [48]. In France, the 2012 ObEpi survey found that the prevalence of obesity and severe obesity above the age of 65 years was 18.7% (men) and 1.1% (women) [49]. Overall, in Europe, the prevalence of obesity in older adults is projected to vary between 20 and 30% in 2015 [50]. In older ages, obesity confers a greater risk for chronic comorbidities as metabolic syndrome, type 2 diabetes, hypertension, coronary heart disease, stroke, respiratory diseases, cancer, osteoarthritis, or cognitive impairments; in older adults, obesity may also alter functionality that leads to loss of autonomy and impaired quality of life [51-53]. Another important aspect, in particular in elderly patients, is represented by the fact that obesity is a risk factor for the development of heart failure

(HF), independent of other established risk factors such as diabetes and hypertension. Ventricular chamber dilation may then lead to increased wall stress, which predisposes to an increase in myocardial mass and ultimately to LV hypertrophy, characteristically of the eccentric type [54] Studies have demonstrated a continuous gradient of HF risk with increasing body mass index [55]. Obesity-related inflammatory, metabolic, and hormonal changes have been postulated to contribute to the development of HF with obesity (Figure 4).

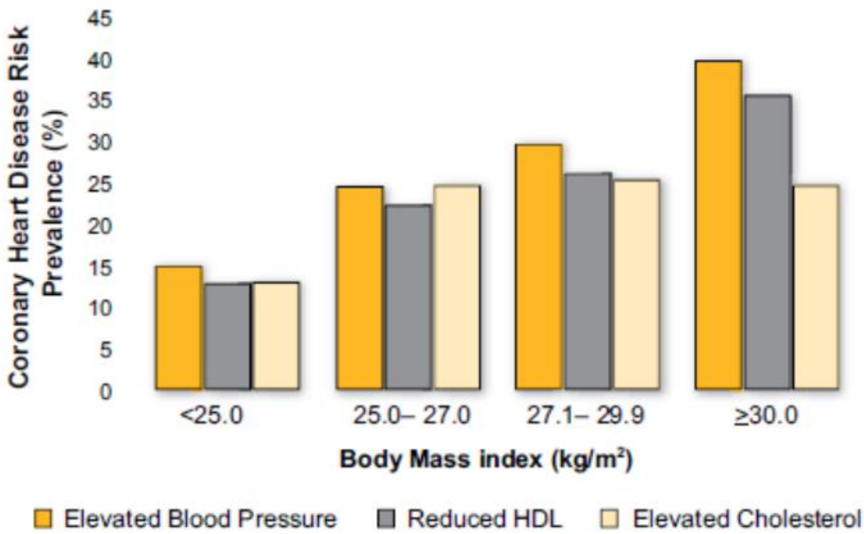


Figure 4. Body mass index and coronary heart disease risk prevalence.

International guidelines recommend weight loss for overweight and obese patients for primary or secondary prevention of CAD. The role of adipose tissue and its secretory products (adipokines), which can be considered as an active endocrine organ, is gaining importance in the investigation of obesity-associated diseases. In obese older adults, moderate weight loss may have beneficial effects on comorbidities, functional performances, and quality of life provided that regular physical activity can be associated [56]; thus, the development of treatment strategies based on changes in the eating habits on one side and on physical exercise on the other, are strongly advised.

According to the relation between UDH and CVD, a significant role can be assigned to **cholesterol**. As a natural *part* of our body composition, this biological molecule is really essential to cell membrane structure and function. However, its main importance lies in its role in the degenerative process that affects medium and large calibre arteries called **atherosclerosis,** the leading cause of death worldwide.

This process may start at an early age moving as an accumulation of cholesterol in the intimal layer of arteries, producing lesions that in the advanced form become atherosclerotic plaques. The growth of this plaque towards the lumen of the vessel may produce ruptures with subsequent thrombosis leading to ischemic diseases presenting as coronary disease (CAD) or ischemic stroke.

Several studies inform us that the reduction of sodium chloride (one component of table salt) in our diet lowers blood pressure, helping to prevent onset of arterial hypertension, one of the major risk factors in CVD. Vegetables, fruits are low in sodium, calories and saturated fats and must take an important place in healthy dietary habits. Instead of using salt or added fat to flavour foods, it will be important to reach the use of spices and herbs.

As far as the relation with UDH is concerned, high cholesterol can indicate that the individual has dietary habits rich in cholesterol: too much lipid-rich foods and processed food and not enough vegetables, fruit and healthy protein. A cholesterol panel that shows elevated triglycerides might also indicate too much sugar in the diet: also, it cannot be overstated how important it is to avoid bad hydrogenated or partially hydrogenated oils and instead take in polyunsaturated (healthy) fats.

The majority of CVD cases and deaths occurs in the elderly (>65 years) and very elderly (> 90 years), and it is in part caused by UDH [57-60].

4.1.2 Effects of UDH on neurological diseases

The major dietary nutrients needed by living organisms can be grouped into macro and micronutrients. The first group, are the energy-yielding nutrients — proteins, carbohydrates and fat — and micronutrients are the vitamins and minerals. The macronutrients have a double function, being both "firewood" and "building blocks" for the body, whereas the micronutrients are special building items, mostly for enzymes to function well. UDH such as micro and macronutrients deficiencies are often associated to neurological disorders and *dehydration* – the lack of intra-and extracellular water - is one of the most common effects strictly linked on neurological diseases.

Seniors suffering from dehydration can have a difficult time making even the simplest decisions. Headaches and high stress levels contribute to a decreased level of mental alertness. Short-term memory loss, confusion and mental fogginess are also reported by seniors suffering from dehydration.

According to a 2012 study published in the *Journal of Nutrition*, this is a very common status in the elderly because even if they actually drink fluids throughout the day, it is not enough for what their bodies need. This can lead to the development of difficulties and conditions such as confusion, anxiety, irritability without apparently causes; it can also cause people to perceive tasks as harder than they are and cause difficulty to solve everyday life problems: all these signs are commonly mistaken for signs of dementia and dehydration goes often undetected. [61-64].

According to the WHO *"Neurological disorders: a public health approach "*, UDH affect a variety of organ systems including the central nervous system: for example the long term use of alcohol (ethanol as a toxic compound) is strictly associated with severe damages to the brain structure responsible for cognitive abilities and emotional functions. Cerebral atrophy and other anomalies too are often symptoms of alcohol-related neurological disorders.

As far as the influence on the onset *nutrition and evolution* of Parkinson Disease, an alteration of the antioxidant protection may contribute to the onset and progression: a protective function against Alzheimer Disease (AD) is probably ruled by the assumption of omega-3 poly-unsaturated fatty acids (n-3PUFA) [65-67].

The objective of the "IANA TASK FORCE ON NUTRITION AND COGNITIVE DECLINE WITH AGING" is to review data relating diet to risk of cognitive decline and dementia especially AD. High intake of saturated and trans-unsaturated fats are in association with risk of AD, whereas intake of polyunsaturated and monounsaturated fats were protective against cognitive decline in the elderly in prospective studies.

Indeed, the influence of cognitive ageing by different consumption levels of the major specific fat types, rather than total fat intake itself, is confirmed by a study on American women's health, published in "Annals of Neurology", conducted over 4 years among 6000 women aged over 65 [68]. Outcomes highlight that higher Saturated Fatty Acid (SFA) intake is associated with worse global cognitive (p for linear trend = 0.008) and verbal memory (p for linear trend = 0.01) trajectories, as well as a higher risk of worst cognitive change. On the other hand, higher Monounsaturated Fatty Acids (MUFA) intake is related to better global cognitive (p for linear trend < 0.001) and verbal memory (p for linear trend = 0.009) trajectories, and lower OR (95% CI) of worst cognitive change in global cognition (0.52 [0.31–0.88]) and verbal memory (0.56 [0.34–0.94]).

Malnutrition, nutrient deficiencies and ingestion of toxic compounds, continue to be associated to neurological disorders and cognitive dysfunctions: nowadays this may suggest the importance of having a balanced intake of several nutrients which play a significant role in the prevention of most of them.

For example, several studies have demonstrated that higher adherence to the Mediterranean diet, characterized by unsaturated fatty acids - mostly in the form of olive oil, high intake of fish, vegetables, legumes, fruits, cereals, and low intake of dairy products, meat, and saturated fatty acids, and a regular but moderate intake of alcohol is associated with a trend for reduced risk of developing Mild Cognitive Impairment (MCI) and with reduced risk of MCI conversion to AD [69-71].

4.1.3 Effects of UDH on metabolic alterations (type 2 diabetes, metabolic syndrome)

Aging is an important risk factor for metabolic disorders, including obesity, impaired glucose tolerance, and **type 2 diabetes**. Diabetes and its complications remain major causes of morbidity and mortality in the USA [72]. It is reported that the prevalence of type 2 diabetes increases with age and peaks at 60–74 [73,74]. Almost one third of the elderly in USA have diabetes and three quarters have diabetes or pre-diabetes [74]. Among the lifestyle factors that can favour the onset of type 2 diabetes are being overweight and obese, which are consequences of an unbalanced diet, rich of saturated fats and simple sugars. The higher incidence of diabetes is especially alarming considering that diabetes in itself increases the risk for multiple other age-related diseases such as CVD, atherosclerosis, stroke, AD, Parkinson’s disease, non-alcoholic fatty liver disease, and cancer. The pathogenesis of type 2 diabetes in aging is characterized by two major features: peripheral insulin resistance and impaired insulin secretion from β cells. Whole body glucose homeostasis is a complex balance of glucose production and utilization by different tissues. Food intake and hepatic glucose production are the two sources of glucose production, while skeletal muscle contributes to the majority of the glucose uptake and utilization. While hepatic glucose production does not increase with age, when adjusted for lean body mass, the European Group for the Study of Insulin Resistance demonstrated that glucose uptake, although not altered as a function of aging per se, is secondarily affected by increases in body fat accumulation [75]. Moreover, the decrease of lean body mass [76] and contractile strength with age are other factors that contribute to the reduction in insulin stimulated glucose uptake. Therefore, a mismatch between lean and fat body mass in the elderly, associated with sedentariness-related loss of muscle strength, are key mechanisms favouring insulin resistance and onset of type 2 diabetes. Today, living healthy with diabetes is feasible, if food intake and exercise are balanced, helping to control the weight and keeping blood glucose levels in the healthy range. Making healthy food choices and learning how different foods affect glucose levels is mandatory. For weight loss, the advices is to seek out foods that are low in fat and sugar and let the doctor know if a help with meal planning is needed. Community food programs, either as congregate meals or home-delivered nutrition services, are a great way to meet and socialize and deliver healthy meals, respectively, a strategy that has been proved to prevent diabetes progression and its related sequels.

According to the new International Diabetes Federation, the **metabolic syndrome** is defined as a cluster of cardio-metabolic risk factors which are related to insulin resistance. Beyond the importance of each risk factor, the aggregation of abdominal obesity (waist circumference ≥ 94 cm for men and ≥ 80 cm for women), impaired glucose metabolism (raised fasting plasma glucose (FPG) ≥ 100 mg/dL (5.6 mmol/L), dyslipidaemia (reduced HDL cholesterol:< 40 mg/dL (1.03 mmol/L) in males and < 50 mg/dL (1.29 mmol/L) in females) and hypertension (raised blood pressure: systolic BP ≥ 130 mm Hg or diastolic BP ≥ 85 mm Hg), summarized as the metabolic syndrome, characterizes individuals with a significant increase at risk for type 2 diabetes and cardiovascular disease.

In the complex pathophysiology of the metabolic syndrome (Figure 4), malnutrition linked to central obesity and insulin resistance are acknowledged as important causative factors [77,78].

As a matter of fact, over-nutrition tending to obesity, increases the risk for various co-morbidities, and recent advances in the understanding of adipose tissue biology offer an insight into this complex pathophysiological mechanisms (Figure 5). Various endocrine and pro-inflammatory products from the visceral adipose tissue, which interact with the insulin signalling cascade, can be identified [79]. Among these products, adiponectin protects from insulin resistance and cardiovascular disease, while free fatty acids, leptin, resistin and pro-inflammatory substances promote the development of insulin resistance [80,81]. Leptin, the product of the obesity gene, is primarily produced by the adipose tissue, regulates food intake and energy expenditure, skeletal muscle fatty acid metabolism and hepatic glucose production. Leptin reveals structural similarities with pro-inflammatory cytokines, such as interleukin-6 (IL-6), which interferes with insulin action. Cells of the stromal vascular fraction in adipose tissue, and especially in visceral fat, are important sources of IL-6 production [82-84].

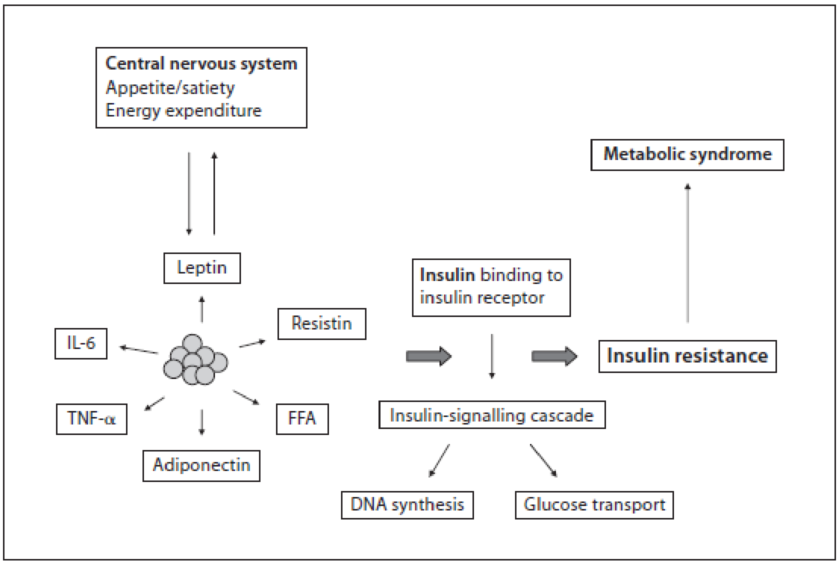


Figure 5. Pathophysiology of the metabolic syndrome.

Epidemiologic data indicates that the prevalence of metabolic syndrome is about 20% in the overall population, and increases with increasing age. Data from the Third National Health and Nutrition Examination Survey recently demonstrate that the presence of the metabolic syndrome is 7% in the age group of 20–29 years, increases to 44% in the age group of 60–69 years and reaches 42% in people aged 70 years or older [85].

It is commonly stated that achievement of weight loss and the maintenance of a lower weight, is the first priority in elderly people with abdominal obesity, assuming that weight loss will reduce the severity of most of the metabolic risk factors and the related CV events. However, relevant parameters not detectable by the simple measurements of weight or BMI, such as body fluid amount or body lean, may better allow to monitor fluid and tissue composition in the body, providing important information on body composition in subject with metabolic syndrome, sarcopenia, obesity, or other forms of malnutrition.

Diet should be low in saturated fats, cholesterol, sodium and simple sugar; the correct intake of vegetables, whole grains, fish and fruits, as well as a correct hydration, should be encouraged in the vision that maintenance of physiologic lean mass and fluid balance control in the elderly needs a combination of healthy dietary habits, physical activity and motivation. This will be an innovative approach of DOREMI project.

4.1.4 Effects of UDH on osteoporosis

To define osteoporosis as a systemic skeletal disease characterized by low bone mass and deterioration of bone tissue with the determination of bone fragility, can be nowadays reductive. In fact, even if preventable and treatable, there are **no warning signs prior to fractures**, and this makes it a silent disease generating fractures that often occur as a result of minimal trauma in the elderly ADL. The osteoporotic fractures represent a major cause of morbidity in aging, being really common and place an enormous medical and personal burden on older individuals and a major economic toll on nations.

In the lifestyle factors associated with an increased risk of osteoporosis-related fractures, UDH is on the top scale: a not well-balanced supply of nutrients is related to several diseases that involves different organs as liver, heart, brain, as well as the muscle-skeletal system. In particular, with the latter, in elderly people it is common for the development of the depletion of calcium reserves which is linked to excessive thinness, an insufficiency of vitamin D linked to immobilization, and an excess of vitamin A linked to active or passive smoking, alcohol abuse linked to the risk of balance.

In 1998, Riggs [86] shows how, not only hormonal imbalances, but also calcium malnutrition and malabsorption are strongly related to development of diseases in both genders with the consequent need of calcium supplementation in diet. Further analysis takes into account how not only calcium but also the contemporary administration of Vitamin D is fundamental to reduce the risk of hip fractures [87]. This study is confirmed also by Tang, showing how a well-balanced supply of calcium and vitamin D in people aged 50 years or older have the best therapeutic effect to prevent fractures and bone loss [88].

On the other hand, the role of obesity is not completely clear in osteoporosis evolution. Traditionally, the mechanical loading generated by body weight is a stimuli for bone formation [89]. However, recently studies have shown how obesity, evaluated as percentage body fat or waist circumference after adjusting for weight, is a risk factor for osteoporosis. In particular, elderly women present a decrease of oestrogen concentrations, with consequently a negative effect on osteoblast number in bone marrow [90]. Furthermore, fat tissue secretes inflammatory cytokines (e.g., Interleukin-6, TNF-alfa), that are negatively related to bone mineralization and bone loss [91,92].

According to the "CLINICIAN'S GUIDE TO PREVENTION AND TREATMENT OF OSTEOPOROSIS" - developed and revised by NOF in 2013, the advise on a diet rich in fruits and vegetables which includes adequate amounts of total calcium intake (1,000 mg per day for men 50-70; 1,200 mg per day for women 51 and older and men 71 and older) and the advise on vitamin D intake (800-1,000 IU per day), including supplements if necessary for individuals age 50 and older, are the priority council in the modification of UDH [93].

4.1.5 Effects of UDH on cancer

The risk of cancer is strongly related to malnutrition, in terms altered (inadequate or excessive) daily nutrient supply. In a study conducted in UK, researchers have estimated that unhealthy diet is at the base of 10% of cancer cases [94]. Design studies that are able to specifically look at the effect of a single food on cancer development and progression are very difficult for the variety of nutrients, which compose a person's diet. Despite this, some specific foods have shown a remarkable effect on increasing or reducing the risk of cancer.

In the EPIC (European Prospective Investigation into Cancer and Nutrition) study [95] it is highlighted how a reduced supply of fibre is related with an increase of bowel cancer, and an approximate doubling of total fibre intake from foods could reduce the risk of developing the disease by 40%.

This European study has found also how fruits and vegetables are able to reduce the risk of mouth, oesophageal and lung cancers, [96,97] as well as also some types of stomach [98] breast, prostate, ovarian and kidney cancers [99-101]. This is related to their content in vitamins and nutrients able to protect, for example, against the oxidative stress [102-104].

Many studies have focused, instead, on meat, which has been shown to be related with cancer development. An unbalanced supply of red meat (such as fresh, minced and frozen beef, pork and lamb) including processed meats (such as ham, bacon, salami and sausages) can increase the risk of bowel cancer by a third [105].

Red and processed meats contain a red pigment called haem, which is able to stimulate bacteria in production of N-nitrous compounds (NOCs) [106]. These substances are alkylating agents that damage cell cycle. Cells contrast this action with a deregulated increase of cellular division, which can evolve in tumour mass.

Furthermore, some processed meat also contains chemicals called nitrites. These substances are used to improve the colour of products, making them more attractive. In the bowel, nitrites are converted into NOCs, which could cause stomach cancer [107].

Salty foods are also related to cancer development, not only to atherosclerosis. In fact, an excess of sodium chloride can damage the lining of the stomach and cause inflammation. Salt can interact also with Helicobacter pylori, which causes stomach ulcers and stomach cancer [108].

In industrial countries, the common use of pre-cooked and industrial products is linked to the presence of saturated fats in high concentrations. The EPIC study evidenced how women who eat saturated fats have a higher risk of developing breast cancer [109,110], probably related to the action related to the increase of oestrogen and other hormones in blood [111].

The foods and the nutrients described above show how an unbalanced supply, in excess or in defect, can be linked with several types of cancer and its development.

4.2 Sedentariness

Physical activity (PA), health and quality of life are closely interconnected: the human body was designed to move and therefore needs regular physical activity in order to function optimally and avoid illness. It has been observed in literature that a sedentary lifestyle is a risk factor for the development of many chronic illnesses, including cardiovascular diseases.

Based on the epidemiological studies carried out in Europe, it is evident that the absence of physical activity seems to reach unfortunately the population most likely to benefit, such as the over 65s [112]. For this purpose, the implementation of European wide policy to improve active living is strongly needed, especially if supported by methodologies and technologies able to make physical activity easy and to improve personal responsibility in the over 65s with the main aim of preventing physical and mental diseases. Sedentary people who become more physically active report feeling better from both a physical and a mental point of view, and enjoy a better quality of life.

For adults aged over 65s, the same goals as for healthy younger adults should be achieved with additional exercises like strength training and balance exercises to prevent falls. These are in addition to the routine daily activities [113].

In March 2005 the "European Network for Action on Aging and Physical Activity" (EUNAAPA) was established as an informal network for people supporting the vision of giving an optimal health and quality of life for the older people in Europe, through physical activity. In mutual efforts, two projects *(EUNAAPA project and PASEO project)* were formulated and funded by the DG-Sanco Public Health Programme of the European Union.

In 2009 the *American College of Sports Medicine (ACSM)* came up with a position stand on *Aging and Physical activity* [114] describing all the evidence in the area. This position stand underpinned also the physical activity guidelines as published earlier [115].

It was concluded that:

"Although no amount of physical activity can stop the biological aging process, there is evidence that regular exercise can minimize the physiological effects of an otherwise sedentary lifestyle and increase active life expectancy by limiting the development and progression of chronic disease and disabling conditions. There is also emerging evidence for psychological and cognitive benefits accruing from regular exercise participation by older adults"

Following the *ACSM, the European College of Sport Sciences (ECSS)* will shortly come up with a position paper on physical activity and behavioural change in all age groups (co-authored by Stuart Biddle, Walter Brehm and Marijke Hopman-Rock).

All together, these developments clearly show a range of challenges, which are of significance for the further work of EUNAAPA (Figure 6). However, as a starting point, the main focus will be on education and training about the role of physical activity in the aging process.

PA, able to cause a noticeable increase in heart rate, is beneficial for disease prevention. Some studies show that walking briskly for even one to two hours a week (15 to 20 minutes a day) starts to decrease the chances of having a heart attack or stroke, developing diabetes, or dying prematurely [116].

Walking is an ideal exercise for many people—it doesn't require any special equipment, can be done any time, any place, and is generally very safe. Several studies, such as the Health Professionals Follow-up Study [117], Women's Health Study [118], National Health Interview Survey [119], Women's Health Initiative [120], and others [121,122] have demonstrated that this simple form of exercise substantially reduces the chances of developing heart disease, stroke, and diabetes in different populations.

The 2008 Physical Activity Guidelines for Americans recommended that adults get a minimum of 2-1/2 hours per week of moderate-intensity aerobic activity, or get a minimum of 1-1/4 hours per week of vigorous-intensity aerobic activity, or a combination of the two [123]. Moderate-intensity aerobic activity is any activity that causes a slight but noticeable increase in breathing and heart rate. One way to gauge moderate activity is with the “talk test”—exercising hard enough to break a sweat but not so hard you can’t comfortably carry on a conversation. Vigorous-intensity aerobic activity causes more rapid breathing and a greater increase in heart rate, but you should still be able to carry on a conversation—with shorter sentences.

According to *“Physical Activity Guidelines in the UK: Review and Recommendations”*, the final protocol for PA guidelines for the older population present 13 recommendations for revising the UK Guidelines on PA for this specific target group. All 13 recommendations are agreed to be applicable to the development of specific Guidelines on physical activity for elderly people; each of them is considered to be an accurate and evidence-based item. Last but not least, two additional recommendations are identified as important for new UK guidelines for older adults, informing on the gradual increase of PA level, and the importance of involving balance training by way of preventing risk of falls [124].

On July 2011 the Department of Health published a UK-wide document that presents guidelines on the volume, duration, frequency and type of physical activity required. “*Start Active, Stay Active: A report on physical activity for health from the four home countries’ Chief Medical Officers (2011)”*, includes a special factsheet for over 65s, gives examples of PA, gives advice on improving balance and co-ordination, and minimizing sedentary behaviour, and shows the benefits of being active today.

According to the WHO, for adults over 65s, PA includes recreational or leisure-time physical activity, transportation (walking or cycling), occupational (if the person is still engaged in work), household, in order to improve cardiorespiratory and muscular fitness, bone and functional health and reduce the risk of Non-Communicable diseases (NCDs), depression and cognitive decline [125].

Analysing the fact that a high number of elderly people are overweight or obese, performing PA will provide substantial health benefits, even in the absence of reductions in body weight. As a matter of fact, engaging physical function is difficult for older adults because of loss of muscle mass, strength and bone density. Excess weight further reduces mobility, especially among obese people. As a key component of daily energy expenditure, PA has an important role to play in the maintenance of a healthy weight. For older adults who currently have low physical activity levels, reaching the recommended 150 minutes of moderate intensity activity each week will substantially increase their energy expenditure. Overweight and obese older adults should therefore develop a weight loss program combining reduction in calorie intake and increase in physical activity. This will produce greatest benefit for fat loss, retention of muscle mass, physical function and health [126].

EUNAAPA Roadmap 2011-2016

EUNAAPA priority	Way to go	Milestones 2011-2016
Training and education	• Adjustment of international training curriculum (see http://www.isapa.org/guidelines/index.cfm) to EUNAAPA goals and European situation (coordination by XX?)	• Summer school (The Netherlands, October 2011) Lead by Ger Kroes, Nina Waaler Loland, Christophe Delecluse and Federico Schena)
	• Preparation and publishing of EUNAAPA reviews (coordination by Kerstin Frändin, Sweden) • To provide information on physical activity and elderly among health care professionals (medical doctors, physiotherapists, nurses). • Consultation of international advisory board and HEPA and PROFANE partners (coordination by Nina Waaler Loland and Marijke Hopman-Rock)	• Oversight of effective measurements (reviews available or in development) and intervention programmes (overview under development lead by Ger Kroes) • Cooperation with European partners (HEPA, PROFANE (Prevention of Falls Network Europe; etc)
Awareness of health care personnel about role of physical activity in the aging process	• Contact with gerontological and geriatric associations in EU countries and in Europe (coordination by Ellen Freiberger) • Contact with physiotherapists organisations (coordination by Kerstin Frändin?) • Development of presentations and short publications (for patient populations and care personnel) (action for country members) • Contact with ECSS and sport doctors to improve attention for sport stimulation in older people (Nina Waaler Loland and Marijke Hopman-Rock)	• Symposia during relevant conferences (steering committee and individual members) • Short publications in relevant practical journals • Draft text for leaflets in country languages • Overview of existing and effective interventions
Policy strategies	• Develop a unified consensus statement regarding policy strategies (coordination by Alfred Rütten). • Convene a meeting of policy experts to guide the policy research agenda. • Make existing research appropriate for older adults and identify gaps in research knowledge.	• PASEO end conference Brussels (lead by Alfred Rütten and Nina Waaler Loland etc) • Continuation of national PASEO coalitions (country members actions) • 100-500 EUNAAPA members
Supportive strategies	• Continuation of EUNAAPA website and newsletter (coordination by TNO Leiden, Erwin Tak) • Coordinated action on funding of new European proposals in the area of PA and Aging	• New project funded

Figure 6. EUNAAPA roadmap.

4.2.1 Effects of Sedentariness on cardiovascular impairments

Sedentary behaviour is a cluster of behaviours adopted in a sitting or lying posture where little energy is being expended. It has been recently reported in a survey of more than 600 subjects, that nearly 67% of the older population is sedentary for more than 8.5 hours daily of waking time, objectively evaluated by accelerometer [127,128]. According to the WHO, lack of physical activity is ranked as the fourth leading cause of all deaths worldwide [129]. The amount of time spent being sedentary is a risk factor by itself, associated with important co-morbidities such as being overweight, obesity and metabolic diseases [128]. On the other hand, PA is an influencing factor for healthy aging; lack of PA has been associated with chronic diseases, such as cardiovascular lung and renal diseases, diabetes mellitus, and cancer [130,131]. In a huge cohort study from the Women's Health Initiative, involving more than 70,000 participants, it has been recently demonstrated that in postmenopausal women without a history of CVD prolonged sitting time is associated with increased CVD risk, independent of leisure-time physical activity and that the combination of low physical activity and prolonged sitting augments CVD risk [132]. Thus, cardiovascular morbidity and mortality are related to physical inactivity through a worsening of conventional risk factors [131,132] but also by direct action on cardiac function. It is well known that physical activity results in better cardiorespiratory fitness by improving maximal workload, end-diastolic volume at rest, stroke index, and cardiac index [133]. Aging is associated with a decline in VO_2max by approximately 10% per decade after age 25 years, mostly due to a 40% reduction in muscle mass and to impaired blood flow distribution to the working muscle [134]. Since with aging a reduction in heart rate (HR) is reported and stroke volume and cardiac output tend to decrease [135], physical activity may improve cardiac output (CO) through a remodelling of LV cavity. This functional improvement may also contribute to an improvement in LV diastolic function which is impaired with advanced aging possibly due to a decrease in compliance for the increased fibrotic component of the myocardium [136]. As a consequence, regular physical activity may positively affect morbidity and mortality eliciting beneficial central and peripheral cardiovascular effects [137]; in healthy elderly individuals, those who have a lifelong physical training show better left ventricular systolic and endothelial function [138]. Moreover, not only does maintaining aerobic fitness throughout the lifespan improves cerebral hemodynamic in later-life [139] but also it has been demonstrated that despite the elderly have reduced cerebral perfusion, cerebral oxygenation and uptake of lactate and glucose are similar during maximal exercise in young and older individuals, further suggesting the importance of physical activity in the elderly population [140].

A recent meta-analysis has shown that to obtain significant effects of physical activity interventions in the elderly, the patient should participate in the exercise programs for at least 12 weeks and that the typical dose of the physical activity prescription is 20–60 min of aerobic activity three times weekly. In very wide population studies it has been shown that higher baseline cardiorespiratory fitness, quantified by treadmill test is associated with lower heart failure and cancer mortality risk in healthy men and women, independent of BMI [141-143].

Since adherence to mobility enhancement recommendations by older patients is generally low, it is important that patients undergoing training should be followed-up by in-person interviews or use of mobility monitoring tools [144].

As far as the relation between a specific risk factor as cholesterol and a sedentary life style, **regular physical exercise** does not reduce total cholesterol and LDL if there is no weight loss, **although it is effective in increasing HDL cholesterol and reducing triglycerides.** It also causes a change in the phenotypic expression of LDL and decreases the amount of small LDLs, which are more atherogenic [145].

4.2.2 Effects of Sedentariness on neurological diseases

Ageing is associated with a progressive decline in activity levels, which are also influenced by education, gender, ethnicity and income. Older adults are more likely to engage in PA of lower intensity, such as walking, gardening, riding a bicycle, or playing golf rather than running, doing aerobics or team sports.

Over the years studies confirm that a sedentary lifestyle is one of the risk factors for a wide range of neurological and psychiatric diseases. In particular, molecular and biochemical evidences on cerebral cortex and hippocampus, support that physical inactivity is connected to a progressive decline in cognitive function [146].

Conversely, increasing PA, intended as any bodily movement produced by skeletal muscle that requires energy expenditure, has various benefits for older adults [146]. For example, it has been shown to decrease depression [147,148], increase overall health through mechanisms such as increasing cardiovascular fitness and bone density and preventing loss of muscle mass [149,150], and improve quality of life [151].

In addition to these general benefits, PA has been shown to influence cognitive performance in MCI, thus preventing or postponing cognitive decline into dementia.

From a social prospective, as physical activity can promote social contact [152] stimuli fostered by relationships can also promote cognitive function by introducing novel social interactions into one's routine.

Conversely, from a physical point of view, the following figure shows possible biological mechanisms through which physical activity can have neuro-protective effects, identified in cognitively normal human and animal models (Figure 7).

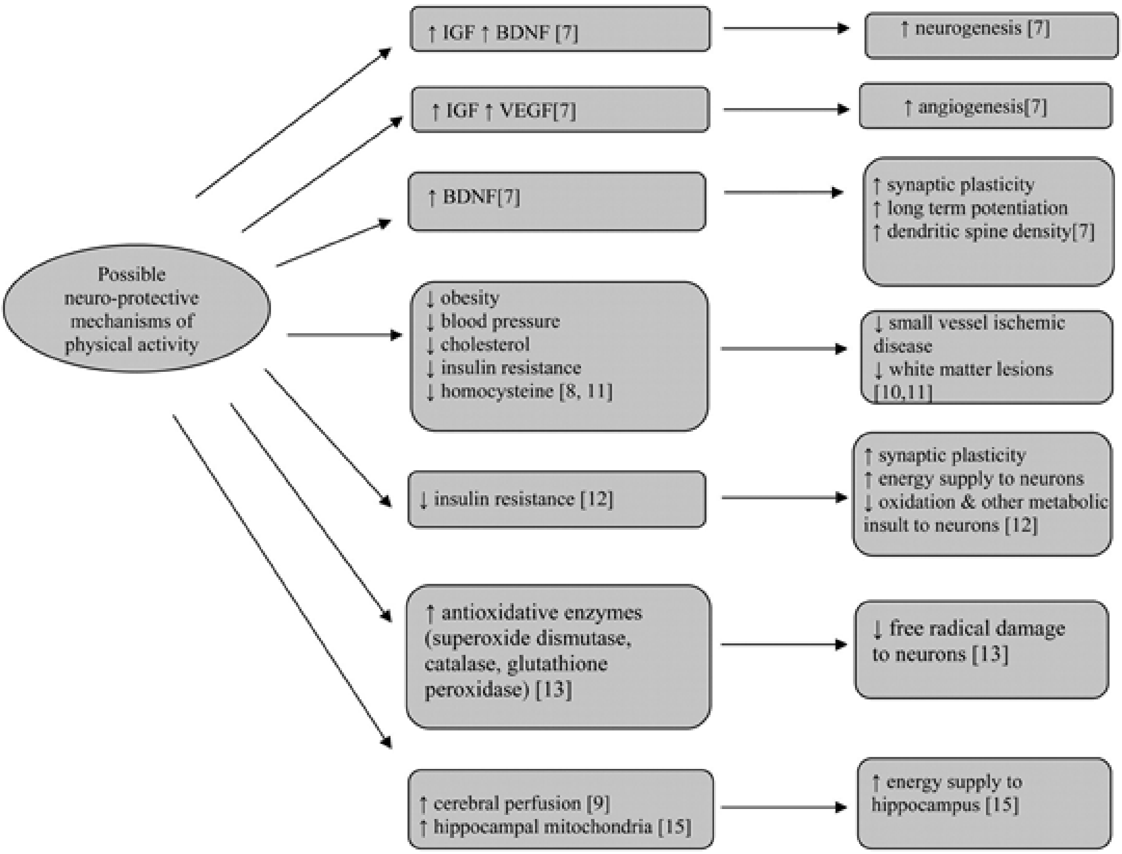


Figure 7. Mechanisms of physical activity-related neuro-protection.

Literature reports many studies confirming biological positive effects on cognition due to exercise training:

- It is shown to up-regulate and increase the activity of several neurotrophic and vascular growth factors, including insulin-like growth factor-1, brain-derived neurotrophic factor and vascular endothelial growth factor. According to the article by Van Pragg [153], this would enhance neurogenesis, angiogenesis, synaptic plasticity and dendritic spine density in the hippocampus.

- It has been shown to enhance the expression of genes that regulate the production of free-radical scavenging enzymes, thus reducing free radical damage to neurons and neurodegenerative diseases [154].

- Increased production of mitochondria in neurons is demonstrated to be an effect of physical exercise, improving energy metabolism in the brain and ensuring energy supply to neurons [155].

- Aerobic exercise is documented to significantly larger hippocampal volumes [156], associated with significant improvement in the primary cognitive outcome measure of spatial memory.

- Besides a brain neuro-protective effect, physical exercise may also attenuate cognitive decline via mitigation of cerebrovascular risk, including the contribution of small vessel disease to dementia [157].

Observational studies on general populations confirm a protective effect of PA on cognition, associated with the factors above mentioned, according to two meta-analysis of 15-16 prospective studies [158,159], respectively one assessing the pooled relative risk of dementia for the most physically active group compared with the least active one, the other examining the association between PA and risk of cognitive decline in cognitively normal older adults.

4.2.3 Effects of Sedentariness on metabolic alterations (type 2 diabetes, metabolic syndrome)

In recent years, studies and trials have demonstrated the importance of fighting a sedentary lifestyle especially in the prevention of obesity and the associated co-morbidities like type 2 diabetes [160]. According to the Finnish Diabetes Prevention Program, in which Subjects in the intervention group received inputs of physical activity joined to correct dietary counselling, the reduction in the incidence of type 2 diabetes was directly associated with changes in the lifestyle of risks subjects [161].

The ***Diabetes Prevention Program Research Group*** conducted a large, randomized clinical trial involving adults in the United States who were at high risk for the development of type 2 diabetes.

The "Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin" study hypothesizes that modifying these factors with a lifestyle-intervention (at least a 7% weight loss and at least 150 minutes of physical activity per week) or the administration of metformin would prevent or delay the development of diabetes. The lifestyle intervention reduces the incidence by 58% (95% confidence interval, 48 to 66%) and metformin by 31% (95% confidence interval, 17 to 43%), as compared with placebo; the lifestyle intervention is significantly more effective than metformin. Lifestyle changes and treatment with metformin both reduce the incidence of diabetes in persons at high risk [162].

In the study *"Sedentary activity associated with metabolic syndrome independent of physical activity"* elderly people with unhealthy dietary habits tending to over-nutrition are enrolled [163]. Data from 1,367 men and women (aged ≥ 60 years who participated in the 2003-2006 National Health and Nutrition Examination Survey – NHANES), are collected and examined. Sedentary time during waking hours is measured by an accelerometer (<100 counts per minute). A sedentary bout is defined as a period of time >5 min. A sedentary break is defined as an interruption in sedentary time (≥ 100 counts per minute). On average, people spent 9.5 hours (65% of wear time) as sedentary. Compared with people without metabolic syndrome, people with metabolic syndrome spent a greater percentage of time as sedentary (67.3 vs. 62.2%), had longer average sedentary bouts (17.7 vs. 16.7 min), had lower intensity during sedentary time (14.8 vs. 15.8 average counts per minute), and had fewer sedentary breaks (82.3 vs. 86.7), adjusted for age and sex (all $p < 0.01$). A higher percentage of time sedentary and fewer sedentary breaks are associated with a significantly greater likelihood of metabolic syndrome after adjustment for age, sex, ethnicity, education, alcohol consumption, smoking, BMI, diabetes, heart disease, and physical activity. The association between intensity during sedentary time and metabolic syndrome is borderline significant. The proportion of sedentary time is strongly related to metabolic risk, independent of physical activity [163]. ***"Current results suggest that older people may benefit from reducing total sedentary time and avoiding prolonged periods of sedentary time by increasing the number of breaks during sedentary time."***

As far as the concept of a sedentary behaviour is concerned, we can pose it as a risk factor, and not only in subjects with CVD or diabetes, but otherwise *in the way to prevent them*. As a matter of fact, the study *"Sedentary behaviour, physical activity and a continuous metabolic syndrome risk score in adults"* [164], investigates the association of sedentary behaviour and leisure time physical activity with a validated continuous metabolic syndrome risk score in adults *without* CVD and diabetes. "Subjects reported time spent in leisure time physical activity and television watching/computer activities. A validated metabolic syndrome risk score, based on waist circumference, triglycerides, blood pressure, fasting plasma glucose and high-density lipoprotein cholesterol, is used. The metabolic syndrome risk score and time spent in sedentary behaviour and physical activity are analysed as continuous variables using multiple linear regression. The results support inclusion of efforts to decrease sedentary behaviour in metabolic syndrome prevention strategies for aging people besides promotion of moderate to vigorous physical activity, since both behavioural changes might show additional effects".

However, longitudinal and intervention studies are needed to clarify the nature of any causal relationship between sedentary behaviour and metabolic syndrome. Current results, although based on cross-sectional findings, emphasize that it might be important to recommend a reduction in sedentary behaviours, such as TV viewing and time on the computer, for the prevention of metabolic syndrome [165].

4.2.4 Effects of Sedentariness on osteoporosis

Fighting sedentariness, avoiding short and long immobilization and improving physical function such as ADL, is "an active drug" against osteoporosis: various studies have demonstrated the role and the relevance of physical activity in improving or maintaining bone mass in all ages. Recent data have shown how some specific exercises are beneficial for bone strength, in the form of short, repetitive and multidirectional mechanical loading [166,167].

This mechanical stress can maintain or increase bone matrix, reducing osteocyte apoptosis, and stimulating osteoblast differentiation. These mechanisms are probably mediated by calcium signalling associated to mechano- and voltage-activated channels, second messengers such as nitric oxide as well as Wnt/β-catenin, prostaglandin, and other intracellular pathways [168-170].

To produce a "osteogenic" exercise it is necessary that this generates a stimulus, as intensity, frequency, amplitude and duration, different from the habitual movements [171]. In particular, these exercises, in accordance with the study of Borer [172] should: be dynamic; exceed a threshold intensity and a strain frequency; be relatively brief but intermittent; impose an unusual loading pattern on the bones; be supported by unlimited nutrient energy; include adequate calcium and vitamin D diet supply.

As shown above, it is not necessary to stimulate the musculoskeletal apparatus with high-impact exercises: Nikander [173] demonstrated that different exercises with high or low impact appear to have the same capability to improve the thickness of femoral neck-cortex respect to sedentary controls.

According to "CLINICIAN'S GUIDE TO PREVENTION AND TREATMENT OF OSTEOPOROSIS", based on the initial condition of the patient, the physical protocols should provide a complete exercise recommendation that includes aerobic activities for the skeleton, postural training, progressive resistance training for muscle and bone strengthening, stretching for tight soft tissues and joints and balance training.

Walking and daily activities, such as housework and gardening, are practical ways to contribute to maintenance of fitness and bone mass. Additionally, progressive resistance training and increased loading exercises, within the parameter of the person's current health status, are beneficial for muscle and bone strength. Proper exercise may improve physical performance/function, bone mass, muscle strength and balance, as well as reduce the risk of falling [174]. For this reason, in particular with the elderly or high-risk fracture population (as can be the DOREMI target), soft and mechanically less demanding odd-impact exercises can be a better option to take in account.

4.2.5 Effects of Sedentariness on cancer

In the last few years a link between physical activity and cancer prevention is demonstrated, as documented by many studies. Epidemiologic data obtained by more than 70 studies around the world indicate, for example, a reduction in the risk of breast cancer (25%) in active women compared to a more sedentary lifestyle [175]. Another piece of work based on the analysis of 19 studies shows an inverse association between kidney cancer and physical activity [176] as also a protective role of exercise in decreasing the risk of many others cancers (lung, endometrial, colon, and possibly prostate cancer) [177-180]

Frequently, physical exercise as a prevention strategy against cancer is most often associated with a means of reducing the negative effects of obesity or in other words, energy imbalance. This may be one reason why the connection between breast cancer prevention and physical exercise is less well established and understood than other preventative strategies. Recent evidence has indicated that physical exercise prevents breast cancer primarily through its ability to reduce sex hormone levels in women. This mechanism is crucial since oestrogens promote the risk of breast cancer development due to the stimulation of mitosis and regulation of cell proliferation. Friedenreich shows that physical exercise generates a significant decrease in estradiol and increase of sex-hormone binding globulin (SHBG), with no significant impact on levels of estrone, androstenedione, and testosterone [181]. Furthermore, Kossman et al. [182]. conducted a study involving seven healthy premenopausal women at high risk for breast cancer resulted in a beneficial reduction of oestrogen and progesterone after 300 minutes of vigorous physical exercise per week for seven menstrual cycles. In a study of Friedenreich, moderate to vigorous daily activity reduced C-reactive protein levels among post-menopausal women. Previous studies have shown that the immune cells activated by the inflammatory response, such as macrophages and neutrophils, release reactive elements like oxygen and nitrogen that can damage DNA [183].

4.3 Cognitive Decline

Averagely at the age of 30, due to a process called “apoptosis”, standing for “programmed cell death”, neurons start collapsing or dying.

The first consequence of apoptosis is the progressive decrease of brain weight (up to 10% between 30 and 75 years) and loss up to 20% of the blood supply to the brain.

With the gradual advancement of age, especially from the age of seventy onwards, the subjects may have more difficulties in retrieving information that are usually easy to recall, as well as in saving new data and focusing their attention [184]. In addition to memory and concentration functions, the person may lose interest and initiative, and have problems in properly organizing actions. They also present less capacity with abstract thinking and less plasticity in problem solving activities. The decline of these skills, within certain limits, can be considered physiological. Nevertheless, whenever decline is significantly higher with respect to the standard, specific monitoring and treatments become crucial, because it is more likely to develop into a dementia such as Alzheimer’s Disease in the following years, a condition that significantly affects a person's autonomy and quality of life.

The studies reported in the previous sections illustrate how physical exercise, along with a healthy diet and social relations can positively influence the maintenance of cognitive functions in healthy people.

The report called "Dementia: a public health priority" (Geneva, April 11th , 2012) [185] - developed by the World Health Organization (WHO) and Alzheimer's Disease International, with the support of patient organizations and their family members, shows how dementia will become more and more widespread in the following decades, thus leading to huge health-care costs as well as a heavy psycho-physical and economic burden for families and caregivers.

According to the report, by 2030 the number of people suffering from dementia will reach 63 million and in 2050 it will reach 114 million.

Since the onset of severe dementia disorders is often very gradual, physicians and health care professionals try to identify and define the early stages of disease in which certain symptoms (such as loss of memory, attention and concentration) are already present, but in a mild form, when the person is still able to live independently. The term used to define this condition is MCI (Mild Cognitive Impairment).

Cognitive rehabilitation, as well as the adoption of a healthy diet and physical exercise may have a positive effect in this intermediate status.

Being a sometimes reversible but abnormal state, MCI is a heterogeneous syndrome in terms of aetiology, incidence, prevalence, presentation, and overall prognosis.

Most recently, MCI has been defined as the sum of the items quoted below:

- Subjective memory complaints, preferably qualified by another person
- Memory impairment, with consideration for age and education
- Preserved general cognitive function
- Intact activities of daily living
- Absence of overt dementia.

Several studies have shown that the annual risk of progression to dementia for patients with MCI is 5% to 10% in community-dwelling populations and up to 15% in specialty-clinic patients. In comparison, the incidence of dementia in the general elderly population is 1% to 3% per year[184,186].

On the other hand, a number of studies show that MCI improves significantly in up to 15% to 40% of patients and sometimes reverts to a normal cognitive state. Nonetheless, prospective studies of patients with clinically diagnosed MCI usually find a low rate of reversion to a normal state [187].

4.3.1 Effects of Cognitive Decline on cardiovascular impairments

Cardiovascular impairment as well as being a primary cause for the increased risk for survival, plays an important role in cognitive degeneration of elderly and young people.

The correlation between these two conditions basically indicates that heart problems and heart disease are linked to an increased risk of cognitive decline.

Rosebud Roberts (a researcher in health sciences at the Mayo Clinic), in a study of 2013 [188] showed that people who suffer from some cardiovascular disease (women in particular), are more likely to be affected by a kind of decline cognitive that does not include memory loss. Usually this condition is considered to be a precursor to dementia. The study involved the participation of 2,719 people aged between 70 and 89 years at baseline. It identified a significant association on the basis of sex: heart disease and mild cognitive impairment appear together more often in women than in men.

A further study from 2012 [189] highlighted how higher cardiovascular disease risk and higher stroke risk were associated with greater cognitive decline in all tests relating to reasoning, vocabulary, and global cognitive scores. The only area that seemed less involved was the memory. Compared with the dementia risk score, cardiovascular and stroke risk scores showed slightly stronger associations with 10-year cognitive decline; these differences were statistically significant for semantic fluency and global cognitive scores. Furthermore, Raymond L.C. Vogel et al. [190], showed diminished neuropsychological performance among HF (heart failure) patients. In a pooled sample of 2,937 heart-failure patients and 14,848 control subjects, the odds ratio for cognitive impairment was 1.62 (95% confidence interval:1.48–1.79, $p<0.0001$) among subjects with heart-failure. In the study, the authors have called for adequate neuro-imaging from representative populations of HF patients. Friedman [191] took into account a range of specific population (patients with schizophrenia) to investigate the relationship between cognitive impairment and cardiovascular disorders.

The authors investigated whether vascular risk factors influenced the cognitive impairment of people with schizophrenia and whether the effects on cognition in schizophrenia are different from those observed in non-psychiatric comparison subjects. There was no significant interaction effects between a schizophrenia diagnosis and hypertension on any of the cognitive measures; a BMI above 25 was associated with negative effects on delayed memory in both groups, a BMI ≥25 had no significant effect on any other cognitive measures, and no interaction effects were observed between a schizophrenia diagnosis and BMI on any cognitive measures.

4.3.2 Effects of Cognitive Decline on metabolic alterations

In order to maintain a physiological function of the brain, we require a constant supply of micronutrients for energy metabolism of neurons and glial cells, neurotransmitter synthesis and action, nerve impulse propagation and homocysteine metabolism. Deficiencies in various micronutrients, especially the B vitamins, have adverse effects on cognition [192].

Several studies have pointed out the impact of **Metabolic Syndrome** on cognitive functioning and brain integrity in functionally. Kristine Yaffe et al. [193] shows that the metabolic syndrome may be a risk factor for cognitive decline because it summarizes the joint effects of abdominal obesity, hypertriglyceridemia, low HDL level, hypertension, and hyperglycaemia. Gregg EW et al. [194], instead, investigated the relationship between metabolic disorders (diabetes) and cognitive disease specifically in the female population. In this study, they used three tests of cognitive function, the Digit Symbol test, the Trails B test, and a modified version of the Mini-Mental State Examination (m-MMSE). The study highlighted that diabetes is associated with lower levels of cognitive function and with greater cognitive decline among older women. There are scarce evidences in literature that cognitive decline causes metabolic disorders.

4.3.3 Effects of Cognitive Decline on osteoporosis

No studies which show direct correlations between osteoporosis and cognitive decline were found. However, Kristine Yaffe, et al. [195] Studied the cognitive decline in women in relation to non-protein-bound estradiol (1) concentrations. They found that women with high serum concentrations of non-protein-bound and bioavailable estradiol, but not testosterone, were less likely to develop cognitive impairment than women with low concentrations. This finding supports the hypothesis that higher concentrations of endogenous oestrogens prevent cognitive decline investigated in previous studies [196-198].

(1) The active ingredient is used as a prevention against genitourinary symptoms, caused by lack of oestrogen in the body and in the prophylaxis of osteoporosis.

4.3.4 Effects of Cognitive Decline on cancer

In the literature correlation between cognitive decline and some forms of cancer is scanty. But there is an interesting study [199] that correlates the effect which treatment for breast cancer has on a possible cognitive impairment. The study population consisted of 34 patients treated with high dose chemotherapy plus tamoxifen, 36 patients treated with standard-dose chemotherapy plus tamoxifen, and 34 control patients. For all patients, the average time since the completion of last non hormonal therapy was 2 years. High-dose chemotherapy appears to impair cognitive functioning more than standard-dose chemotherapy. Central nervous system toxicity may be a dose limiting factor in high-dose chemotherapy regimens.

5. MOTIVATIONAL ASPECTS AND SOCIAL INTERACTION IN MANAGEMENT OF UDH, SEDENTARINESS, AND COGNITIVE DECLINE

In the previous paragraph we have discussed about the negative effects of unhealthy lifestyles on the physiological and clinical conditions as well as the cognitive decline of aged persons. Moreover, we have also argued how good healthy lifestyle, such as positive dietary habits and physical activities, can, vice-versa, have an important role in preventing, or, at least slow down the progressive psycho-physical and cognitive decline of an individual in older age.

In this chapter we argue that the up-taking of healthy practices for a young and older adult (as the target persons of DOREMI project) implies a direct engagement of the person in his/her care management. In particular we explain which are the determinants for health-related behavioural changes driving an aged person towards a healthier lifestyle that could have as a consequence the positive clinical outcomes discussed in the previous chapters.

In particular, we try to see the motivational aspects and social interaction issues as a consequence of the engagement of the target group with DOREMI solution and related service.

According to the scientific and grey literature that we have analysed, engagement on lifestyle management looks at the individuals' capacity to take decisions about their health-behavioural choices and to have, or to take control over their health care status and risk factors that could affect their quality of life [200].

Assumptions are that health engaged individuals could make more rational healthcare decisions to maximize benefits for their health, decrease dependencies on health care services and, ultimately, contribute to more cost-effectiveness health care processes [201]. These assumptions go beyond the self-reported and self-efficacy of the health care services, to give more importance to the self-determination in health behavioural choice of each individual entity [200].

Scientific literature identifies three main perspectives under which individuals could be engaged with respect to their health status:

- the professional perspectives [202] where each individual that is subject to health matters related to his/her health conditions acquires expert knowledge and usually put it into practice for preventive actions or proactive treatment of their disease;
- the consumer logic [203] that emphasizes the process of personal affirmation to make decision based on personal judgment and resources. This logic refers to the sense of responsibility that steers an individual into more preventive health care risk management practices;
- the community logic, that, according to Hoey et al. [204], addresses the issues of inclusion in actions and social changes due to the participation of an individual to a social network or an advocacy group.

Moreover, the engagement issues are more and more important when the individuals have to face off with health-behaviour that are related to their daily choices that imply to integrate a number of new lifestyle or treatment-related behaviours into their everyday life [205] (e.g. making a physical activity; choosing more healthy food; etc.) as in the case of DOREMI project.

Under this perspective, there is consensus in the scientific community [200,206,207] around the fact that the psychological and life-related outcomes of individuals engaged in prevention and treatments of their health status can produce the following benefits:

- enhancement of psycho-physical and cognitive conditions (see previous chapters);
- improve quality of life (see previous chapters);
- enhancement of capacity to cope with negative feelings;
- self-transformation in relation with one’s environment;
- better psychosocial adaptation;
- enhancement of control;
- personal satisfaction;
- self-responsibility;
- self-esteem;
- decision and implementation of behaviour changes.

Therefore engagement can have appositive effects on motivational aspects related to better lifestyle management of an individual. In other world, engagement is the trigger to increase positive lifestyle related motivation, which is the expression of the reasons that induce a person to perform or tending towards a particular healthy action. It’s an important factor to keep in mind when working on the modification of behaviours, as shown in Figure 8, which describes the Maslow's hierarchy of needs (is a theory in psychology proposed by Abraham Maslow in his 1943 paper "A Theory of Human Motivation" in Psychological Review [208]).

The figure below clearly shows how after having satisfied the primarily needs in the bottom of the Maslow’s pyramid, individuals need to address more complex needs related to the social interaction and self-esteem and actualization. However, as described in DOREMI project objectives, in the case of elderly persons, it is necessary to define engagement mechanisms (e.g. gaming, recommendations, interactions with caregivers, families, friends and others) to stimulate and encourage a change in their attitudes, recognized as wrong or harmful to their health.

The engagement can have two opposite prospects, of punishment or reward. The former tends to highlight the negative consequences (death, illness, etc.) caused by the continuation of their bad lifestyle health-related behaviours, while the second outlines the benefits resulting from the changes suggested by caregivers, families, friends or social contacts, etc., regarding physical activation and stimulation.

In this perspectives we should see the engagement of individuals through the positive stimuli provided through DOREMI platform and related services: physical exercises; gaming and social interaction.

In particular, the social involvement and interaction with the group of "friends-participants" to compare one another on their achievements, to "challenge" the others to serious games or maybe share diets and recipes represents an important factor to improve positive lifestyle behavioural changes.

In such perspective two other positive outcomes could be achieved during the project activity: the willingness to extend the use of the "DOREMI Protocol" also after the project’s conclusion and the reinforcement of intrinsic motivation of the target users.

To this end it is necessary to evaluate clear positive causality relationships between the stimuli (physical exercises, gaming and social interactions ones) proposed by DOREMI project platforms for engaging young adults and their behavioural changes in undertaking healthier lifestyles.

The above perspectives and related benefits need also to be analysed in relation to the use of information and communication technologies to enable patient engagement in their care management processes [209]. This is another important aspect that we should consider during the project evaluation activity, because of DOREMI project dealing with the use of ICT solutions and social web technologies to engage young and older adults to a better life style management.

The most important issue to this end is to provide evidences of an effective acceptability of the ICT solution applied for engaging the target population in better lifestyle management [210].

The reason for considering this issue in the project results evaluation relies in a recent analyses [211], conducted on several examples of successful e-health cases, especially in tele-health and tele-monitoring domains. The paradox underpinning this analysis is evident: despite to the fact that such analyses provide clear positive evidences in terms of benefits for the target population, health care systems cost cutting in hospitalization, and home treatments, there is still a lack of significant rise in the adoption of e-health solutions [210] by their target potential adopters.

In paragraph 6 we provide some metrics that we propose to use for the measurement of motivation and social interaction of the target population engaged with DOREMI platform and related services during the Pilots' Trials.

Motivation is the expression of the reasons that induce a person to perform or tend towards a particular action. It is an important factor to keep in mind when seeking to inspire changes participant behaviours.. Maslow's hierarchy of needs (Figure 8) is a psychological theory proposed by Abraham Maslow in his 1943 paper "A Theory of Human Motivation" in Psychological Review [208].

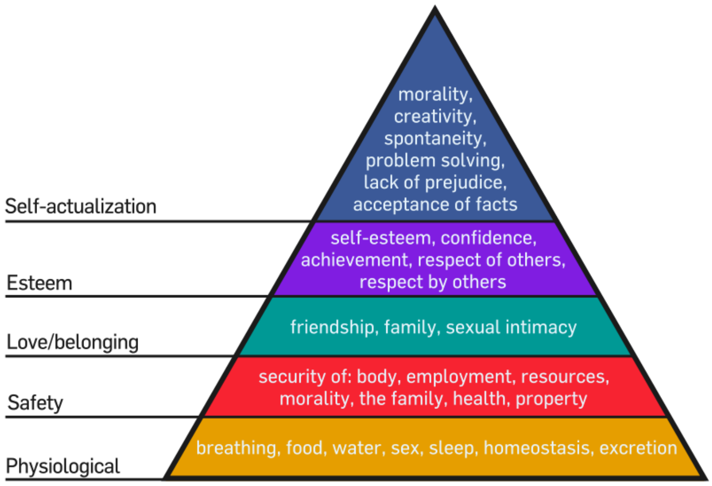


Figure 8. Maslow's hierarchy theory of needs.

There are a lot of negative stereotypes about the skills and productivity of the elderly. Peterson and Coberly [212] concluded in their studies, that senior workers are considered physically unable to do their work, less productive, less motivated, less receptive to innovation than younger workers, unable to learn, and subject to high rates of absenteeism and work-related accidents. For instance, in the literature on ageing, research has found that a metacognitive deficit (changes in implicit theories and beliefs, self-efficacy, causal attributions and strategy use) in elderly people implies an age-related memory decline, which in turn has an effect on implicit theories and beliefs, self-efficacy, causal attributions and strategy use [213,214].

Nevertheless, different studies confirm that behaviour, attitudes and erroneous metacognitive attitudes can be changed and implemented through appropriate training and incentives. [215-217].

When managing activities with the elderly it is necessary to stimulate and encourage a change in their attitudes, recognized as wrong or harmful to their health.

The incentive can have two opposite relapses, punishment or reward. The former tends to highlight the negative consequences (death, illness, etc.) caused by the continuation of their behaviours (social approach, diet, etc.) while the second outlines the benefits resulting from the changes suggested by caregivers, regarding physical activation and stimulation.

A study conducted by *Clara Maria Silvestre Monteiro de Freitas* et al., on 120 subjects from two physical exercise programs, indicates that the most important motives are positive to improve health (84.2%), to improve physical performance (70.8%), to adopt a healthy lifestyle (62.5%), to reduce stress (60.8%), to comply with doctor's orders (56.7%), to recover from injury (55%), to improve self-image (50.8%) and to enhance self-esteem and relax (47.5%) [218].

The social involvement and interaction with the group of "friends-participants" to compare one another on their achievements, to "challenge" the others to serious games or maybe share diets and recipes represents the most relevant key factor to improve the integration. In such a way two other positive results could be achieved: the willingness to extend the use of the "DOREMI Protocol" also after the project's conclusion and the reinforcement of intrinsic motivation. This last factor, illustrated by the study of Bonfiglio D and Pioggia G. [219], is a key element to ensure that the person undertakes an activity because it is in itself motivating (Figure 9).

Motivation and social interaction will contribute to restore and improve the user psychological wellbeing, considered as major component of active ageing. Wellbeing, viewed as an integration of mental, physical, and social domains, is associated with numerous benefits to health, family, work, and economic status. This element will be taken in account as key success element of DOREMI protocol, thanks to its metric evaluation by the use of Wellbeing Evaluation Scale, a test measuring well-being through 6 structural properties: Integrity of self; Integrity of others, Belonging, Agency; Enrichment; Security [220]

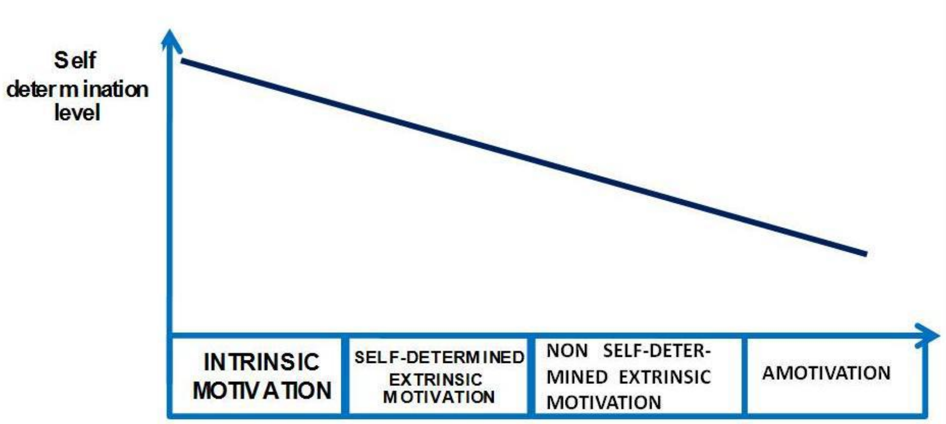


Figure 9. Correlation between motivation and self determination level.

6. SCREENING: SELECTED SET OF PARAMETERS AND SCALES

6.1 UDH - Malnutrition

In the elderly, there are two major events of **UDH**, namely **malnutrition for "excess or defect",** due to behaviours like the difficulty to modify dietary needs according to changes in age and association of novel diseases, the difficulty to maintain the right caloric intake by paying attention to the amount of portions, to the method of preparation, intake of fat and carbohydrates, especially sugar. As a screening tool to help identification of the nutritional status of the elderly in malnutrition for "defect", the Mini Nutritional Assessment (MNA®) has been increasingly employed worldwide and recommended by the European Society for Clinical Nutrition and Metabolism, since its publication.

What is the MNA®?

The MNA® is a validated nutrition screening and assessment tool that can identify geriatric patients age 65 and above who are malnourished or at risk of malnutrition (excess or defect). Originally comprising a 18-item questionnaire (published in 1994 by Guigoz, et al.) [221], it was developed 20 years ago and is the most well validated nutrition screening tool for the elderly.

The **MNA**® is effective because it:

- Targets the frail and elderly and at-risk geriatric population
- Identifies the malnourished so intervention can being immediately
- Identifies at-risk persons before weight loss occurs and serum protein levels fall,
- Includes criteria specific to issues of ageing- functionality, depression, dementia
- Not only identifies people who are at nutrition risk, but allows healthcare professionals to target intervention to specific causes of malnutrition as identified in the MNA®

The **MNA**® (18 questions, Table 1), is composed of an anthropometric assessment, a questionnaire about diet characteristics, food intake, fluids intake, weight loss, mobility, psychological stress or acute disease, drugs, presence of dementia or depression, global health and environment, and a self-evaluation of health and nutritional state (**assessment**).

The revised **MNA® Short Form - SF** developed by Nestlé and leading international geriatricians, makes the link to intervention easier and quicker and is now the preferred validated screening tools for clinical use. It has been thoroughly validated in international studies in a variety of settings and correlates with morbidity and mortality; it now consists of 6 questions and streamlines the screening process. The **MNA® SF** retains the validity and accuracy of the original **MNA**® in identifying older adults who are malnourished or at risk of malnutrition [221].

Although the literature suggests the use of the **MNA® - SF**, DOREMI will use **the original MNA®**. The project seeks to investigate the parameters of <u>dietary habits</u>, of <u>hydration</u> and <u>consciousness of the level of nutrition</u> and the full version has a number of questions appropriate to the definition of the nutritional profile, not provided in the short form assessment.

As a result of the screening score and the assessment, the final **MNA® MALNUTRITION INDICATOR SCORE** classifies nutritional state as:

Normal nutritional status	(score 24-30)
at risk for malnutrition	(23.5-17)
and malnourished	(<17)

Nestlé NutritionInstitute

Mini Nutritional Assessment MNA®

Last name: First name:

Sex: Age: Weight, kg: Height, cm: Date:

Complete the screen by filling in the boxes with the appropriate numbers. Add the numbers for the screen. If score is 11 or less, continue with the assessment to gain a Malnutrition Indicator Score.

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake ☐

B Weight loss during the last 3 months
0 = weight loss greater than 3kg (6.6lbs)
1 = does not know
2 = weight loss between 1 and 3kg (2.2 and 6.6 lbs)
3 = no weight loss ☐

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out ☐

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no ☐

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems ☐

F Body Mass Index (BMI) (weight in kg) / (height in m²)
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater ☐

Screening score ☐☐
(subtotal max. 14 points)

12-14 points:	Normal nutritional status
8-11 points:	At risk of malnutrition
0-7 points:	Malnourished

For a more in-depth assessment, continue with questions G-R

Assessment

G Lives independently (not in nursing home or hospital)
1 = yes 0 = no ☐

H Takes more than 3 prescription drugs per day
0 = yes 1 = no ☐

I Pressure sores or skin ulcers
0 = yes 1 = no ☐

J How many full meals does the patient eat daily?
0 = 1 meal
1 = 2 meals
2 = 3 meals ☐

K Selected consumption markers for protein intake
- At least one serving of dairy products (milk, cheese, yoghurt) per day yes ☐ no ☐
- Two or more servings of legumes or eggs per week yes ☐ no ☐
- Meat, fish or poultry every day yes ☐ no ☐

0.0 = if 0 or 1 yes
0.5 = if 2 yes
1.0 = if 3 yes ☐.☐

L Consumes two or more servings of fruit or vegetables per day?
0 = no 1 = yes ☐

M How much fluid (water, juice, coffee, tea, milk...) is consumed per day?
0.0 = less than 3 cups
0.5 = 3 to 5 cups
1.0 = more than 5 cups ☐.☐

N Mode of feeding
0 = unable to eat without assistance
1 = self-fed with some difficulty
2 = self-fed without any problem ☐

O Self view of nutritional status
0 = views self as being malnourished
1 = is uncertain of nutritional state
2 = views self as having no nutritional problem ☐

P In comparison with other people of the same age, how does the patient consider his / her health status?
0.0 = not as good
0.5 = does not know
1.0 = as good
2.0 = better ☐.☐

Q Mid-arm circumference (MAC) in cm
0.0 = MAC less than 21
0.5 = MAC 21 to 22
1.0 = MAC 22 or greater ☐.☐

R Calf circumference (CC) in cm
0 = CC less than 31
1 = CC 31 or greater ☐

Assessment (max. 16 points) ☐☐.☐

Screening score ☐☐.☐

Total Assessment (max. 30 points) ☐☐.☐

Malnutrition Indicator Score

24 to 30 points	☐	normal nutritional status
17 to 23.5 points	☐	at risk of malnutrition
Less than 17 points	☐	malnourished

Ref. Vellas B, Villars H, Abellan G, et al. *Overview of MNA® - Its History and Challenges.* J Nut Health Aging 2006; 10: 456-465.
Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for Undernutrition in Geriatric Practice: *Developing the Short-Form Mini Nutritional Assessment (MNA-SF).* J. Geront 2001; 56A: M366-377.
Guigoz Y. The Mini-Nutritional Assessment (MNA®) *Review of the Literature – What does it tell us?* J Nutr Health Aging 2006; 10: 466-487.

For more information: www.mna-elderly.com

Table 1. Mini Nutritional Assessment form.

The administration and scoring instruction manual for the complete **MNA®** prepared by Nestle', can be downloaded from the website: www.mna-elderly.com .

MNA® BMI Table for the Elderly (age 65 and above)

Height (feet & inches)

Weight (kg)	4'11"	5'0"	5'1"	5'2"	5'3"	5'4"	5'5"	5'6"	5'7"	5'8"	5'9"	5'10"	5'11"	6'0"	6'1"	6'2"	6'3"	Weight (pounds)
45	20	20	19	18	18	17	17	16	16	15	15	14	14	14	13	13	13	100
48	21	21	20	19	19	18	17	17	16	16	16	15	15	14	14	14	13	105
50	22	22	21	20	20	19	18	18	17	17	16	16	15	15	15	14	14	110
52	23	23	22	21	20	20	19	19	18	18	17	17	16	16	15	15	14	115
55	24	23	23	22	21	21	20	19	19	18	18	17	17	16	16	15	15	120
57	25	24	24	23	22	22	21	20	20	19	19	18	17	17	17	16	16	125
59	26	25	25	24	23	22	22	21	20	20	19	19	18	18	17	17	16	130
61	27	26	26	25	24	23	23	22	21	21	20	19	19	18	18	17	17	135
64	28	27	26	26	24	24	23	23	22	21	21	20	19	19	18	18	18	140
66	29	28	27	27	26	25	24	23	23	22	21	21	20	20	19	19	18	145
68	30	29	28	27	27	26	25	24	24	23	22	22	21	20	20	19	19	150
70	31	30	29	28	28	27	26	25	24	24	23	22	22	21	20	20	19	155
73	32	31	30	29	28	28	27	26	25	24	24	23	22	22	21	21	20	160
75	33	32	31	30	29	28	28	27	26	25	24	24	23	22	22	21	21	165
77	34	33	32	31	30	29	28	27	27	26	25	24	24	23	22	22	21	170
80	35	34	33	32	31	30	29	28	27	27	26	25	24	24	23	23	22	175
82	36	35	34	33	32	31	30	29	28	27	27	26	25	24	24	23	23	180
84	37	36	35	34	33	32	31	30	29	28	27	27	26	25	24	24	23	185
86	38	37	36	35	34	33	32	31	30	29	28	27	27	26	25	24	24	190
89	39	38	37	36	35	34	32	32	31	30	29	28	27	26	26	25	24	195
91	40	39	38	37	35	34	33	32	31	31	30	29	28	27	26	26	25	200
93	41	40	39	38	36	35	34	33	32	31	30	29	29	28	27	26	26	205
95	42	41	40	38	37	36	35	34	33	32	31	30	29	29	28	27	26	210
98	43	42	41	39	38	37	36	35	34	33	32	31	30	29	28	28	27	215
100	44	43	42	40	39	38	37	36	35	34	33	32	31	30	29	28	28	220
102	45	44	43	41	40	39	37	36	35	34	33	32	31	31	30	29	28	225
105	47	45	44	42	41	40	38	37	36	35	34	33	32	31	30	30	29	230
107	48	46	44	43	42	40	39	38	37	36	35	34	33	32	31	30	29	234
109	48	47	45	44	43	41	40	39	38	37	35	34	34	33	32	31	30	240
111	49	48	46	45	43	42	41	40	38	37	36	35	34	33	32	32	31	245
114	51	49	48	46	44	43	42	40	39	38	37	36	35	34	33	32	32	250
Height (cm)	150	152.5	155	157.5	160	162.5	165	167.5	170	172.5	175	177.5	180	182.5	185	188	190	

0 = BMI less than 19

1 = BMI 19 to less than 21

2 = BMI 21 to less than 23

3 = BMI 23 or greater

Figure 10. BMI table.

Associated with important changes in body composition and metabolism, the prevalence of malnutrition from excess until obesity, is rising progressively among over 65 [222].

According to WHO definition, as the international tool in the classification of overweight and obesity, the **B**ody **M**ass **I**ndex (**BMI**) is commonly used as a simple and validated index of weight-for-height, to categorize both situations.

The abbreviated **BMI** table shown above (Figure 10) is provided for convenience and facilitates completing **MNA®** and it is accurate for it. In some cases, calculating the BMI may yield a more precise **BMI** determination, defined exactly as a person's weight in kilograms divided by the square of his height in meters (kg/m^2):

BMI Formula – US units

BMI = (Weight in Pounds / [Height in inches x Height in inches]) x 703

BMI Formula – Metric units

BMI = (Weight in Kilograms /Height in Meters x Height in Meters])

1 Pound = 0.45 Kilograms

1 Inch = 2.54 Centimetres

The standard weight status categories associated with BMI ranges for adults are shown in the following table:

BMI	WEIGHT STATUS	DOREMI DEFINITION
BMI ≤ 18.5	underweight	unhealthy dietary habits for deficiency
BMI 18.5-24.9	normal range	
BMI 25-29.5	mild overweight	unhealthy dietary habits for excess
BMI≥ 30	obesity	unhealthy dietary habits for excess

As far as this anthropometric measurement is concerned, it presents two limits:

- It does not investigate the real level of fatness and leanness among subjects;
- And it does not evaluate the level of hydration of our subject.

The complementary method for body-composition assessment is **Bioelectrical Impedance Analysis (BIA)** – whole body, which is able to evaluate the hydration and body mass composition in any clinical condition, regardless of weight [223].

Bio-impedance and bio-electrical impedance are interchangeably used and properly employed, are able to capture clinical changes in tissues hydration, for direct measurement of electrical quantities and specifics dependent only from tissue hydration.

It should be noted that under abnormal conditions even the most validated algorithms can produce serious bias in the estimates of the components. How is it possible to detect directly the presence of alterations of fluid and electrolyte and to avoid bias in the estimates?

The BIA vector analysis (**BIVA**) **Biavector®** provides:

- semi-quantitative assessment of body composition based on direct measurements;
- confirmation of the applicability of conventional BIA using the fixed coefficient of hydration.

As in the electrocardiogram, the BIA aims to transform the electrical properties of the tissues in a clinical setting: the electrocardiogram records graphically, through surface special electrodes, the electrical potential of the heart and the abnormality of certain waveforms is determined by comparison with the reference waveforms of the healthy population.

The clinical application of the analysis BIA is now possible, following the same methodology of interpretation of an electrocardiogram: **BIVA Biavector**® allows clinician to draw on interpretative schemes "nomograms" that permit an immediate diagnosis of states of fluid overload, dehydration, normal-hydration, cachexia, malabsorption, muscle recovery, nutritional follow-up [224,225].

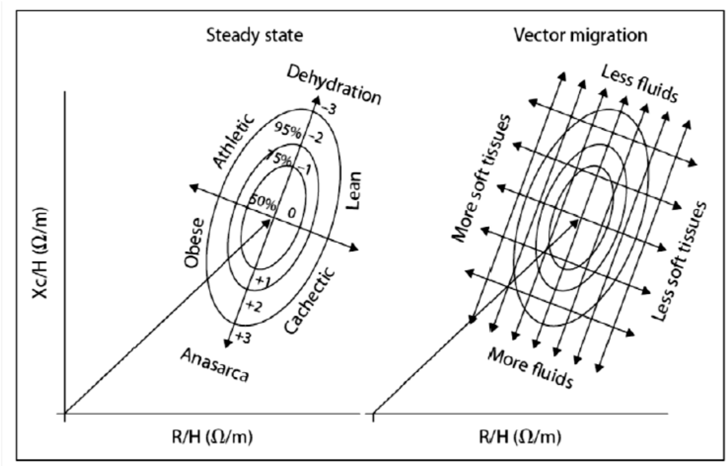
The system of assessment the body composition **Akern Biavector®**, is the first validated system based on the normalization of the measure bioelectrical direct.

The impedance vector analysis using the nomogram **Biavector®**, provides the clinician with an instant interpretative scheme about the state of hydration and nutrition of the subject. The values of bioelectrical resistance (RZ) and reactance (Xc) measured by the instrument, are divided by the height of the subject (conductivity/meter) and plotted on the diagram.

Taking advantage of the direct measurement of impedance using the method of Grafo RXC, it is possible to obtain a semi-quantitative evaluation (in percentiles) of hydration status of a person, from the age of 15 to 85 years by comparing the impedance vector measured by the variability of the reference population described by ellipses of tolerance; these are gender-specific.

The nomogram **Biavector®** graphically (Figure 11) shows the physiological state of a subject, allowing a quick check of the results. The nomogram is composed of three areas, defined ellipses of confidence (50%), tolerance (75%) abnormalities (95%) and is able to highlight with excellent sensitivity and specificity of the real state of hydration in any clinical condition.

GENERAL RULES FOR THE INTERPRETATION OF THE NOMOGRAM graph R-Xc



A STEP AHEAD IN BODYCOMPOSITION

Image provided by the author Prof. A. Piccoli contrib nephrolog 2005; 49:150-161

Figure 11. Normogram graph.

The nomogram is divided in 4 parts, corresponding to four different nutritional and hydration condition.

All changes in hydration are associated with a shortening (over-hydration) or an extension of the vector impedance along the major axis (de-hydration). The hydration status is well-balanced, when the carrier is approaching the centre of the graph.

The human body consists of about two-thirds water, divided into extracellular (outside the cells) and intracellular (inside the cell) compartments. A well-balanced state of hydration is the first condition for proper metabolic functioning.

Starting from this fundamental assumption, it is possible to calculate:

1. **PA phase angle** is the ratio between the two electric measurements of resistance and reactance.
   It represents an indicator of the general conditions of the body.
   Standard values are within 4 - 9 degrees range.
2. **TBW - total body water** is divided into 2 compartments called:
   ECW - extracellular water represents the volume of the fluid outside the cells.
   ICW **-** intracellular water is the water contained inside the cell.
   Healthy cells maintain their integrity and maintain their fluids inside
3. **FFM** - **fat free mass** consists of muscles, bones, minerals and other non-fat tissues.
   It contains approximately 73% of water, 20% of proteins and 7% of minerals.
   It is divided into Cellular Mass and Extracellular Mass.
4. **BCM** - **body cell mass** is expression of the active cellular mass, and represents the total volume of the total volume of the living cells.
   It is the metabolically active tissue of the body.
   Normal values are approx.: 35% -40% of the body weight.
5. **FM - fat mass** consists of all the lipids that can be extracted from the adipose tissues and other tissues of the body.
   The external adipose tissues are often identified as cutaneous fat, while the internal adipose tissues are identified as visceral fat.
   The fat mass parameter can be a variable since it is calculated by difference between their.
   <u>It is reliable only if the measured subject has a standard hydration condition</u>.
6. **MM** - **muscle mass** is the skeletal component of the muscle tissue consisting mainly of red and white fibres.

It differs from the cellular mass component since it is an actual anatomical component.

The muscle mass in the standard subject (healthy, young) represents approx. 50% of the **FFM**.

7. **BMR - basal metabolic rate** is the energy consumption of a body at rest and includes the energy required for vital metabolic functions (breathing, blood circulation, digestion, activity of the nervous system, etc.). It represents approximately 45-75% of the daily total energy consumption.

Published estimate equations parameters for adults of the FFM, BCM, FM , TBW , ECW , MM [226,227**]:**

Males: TBW = 1.2 + 0.45 * (HTM ^ 2) / RZ + 0.18 * WTM

FFM = -10.68 + 0.65 * (HTM ^ 2) / RZ + 0.26 * WTM + 0.02 * RZ

Females: TBW = 3.75 + 0.45 * (HTM ^ 2) / RZ + 0.11 * WTM 'females

FFM = -9.53 + 0.69 * (HTM ^ 2) / RZ + 0.17 * WTM + 0.02 * RZ

FAT (M & F) = WTM – FFM

Note: TBW= Total Body Water in litres

FFM= Fat Free Mass in kilograms

HTM= Height in centimetres;

WTM= Weight in kilograms, ;

BCM= Body Cell Mass in kilograms;

ECW= Extra Cellular Water in litres.

Rz Resistance; Xc= Reactance in Ohm, measured with BIA Akern/Rjl system

The excesses or depletions of fat and FFM are associated with an increased risk of some chronic diseases and the amount of FFM is considered to be directly correlated with health and longevity [228].

6.2 Sedentariness

6.2.1 Physical Activity Scales

In the Elderly, it is important to determinate the level of physical capacity by way of understanding their ability to lead an independent life and to have an active participation in society. As a screening tool to help the identification of the physical status of the Elderly, the **PASE** test (Physical Activity Scale for the Elderly) (Table 4) is a brief, easily scored, reliable and valid instrument for the assessment of physical activity in studies of older people. The detection of physical activity suitable for a general population is not sufficiently sensitive and accurate when used in an elderly population. In fact, for the elderly, even simple everyday action like moving into the house, going up and down stairs or a short walk, cannot be ignored in the calculation of the amount of exercise [229].

The PASE questionnaire consists of questions regarding the frequency and duration of leisure activity (e.g., sports, jogging, swimming, strengthening and endurance exercise), household activity, and work-related activity during the previous 7-day period and can be administered by telephone, mail or in-person.

The questions are scored differently. Participation in leisure-time and strengthening activities are scored as never, seldom (1-2 days per week), sometimes (3-4 days per week), and often (5-7 days per week). The duration of these activities is scored as less than 1 hour, 1-2 hours, 2-4 hours and more than 4 hours. Household and work related activities are scored as yes or no. In work related activities, paid or unpaid work is scored in hours/week. The total PASE score is computed by multiplying either the time spent in each activity (hours per week) or participation (i.e., yes/no) in an activity, by empirically derived item weights and then summing overall activities [230].

According to the different categories of the 12 activities, PASE scores are calculated from weight and frequency of each of them. **Weight** for individual activities was estimated by regressing component scores on the complete set of items in the original version of the PASE**.**

Frequency is the number of day per week and then the number of hour per day related to the performance of the leisure activities. Activity frequencies (time spent) are multiplied by the activity weight (assigned to each item) and summed for all activities.

The computation algorithm provides that the duration and frequency of generic activities are not included in the calculation: these are only recorded as performed or not performed. [229,231,232].

It should be emphasized that the **PASE** questionnaire does not estimate the energy expenditure, rather it produces a score that allows comparisons.

PASE activity	Sample mean	PASE weight	Contribution to total PASE score
Muscle strength/ endurance	0.05 hr/day	30	1.5
Strenuous sports	0.07 hr/day	23	1.6
Moderate sports	0.11 hr/day	23	2.5
Light sports	0.09 hr/day	21	1.9
Job involving standing or walking	0.53 hr/day	21	11.1
Walking	0.65 hr/day	20	13.0
Lawn work or yard care	45.6%*	36	16.4
Caring for another person	24.2%*	35	8.5
Home repairs	22.0%*	30	6.6
Heavy housework	47.4%*	25	11.8
Light housework	89.5%*	25	22.4
Outdoor-gardening	26.8%*	20	5.4
			102.7

*Percentage of sample engaging in that activity during week.

Table 2. PASE item weights and contributions to total score (n=314).

Table 2 shows an example of the contribution of each questionnaire item, to the overall PASE score, as calculated by the product of the sample mean and activity weight. A population of 314 elderly people contributed to the generation of the computational algorithm.

To evaluate the effect on the measurement of quality of life of many covariates available and the strength of this relationship, the regression model quantile has been used**.** Whereas the method of least squares results in estimates that approximate the conditional *mean* of the response variable given certain values of the predictor variables. Quantile regression aims at to estimate either the conditional median or other quantiles of the response variable.

Starting from the quartiles of PASE score, it is possible to divide the elderly into four categories of physical activity: inactive, low physical activity, activity moderate physical activity and vigorous physical activity [229] (Table 3). From the results of the model it is clear that even a poor physical activity, compared to the complete inactivity, is positively associated with the perception of health status.

PHISICAL ACTIVITY - QUARTILES	PASE SCORE
INACTIVITY - SEDENTARINESS	<42
LOW PA – BOTTOM QUARTILE	43-105
MODERATE PA– MIDDLE QUARTILE	106-145
HIGHT PA– TOP QUARTILE	>146

Table 3. Categories of physical activity according to the PASE scales.

According to the study *"The Physical Activity Scale for the Elderly (PASE) Questionnaire; Does It Predict Physical Health?"*, PASE questionnaire **cannot be used to predict** clinically healthy physical measures of body composition, cardiovascular and blood parameters, and flexibility and strength measures. It can be used for monitoring tools which correlate well with daily physical activity; health parameters warrant additional research to determine and monitor whether older adults are achieving adequate physical activity for desirable physical parameters, and to increase awareness regarding the importance of physical activity in maintaining and/or increasing the quality of life. With the decreasing of physical activity with age and the increasing numbers of seniors, the need for such a measure is timely [233]. Despite the declared limit of this study "that the cohort was relatively healthy", it goes on giving important inputs: "Future research should attempt to recruit adults who are in unfavourable categories of health and investigate the relationship between their activity level and the various health parameters, especially body composition and strength, which may provide stronger relationships between activity level and health. A large intervention study would be optimal to first quantify the amount of physical activity performed over a 7 day period and relate this amount to the participant's PASE score and health parameters. The Authors would have further test this relationship by increasing an individual's PASE score, by increasing physical activity over a period of time (about 12 weeks) and measure the influence on the health parameters. This would theoretically provide a monitoring tool to advise adults on the amount of activity needed to move their physical measure to a more favourable health category" [234].

As far as PASE validation in concerned, the *Journal of Clinical Epidemiology – 1999,* published an important study in which the evidence of validity of this test was proved. "We assessed the validity of the Physical Activity Scale for the Elderly (PASE) in a sample of sedentary adults (56 men, 134 women, mean age ± [SD] 66.5 ± 5.3 years) who volunteered to participate in a randomized controlled trial on the effect of aerobic conditioning on psychological function. Construct validity was established by correlating PASE scores with physiologic and performance characteristics: peak oxygen uptake, resting heart rate and blood pressure, % of body fat, and balance. The mean PASE scores were higher in men than in women (men = 145.8 ± 78.0; women = 123.9 ± 66.3, $P < 0.05$), and in those aging 55–64 years, compared with those aging 65 years and over (55–64 = 144.2 ± 75.8; 65 and over = 118.9 ± 63.9, $P < 0.05$). PASE scores were also significantly higher in those who did not report a chronic health condition (cardiovascular disease, hypertension, cancer, or recent surgery). PASE scores were significantly associated ($P < 0.05$) with peak oxygen uptake ($r = 0.20$), systolic blood pressure ($r = -0.18$) and balance score ($r = 0.20$). No significant associations of PASE score and diastolic blood pressure, resting heart rate, or % of body fat were noted. These results provide additional evidence for the validity of the PASE as a measure of physical activity suitable for use in epidemiology studies on the association of physical activity, health, and physical function in older individuals [218]. The administration and scoring instruction manual, prepared by the New England Research Institute – NERI, can be downloaded from the website www.neriscience.com.

PHYSICAL ACTIVITY SCALE FOR THE ELDERLY (PASE)
NERI – NEW ENGLAND RESEARCH INSTITUTION Inc.

LEISURE TIME ACTIVITY

1. Over the past 7 days, how often did you participate in sitting activities such as reading, watching TV or doing handcrafts?

[0.] NEVER	[1.] SELDOM	[2.] SOMETIMES	[3.] OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q.#2	↓	↓	↓

1a. What were these activities?

____

1b. On average, how many hours per day did you engage in these sitting activities?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

2. Over the past 7 days, how often did you take a walk outside your home or yard for any reason? For example, for fun or exercise, walking to work, walking the dog, etc.?

[0.] NEVER	[1.] SELDOM	[2.] SOMETIMES	[3.] OFTEN
↓	(1-2 DAYS)	(3-4 DAYS)	(5-7 DAYS)
GO TO Q.#3	↓	↓	↓

2a. On average, how many hours per day did you spend walking?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

5. Over the past 7 days, how often did you engage in strenuous sport and recreational activities such as jogging, swimming, cycling, singles tennis, aerobic dance, skiing (downhill or cross-country) or other similar activities?

[0.] NEVER ↓ GO TO Q.#6	[1.] SELDOM (1-2 DAYS) ↓	[2.] SOMETIMES (3-4 DAYS) ↓	[3.] OFTEN (5-7 DAYS) ↓

5a. What were these activities?

____

5b. On average, how many hours per day did you engage in these strenuous sport and recreational activities?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

6. Over the past 7 days, how often did you do any exercises specifically to increase muscle strength and endurance, such as lifting weights or pushups, etc.?

[0.] NEVER ↓ GO TO Q.#7	[1.] SELDOM (1-2 DAYS) ↓	[2.] SOMETIMES (3-4 DAYS) ↓	[3.] OFTEN (5-7 DAYS) ↓

6a. What were these activities?

____

6b. On average, how many hours per day did you engage in exercises to increase muscle strength and endurance?

[1.] LESS THAN 1 HOUR [2.] 1 BUT LESS THAN 2 HOURS

[3.] 2-4 HOURS [4.] MORE THAN 4 HOURS

HOUSEHOLD ACTIVITY

7. During the past 7 days, have you done any light housework, such as dusting or washing dishes?

   [1.] NO [2.] YES

8. During the past 7 days, have you done any heavy housework or chores, such as vacuuming, scrubbing floors, washing windows, or carrying wood?

   [1.] NO [2.] YES

9. During the past 7 days, did you engage in any of the following activities?

   Please answer YES or NO for each item.

		NO	YES
a.	Home repairs like painting, wallpapering, electrical work, etc.	1	2
b.	Lawn work or yard care, including snow or leaf removal, wood chopping, etc.	1	2
c.	Outdoor gardening	1	2
d.	Caring for an other person, such as children, dependent spouse, or an other adult	1	2

WORK-RELATED ACTIVITY

10. During the past 7 days, did you work for pay or as a volunteer?

[1.] NO [2.] YES

10a. How many hours per week did you work for pay and/or as a volunteer?

_______________ HOURS

10b. Which of the following categories best describes the amount of physical activity required on your job and/or volunteer work?

[1] Mainly sitting with slight arm movements. [**Examples**: office worker, watchmaker, seated assembly line worker, bus driver, etc.]

[2] Sitting or standing with some walking. [**Examples**: cashier, general office worker, light tool and machinery worker.]

[3] Walking, with some handling of materials generally weighing less than 50 pounds. [**Examples**: mailman, waiter/waitress, construction worker, heavy tool and machinery worker.]

[4] Walking and heavy manual work often requiring handling of materials weighing over 50 pounds. [**Examples**: lumberjack, stone mason, farm or general laborer.]

TABLE 1

PASE SCORING FORM

PASE Item	Type of Activity	Activity Weight	Activity Frequency	Weight times Frequency
2.	Walk outside home	20	a.	
3.	Light sport / recreational activities	21	a.	
4.	Moderate sport / recreational activities	23	a.	
5.	Strenuous sport / recreational activities	23	a.	
6.	Muscle strength / endurance exercises	30	a.	
7.	Light housework	25	b.	
8.	Heavy housework or chores	25	b.	
9a.	Home repairs	30	b.	
9b.	Lawn work or yard care	36	b.	
9c.	Outdoor gardening	20	b.	
9d.	Caring for another person	35	b.	
10.	Work for pay or as volunteer	21	c.	
			PASE SCORE:	

Activity Frequency Values:

a. Use hours per day conversion table below
b. 1 = activity reported in past week, 0 = activity not reported
c. Divide work hours reported in Item 10.1 by seven; if no work hours or if job involves mainly sitting with slight arm movements (Item 10.2 = 1), then activity frequency = 0.

ACTIVITY TIME TO HOURS PER DAY CONVERSION TABLE

Days of Activity	Hours Per Day of Activity	Hours Per Day
0. Never		0
1. Seldom	1. Less than 1 hour	.11
	2. 1-2 hours	.32
	3. 2-4 hours	.64
	4. More than 4 hours	1.07
2. Sometimes	1. Less than 1 hour	.25
	2. 1-2 hours	.75
	3. 2-4 hours	1.50
	4. More than 4 hours	2.50
3. Often	1. Less than 1 hour	.43
	2. 1-2 hours	1.29
	3. 2-4 hours	2.57
	4. More than 4 hours	4.29

3

Table 4. PASE test.

To Compute a PASE Score:

1. Review the leisure time activities recorded by respondents or interviewers to ensure that sports and recreational activities are correctly classified as light, moderate, or strenuous. Appendix A shows the appropriate activities for each of these categories; a detailed description of more complex coding situations may be found in Appendix B. Household activities should not be recorded as sports or recreation.

2. Determine the frequency value (hours per day in the one-week reporting period) for each activity. For the walking, exercise, and sports/recreation items, frequency values are derived from the number of days and hours per day of activity, as shown in the conversion table at the bottom of the scoring form. Household activity values are "1" if an activity was reported in the past seven days and "0" if it was not. The frequency value for paid or volunteer work is the number of hours worked in the past week divided by seven. The activity frequency is zero for jobs that involve mainly sitting with slight arm movements.

3. Multiply the activity weight by the activity frequency for each item.

4. Sum the activity weight by the activity frequency products for all 12 items. We recommend that these totals be rounded to the nearest integer. PASE scores may range from zero to 400 or more.

An example of these scoring procedures is presented in Table 5 for a respondent who had a part-time job, walked outdoors, and engaged in light sports, activity. Light housework, and lawn work during the previous week. The PASE score for this respondent is 149.5.

PASE SCORING EXAMPLE

Respondent reports:

- Walking outside home (sometimes; 1-2 hours per day)
- light sports (golf with a cart; seldom; 2-4 hours per day)
- work involving sitting or standing with some walking (20 hours per week)
- light housework and lawn work in past seven days

PASE Item	Type of Activity	Activity Weight	Activity Frequency	Weight times Frequency
2.	Walk outside home	20	.75	15.0
3.	Light sport / recreational activities	21	.64	13.4
4.	Moderate sport / recreational activities	23	0	0
5.	Strenuous sport / recreational activities	23	0	0
6.	Muscle strength / endurance exercises	30	0	0
7.	Light housework	25	1	25.0
8.	Heavy housework or chores	25	0	0
9a.	Home repairs	30	0	0
9b.	Lawn work or yard care	36	1	36.0
9c.	Outdoor gardening	20	0	0
9d.	Caring for another person	35	0	0
10.	Work for pay or as volunteer	21	2.86	60.1
			PASE SCORE:	149.5

Table 5. PASE example.

As far as the concept of physical activity in the Elderly is concerned, the impairment of functional capacity as balance, transferring, turning, etc. may sometimes cause deterioration in physical daily activities (ADL). The functional impairments may be strictly linked to the sedentary lifestyle: for this reason functional capacity must be evaluated by testing certain tasks in the ADL in order to reduce related risks and to receive precious tools in the identification of individual risks. These will be used as indicator in the prevention of falls related to everyday activities helping the identification of high-risks subjects.

The **Berg Balance Scale** (BBS) (Table 6) is considered the gold standard assessment of balance with small intra-inter rater feasibility and good internal validity. The Berg's utility includes grading different patients' balance abilities, monitoring functional balance over time and to evaluating patients' responses to different protocols of treatment [235].

Based on a test of 14 items, it is performance-based and has a scale of 0-4 for each item (higher score for independent performance) with a maximum score of 56.

In 1999, the study *Measuring balance in the elderly: validation of an instrument*, assessed the validity of the Berg Balance Scale by examining how scale scores related to clinical judgments, laboratory measures of postural sway and external criteria reflecting balancing ability. Furthermore, if scores could predict falls in the elderly, and how they related to motor and functional performance in stroke patients.

Elderly residents (N = 113) were assessed for functional performance and balance regularly over a nine-month period and the occurrence of falls was monitored for one year. Acute stroke patients (N = 70) were periodically rated for functional independence, motor performance and balance for over three months. Thirty-one elderly subjects were assessed by clinical and laboratory indicators reflecting balancing ability. The Scale correlated moderately with caregiver ratings, self-ratings and laboratory measures of sway. Differences in mean scale scores were consistent with the use of mobility aids by elderly residents and differentiated stroke patients by location of follow-up. Balance scores predicted the occurrence of multiple falls among elderly residents and were strongly correlated with functional and motor performance in patients [236].

NYC Health

Berg Balance Scale

The **Berg Balance Scale (BBS)** is a 14 item scale to measure balance among older people with impairment in balance function by assessing the performance of functional tasks. It is a valid instrument used for evaluation of the effectiveness of interventions and for quantitative descriptions of function in clinical practice and research.

Instructions: Please document each task and/or give instructions as written. When scoring, please record the lowest response category that applies for each item.

In most items, the subject is asked to maintain a given position for a specific time. Progressively more points are deducted *if the time or distance requirements are not met , the subject's performance warrants supervision* **or** *the subject touches an external support or receives assistance from the examiner.* **A five-point scale, ranging from 0-4. "0" indicates the lowest level of function and "4" the highest level of function. Maximum total score = 56**

Subject should understand that they must maintain their balance while attempting the tasks. The choices of which leg to stand on or how far to reach are left to the subject. Poor judgment will adversely influence the performance and the scoring.

Equipment needed: Ruler, two standard chairs (one with arm rests, one without),footstool or step, stopwatch or wristwatch, 15 ft walkway. **Completion time:** 15-20 minutes.

Name:	**Date:**
Location:	**Administrator:**

	Task	Description of Balance	Pts	Score
1	SITTING TO STANDING	**INSTRUCTIONS: Please stand up. Try not to use your hand for support.**		
		able to stand without using hands and stabilize independently	4	
		able to stand independently using hands	3	
		able to stand using hands after several tries	2	
		needs minimal aid to stand or stabilize	1	
		needs moderate or maximal assist to stand	0	
2	STANDING UNSUPPORTED	**INSTRUCTIONS: Please stand for two minutes without holding on.**		
		able to stand safely for 2 minutes	4	
		able to stand 2 minutes with supervision	3	
		able to stand 30 seconds unsupported	2	
		needs several tries to stand 30 seconds unsupported	1	
		unable to stand 30 seconds unsupported	0	
		If a subject is able to stand 2 minutes unsupported, score full points for sitting unsupported. Proceed to item #4.		
3	SITTING- BACK UNSUPPORTED - FEET SUPPORTED ON FLOOR OR ON A STOOL	**INSTRUCTIONS: Please sit with arms folded for 2 minutes.**		
		able to sit safely and securely for 2 minutes	4	
		able to sit 2 minutes under supervision	3	
		able to able to sit 30 seconds	2	
		able to sit 10 seconds	1	
		unable to sit without support 10 seconds	0	
4	STANDING TO SITTING	**INSTRUCTIONS: Please sit down.**		
		sits safely with minimal use of hands	4	
		controls descent by using hands	3	
		uses back of legs against chair to control descent	2	
		sits independently but has uncontrolled descent	1	
		needs assist to sit	0	

	Task	Description of Balance	Pts	Score
5	TRANSFERS	**INSTRUCTIONS: Arrange chairs for pivot transfer. Ask subject to transfer one way toward a seat with armrests and one way toward a seat without armrests. You may use two chairs (one with and one without armrests) or a bed and a chair.**		
		able to transfer safely with minor use of hands	4	
		able to transfer safely definite need of hands	3	
		able to transfer with verbal cuing and/or supervision	2	
		needs one person to assist	1	
		needs two people to assist or supervise to be safe	0	
6	STANDING UNSUPPORTED WITH EYES CLOSED	**INSTRUCTIONS: Please close your eyes and stand still for 10 seconds.**		
		able to stand 10 seconds safely	4	
		able to stand 10 seconds with supervision	3	
		able to stand 3 seconds	2	
		unable to keep eyes closed 3 seconds but stays safely	1	
		needs help to keep from falling	0	
7	STANDING UNSUPPORTED WITH FEET TOGETHER	**INSTRUCTIONS: Place your feet together and stand without holding on.**		
		able to place feet together independently and stand 1 minute safely	4	
		able to place feet together independently and stand 1 minute with supervision	3	
		able to place feet together independently but unable to hold for 30 seconds	2	
		needs help to attain position but able to stand 15 seconds feet together	1	
		needs help to attain position and unable to hold for 15 seconds	0	
8	REACHING FORWARD WITH OUTSTRETCHED ARM WHILE STANDING	**INSTRUCTIONS: Lift arm to 90 degrees. Stretch out your fingers and reach forward as far as you can. Examiner places a ruler at the end of fingertips when arm is at 90 degrees. Fingers should not touch the ruler while reaching forward. The recorded measure is the subject is in the most forward lean position. When possible, ask subject to use both arms when reaching to avoid rotation of the trunk.**		
		can reach forward confidently 25 cm 10 inches	4	
		can reach forward 12 cm 5 inches	3	
		can reach forward 5 cm 2 inches	2	
		reaches forward but needs supervision	1	
		loses balance while trying/requires external support	0	
9	PICK UP OBJECT FROM THE FLOOR FROM A STANDING POSITION	**INSTRUCTIONS: Pick up the shoe/slipper, which is in front of your feet.**		
		able to pick up slipper safely and easily	4	
		able to pick up slipper but needs supervision	3	
		unable to pick up but reaches 2-5 cm1-2 inches from slipper and keeps balance independently	2	
		unable to pick up and needs supervision while trying	1	
		unable to try/needs assist to keep from losing balance or falling	0	
10	TURNING TO LOOK BEHIND OVER LEFT AND RIGHT SHOULDERS WHILE STANDING	**INSTRUCTIONS: Turn to look directly behind you over toward the left shoulder. Repeat to the right. Examiner may pick an object to look at directly behind the subject to encourage a better twist turn.**		
		looks behind from both sides and weight shifts well	4	
		looks behind one side only other side shows less weight shift	3	
		turns sideways only but maintains balance	2	
		needs supervision when turning	1	
		needs assist to keep from losing balance or falling	0	

PATIENT NAME: **DATE:** **BERG BALACE SCALE 2**

	Task	Description of Balance	Pts	Score
11	TURN 360 DEGREES	**INSTRUCTIONS: Turn completely around in a full circle. Pause. Then turn a full circle in the other direction.**		
		able to turn 360 degrees safely in 4 seconds or less	4	
		able to turn 360 degrees safely one side only 4 seconds or less	3	
		able to turn 360 degrees safely but slowly	2	
		needs close supervision or verbal cuing	1	
		needs assistance while turning	0	
12	PLACE ALTERNATE FOOT ON STEP OR STOOL WHILE STANDING UNSUPPORTED	**INSTRUCTIONS: Place each foot alternately on the step/stool. Continue until each foot has touched the step/stool four times.**		
		able to stand independently and safely and complete 8 steps in 20 seconds	4	
		able to stand independently and complete 8 steps in > 20 seconds	3	
		able to complete 4 steps without aid with supervision	2	
		able to complete > 2 steps needs minimal assist	1	
		needs assistance to keep from falling/unable to try	0	
13	STANDING UNSUPPORTED ONE FOOT IN FRONT	**INSTRUCTIONS: DEMONSTRATE TO SUBJECT Place one foot directly in front of the other. If you feel that you cannot place your foot directly in front, try to step far enough ahead that the heel of your forward foot is ahead of the toes of the other foot. To score 3 points, the length of the step should exceed the length of the other foot and the width of the stance should approximate the subject's normal stride width.**		
		able to place foot tandem independently and hold 30 seconds	4	
		able to place foot ahead independently and hold 30 seconds	3	
		able to take small step independently and hold 30 seconds	2	
		needs help to step but can hold 15 seconds	1	
		loses balance while stepping or standing	0	
14	STANDING ON ONE LEG	**INSTRUCTIONS: Stand on one leg as long as you can without holding on.**		
		able to lift leg independently and hold > 10 seconds	4	
		able to lift leg independently and hold 5-10 seconds	3	
		able to lift leg independently and hold ≥ 3 seconds	2	
		tries to lift leg unable to hold 3 seconds but remains standing independently.	1	
		unable to try of needs assist to prevent fall	0	

TOTAL SCORE (MAX 56) =

Table 6. BERG Scale test.

6.2.2 Objective parameters of Physical Activity

The quantity of habitual physical activity by an individual, is closely associated with all-cause mortality risk, yet the majority of people in many countries do not undertake sufficient exercise to derive health-related benefits [237,238].

With the quantification of the amount of the total daily activity (light, moderate, vigorous), we should be able to study accurately protocols in order to promote active ageing, health, and longevity in the elderly.

Physical **A**ctivity (PA) - with force and movement or only with force – involves however, a variation of mechanical energy evident only in the first case; to support the energy requirement, the human body increases its own metabolism. As far as the control and the monitoring of PA is concerned, *the way* is difficult and with challenges: changes in cognitive abilities and memory loss may lead to difficulties understanding instructions on self - report questionnaires **(indirect PA measures**) and the changing of metabolic cost due to aging, make the use of standard tables and equations used for determining energy expenditure on younger population inappropriate [239].

Indirect PA measures are practical, easy to administer to large groups, and cost efficient however they are prone to either over or under-estimation due to inaccurate recall, social desirability and misinterpretation. Nevertheless, many existing indirect tools fail to measure the lower end of the PA continuum and are susceptible to fluctuations in health status, medical conditions and medications, fatigue, pain, concentration and distractibility, changes in mood, depression, anxiety, and problems with memory and cognition [240-242].

Direct PA measures assess energy expenditure or actual movement and are generally considered more accurate. They are not prone to response and recall biases and are often used to validate indirect measures of PA. Although direct measures do not rely on self-report, there is a subjective element in data analysis and interpretation (i.e., we can choose time lengths and cut-off points/thresholds for intensity groupings) [243-248].

Physiological parameters like heart rate or indices derived by specific wearable sensors like pedometer and accelerometer, are methods to control and quantify levels of habitual activity during daily life [249,250]. Wearable sensors have the ability to measure mobility directly. Heart rate measurements (derived by analysis of R-R beat-to-beat or pulse wave intervals) pedometers or foot-switches measure a person's level of dynamic activity and energy expenditure, however, they do not provide information on static activities. Conversely, wearable accelerometers or gyroscopes are able to distinguish between static position and dynamic activity. Integration of the two systems provides information on PA correlated with energy expenditure, a goal in DOREMI for linking physical work – energy expenditure with energy intake (nutrition).

What is an accelerometer? Acceleration is a measure of how fast the speed of something is changing. An accelerometer is an electromechanical device used as an input to control system, which will measure acceleration forces. These forces may be static, like the constant force of gravity pulling at your feet, or they could be dynamic - caused by moving or vibrating the accelerometer. By measuring the amount of static acceleration due to gravity, you can find out the angle the device is tilted respect to the earth. By sensing the amount of dynamic acceleration, one can analyse the way the device is moving.

In 2008 and 2009, in the trial *Accelerometer-determined physical activity in adults and older people*, PA was assessed objectively for seven consecutive days using this device in 3867 participants age 20-85 yr. A total of 3267 participants provided valid PA assessments [251].

PA was quantified as described below and summarized in Table 7. Sedentary activity was defined as all activities below 100 cpm, a threshold that corresponds with sitting, reclining, or lying down [252,253]. Low-intensity PA was defined as counts between 100 and 759, and time in lifestyle activity (e.g., slow walking, grocery shopping, vacuuming, and child care) was defined as counts between 760 and 2019 [254,255]. Moderate-to-vigorous PA (MVPA) was defined as all activity ≥2020 cpm [256]. This level of activity corresponds to walking at speeds of ≥78 $m*min^{-1}$ as well as more vigorous activities [253]. The numbers of minutes per day at different intensities were determined by summing all minutes where the count met the criterion for that intensity, divided by the number of valid days.

The participants were aged between 20–64 yr had a higher cpm than did those aged between 65–85 yr (347 vs 296). Within the age group of 20–64 yr, cpm did not change with increasing age. By contrast, in the age group of 65–85 yr, the estimated decrease in cpm was 9 per year.

Furthermore, in group 65-85 yr men present a higher cpm respect to women (305 vs 287).

Regarding the means for minutes per day of total accumulated time spent in PA at different intensities and for minutes per day spent in bouts of ≥10 min of MVPA, men in both age groups spent more time being sedentary and achieved more minutes of MVPA compared with women. Women in both age groups completed more minutes of low-intensity PA compared with men. Changes with age were more apparent in the 65- to 85-yr age group. Women and men showed a yearly estimated increase in the amount of sedentary activity with respect to "young group" (+15 and +12 $min*d^{-1}$, respectively). The yearly estimated low- intensity PA and lifestyle activity decreased by 25 $min*d^{-1}$ and 18 $min*d^{-1}$ for women and 21 $min*d^{-1}$ for men. The yearly estimated MVPA decreased by 8.7 $min*d^{-1}$ in women and by 6.3 $min*d^{-1}$ in men.

Interestingly and important to take in account for DOREMI study is also the prevalence of adherence to the PA recommendations. Overall, 20.4% of the study population met the PA recommendations, and this percentage did not differ between women and men.

Accelerometers were able to show that gains in physical performance translated into an increase in accelerometer-derived measures of daily physical activity in the community in contrast to self - reported measures that showed no change [257].

PHYSICAL ACTIVITY	CPM
Sedentary activity	<100
Low-intensity PA	100-759
Lifestyle PA	760-2019
MVPA	>2020

Table 7. Classification of Physical Activity considering the counts per minute

What is a pedometer? The pedometer is a portable device that measures a person's PA level throughout the day. It can be used as a motivational tool. Though they are designed to be worn at the waist, they can also be worn in other locations, such as the arm or ankle.

The pilot study *"Use of a Pedometer to Monitor Physical Activity in Older Adults"* conducted a preliminary test of the reliability of pedometer use to determine physical activity (PA) by older adults living independently.

Step counts along a 10 meter line were determined by observation and pedometer. Each individual then completed a 7-day step count using a pedometer, a 7-day PA log, and a self-reported PA questionnaire**.** The use of pedometer to monitor PA in older adults appears to be reliable and valid [258]. A systematic review of the validity of **pedometers compared to accelerometers**, observation, energy expenditure and self-report concluded that they are a valid method for assessing physical activity when compared to different accelerometers (specifically uniaxial accelerometers), with a reported median correlation of r=0.86, depending on the specific instruments used, monitoring frame and conditions implemented, as well as the manner in which the outputs are expressed [259]. With regards to ambulatory activities only, better accuracy has been reported at faster walking speeds (i.e. 4.8-6.4 km/hr) compared to slower walking speeds but not at running speeds [260]. More sensitive (e.g. piezoelectric) pedometers have been recommended in individuals who naturally ambulate at a slower pace e.g. the elderly [261].

6.3 Cognitive Decline

The characterization of cognitive skills in the elderly population is a useful approach for prevention of a decline linked to other factors, such as malnutrition and/or sedentariness, in addition to the definition of the cognitive impairment.

6.3.1 MMSE test

The Mini Mental State Examination (MMSE) (Table 8), introduced by Folstein Marshall [262] is a screening tool to assess mental status. The MMSE is one of the most used assessment tools to identify older people who have a cognitive impairment. It's one of the tools most commonly used in clinical evaluation. Apart from this, it's easy to apply and allows to monitor the course of a disease and the response of a subject to a treatment in time. It consists of 11 items that measure 5 different areas of cognitive function:

- ✓ Orientation
- ✓ Registration
- ✓ Attention and calculation
- ✓ Recall
- ✓ Language and Praxis

The maximum score is 30 and it takes about 5-10 minutes to administer.

The cut-off score is 24. The score between 24 and 30 indicates a normal cognitive function, between 19-23 it indicates a mild to moderate impairment situation. The score under 19 highlights a severe impairment.

For the test administration, some objects are needed, like a wrist watch, a pencil, an eraser, blank sheets of paper and a paper saying "Close your eyes."

Mini-Mental State Examination (MMSE)

Patient's Name: ________________________________ Date: ____________

Instructions: Score one point for each correct response within each question or activity.

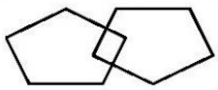
Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 
30		TOTAL

Table 8. MMSE test.

<u>**Instructions for administration and scoring of the MMSE**</u>

<u>Orientation</u> (10 points):

• Ask for the date. Then specifically ask for parts omitted (e.g., "Can you also tell me what season it is?"). One point for each correct answer.

• Ask in turn, "Can you tell me the name of this hospital (town, county, etc.)?" One point for each correct answer.

<u>Registration (3 points):</u>

• Say the names of three unrelated objects clearly and slowly, allowing approximately one second for each one. After you have said all three, ask the patient to repeat them. The number of objects the patient names correctly upon the first repetition determines the score (0-3). If the patient does not repeat all three objects the first time, continue saying the names until the patient is able to repeat all three items, up to six trials. Record the number of trials it takes for the patient to learn the words. If the patient does not eventually learn all three, recall cannot be meaningfully tested.

• After completing this task, tell the patient, "Try to remember the words, as I will ask for them in a little while."

Attention and Calculation (5 points):

• Ask the patient to begin with 100 and count backwards by sevens. Stop after five subtractions (93, 86, 79, 72, 65). Score the total number of correct answers.

• If the patient cannot or will not perform the subtraction task, ask the patient to spell the word "world" backwards. The score is the number of letters in correct order (e.g., dlrow=5; dlrw-dlow drow-dlro=4; dlorw-drlow-dlrwo-dlwor-dlr-lor-dlw=3; dorlw-dl-ow=2; drlwo-ldrwo=1).

Recall (3 points):

• Ask the patient if he or she can recall the three words you previously asked him or her to remember. Score the total number of correct answers (0-3).

Language and Praxis (9 points):

• Naming: Show the patient a wrist watch and ask the patient what it is. Repeat with a pencil. Score one point for each correct naming (0-2).

• Repetition: Ask the patient to repeat the sentence after you ("No ifs, ands, or buts."). Allow only one trial. Score 0 or 1.

• 3-Stage Command: Give the patient a piece of blank paper and say, "Take this paper in your right hand, fold it in half, and put it on the floor." Score one point for each part of the command correctly executed.

• Reading: On a blank piece of paper print the sentence, "Close your eyes," in letters large enough for the patient to see clearly. Ask the patient to read the sentence and do what it says. Score one point only if the patient actually closes his or her eyes. This is not a test of memory, so you may prompt the patient to "do what it says" after the patient reads the sentence.

• Writing: Give the patient a blank piece of paper and ask him or her to write a sentence for you. Do not dictate a sentence; it should be written spontaneously. The sentence must contain a subject and a verb and make sense. Correct grammar and punctuation are not necessary.

• Copying: Show the patient the picture of two intersecting pentagons and ask the patient to copy the figure exactly as it is. All ten angles must be present and two must intersect to score one point.

Ignore tremor and rotation.

Scoring the figure 12:

Correct: score 1

Incorrect: score 0

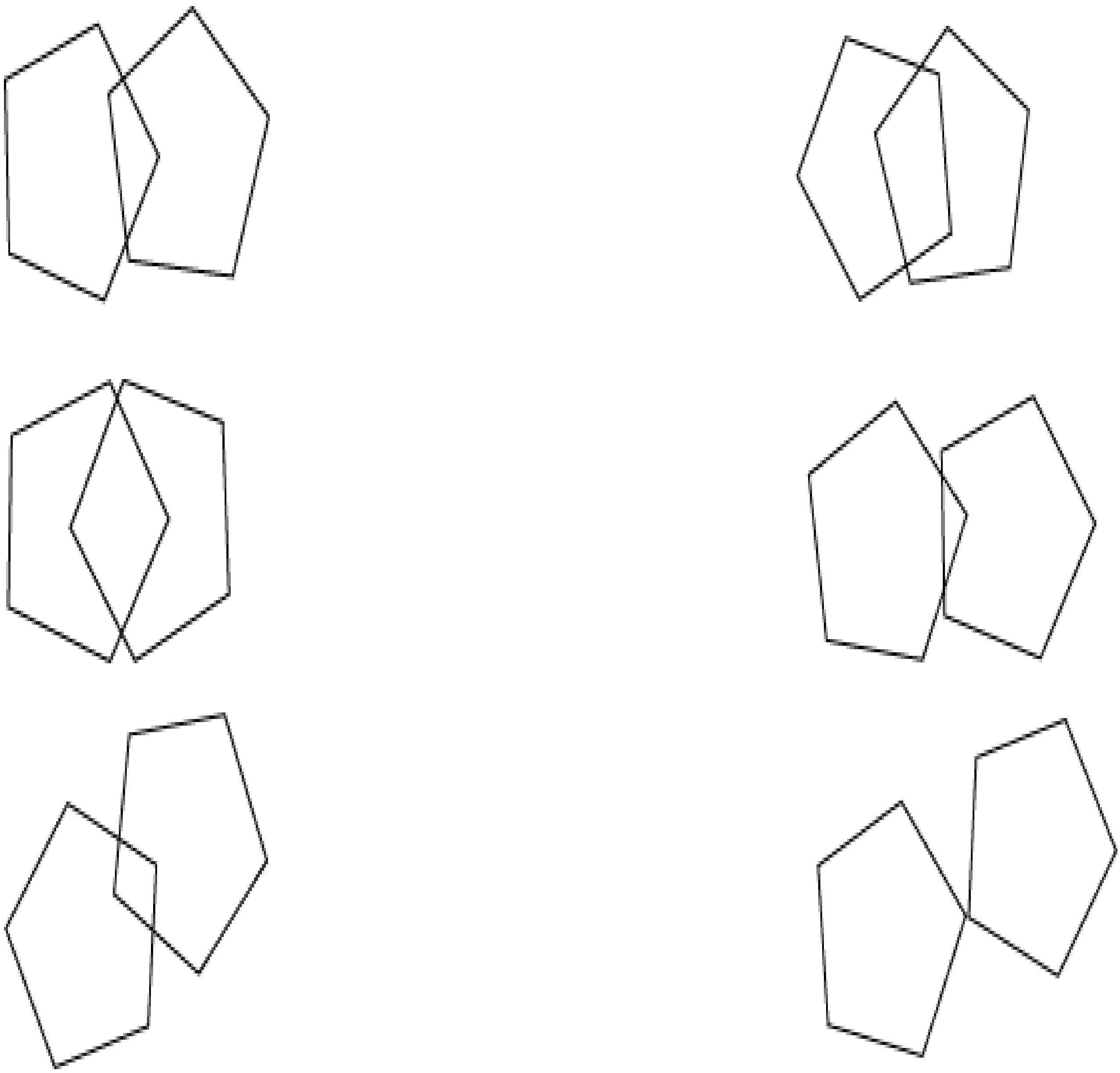


Figure 12. Copying section of MMSE test.

(Folstein, Folstein & McHugh, 1975) Source: www.medicine.uiowa.edu/igec/tools/cognitive/MMSE.pdf

A person's MMSE score can be affected by their level of education. This is because for highly educated people the questions may be too easy and for poorly educated people some may be too difficult. This means that a highly educated person with mild dementia may score in the normal range, whereas a poorly educated person with no problems in cognition may score in the dementia range. The same goes for the question of age (Table 9).

	Schooling (in years)			
	0-4	5-7	8-12	13-17
Age				
65-69	+0.4	-1.1	-2.0	-2.8
70-74	+0.7	-0.7	-1.6	-2.3
75-79	-0.9	-0.3	-1.0	-1.7
80-84	+1.5	+0.4	-0.3	-0.9
85-89	+2.2	+1.4	+0.8	+0.3

Table 9. MMSE score modulation respect to age and scholarization time.

In DOREMI, subjects with score lower than 22 will be excluded.

After the DOREMI interventions we expect to participants reach a value ≥ 27

6.3.2 Token test

Another rating scale of cognitive function is the **Token test** [263,264] (Figure 13 and Table 10). It is an evaluation test of listening comprehension.

The stimuli of the test are made up of thirty-six verbal orders divided into 6 parts, of increasing difficulty which the participant must perform operating on some tokens of different shapes (circle, rectangle), colour (red, blue, yellow, green, white) and size (two sizes). Rating: ranges from a minimum of 0 to a maximum of 36 points, and is given by the sum of items to which the subject gave the correct answer.

The Token test allows also for the discriminate between aphasic patients and not aphasic and is relatively sensitive for the diagnosis of mild deficit language and in subjects with low school attendance.

Score table:

- 1 point for each correct answer to the first presentation;
- 0.5 points for each correct answer to the second presentation;
- 0 points for each incorrect answer after the second presentation (or after the first of the orders of the sixth part)

Figure 13. Token test items.

Instructions: *the examiner tells the patient: "As you can see, here there are tokens (point them) that have different shape, size and colour. Some of them are circles, and other squares, some are large and some small, there are red, yellow, white, green and black ones (indicate each time.) Now I'll tell you to do some things with these tokens, for example, please touch the black one. Wait each time until I've finished explaining what you are requested to do. "*

If the patient doesn't answer within the first 5 seconds, or gives a wrong answer, tidy up the tokens and say, "let's try again." Repeat the request and give to the patient another 5 seconds to answer: if he doesn't answer again, his reply is not correct, proceed with the following request. Only for requests included in Part VI, the order shall never be repeated. If the patient asks for a third repetition or complains of having forgotten part of the order, he should be invited to do anything he can remember.

TOKEN TEST – Short Version

Name: ______________________________

Birth: ______________ **Age:** ____ **yars and** ____ **months.**

Schooling: ______________________ **Date:** __________

Examiner: ______________________________

Part 1 (All tokens)

- ☐ 1- Touch a circle.
- ☐ 2- Touch a square.
- ☐ 3- Touch a yellow token
- ☐ 4- Touch a red one.
- ☐ 5- Touch a black one.
- ☐ 6- Touch a green one.
- ☐ 7- Touch a white onde.

Part 2 (Only large tokens)

- ☐ 8- Touch the yellow square.
- ☐ 9- Touch the black circle.
- ☐ 10- Touch the green circle.
- ☐ 11- Touch the white square.

Part 3 (All tokens)

- ☐ 12- Touch the small white circle.
- ☐ 13- Touch the large yellow square.
- ☐ 14- Touch the large green square green.
- ☐ 15- Touch the small black circle.

Part 4 (Only large tokens)

- ☐ 16- Touch the red circle red and the green square.
- ☐ 17- Touch the yellow square and the black square.
- ☐ 18- Touch the white square and the green circle.
- ☐ 19- Touch the white circle and red circle.

Part 5 (All tokens)

- ☐ 20- Touch the large white circle and the small green square.
- ☐ 21- Touch the small black circle and the large yellow square.
- ☐ 22- Touch the large green square and the large red square.
- ☐ 23- Touch the large white square and the small green circle.

Part 6 (Only large tokens)

- ☐ 24- Put the red circle on the green square.
- ☐ 25- Touch the black circle with the red square.
- ☐ 26- Touch the black circle and the red square.
- ☐ 27- Touch the black circle or the red square.
- ☐ 28- Put the green square away from the yellow square.
- ☐ 29- If there is blue circle, Touch the red square.
- ☐ 30- Put the green square next to the red circle.
- ☐ 31- Touch the squares slowly and the circles quickly.
- ☐ 32- Put the red circle between the yellow square and de green square.
- ☐ 33- Touch all the circles, except the green one.
- ☐ 34- Touch the red circle red. No! The white square.
- ☐ 35- Instead of the white square, Touch the yellow circle.
- ☐ 36- In addition to touching the yellow circle, Touch black circle.

Score: __________

-

Table 10. Token test short version.

6.3.3 Phonemic fluency

The test of phonemic verbal fluency is to say as many words as possible that begin with a certain letter (F, A S for English version; F, L, P for Italian version) (Table 11 and 12). One minute for each letter. You need to provide some examples and discourage the tendency to give proper names and derivatives.

Nr. of Words	Range
From 1 to 16	0
From 17 to 22	1
From 23 to 26	2
From 27 to 31	3
From 32 to over	4

Table 11. Score scale for phonemic fluency test.

	Schooling (in years)				
	0-3	4-5	6-8	9-13	14-17
Age					
25-34	7	4	-1	-6	-10
35-44	8	5	1	-5	-9
45-54	9	6	2	-4	-7
55-64	10	7	3	-3	-6
65-74	12	8	4	-1	-5
>75	13	9	5	0	-4

Table 12. Correction table for phonemic fluency test.

Cut-off: 17 (n. of word), after DOREMI we expect to reach a value >30.

6.3.4 Semantic fluency

The implementing rules are identical to those of the phonemic fluency test (Table 13 and 14). Instead of the letters you use three semantic fields:

- fruits
- animal
- brands cars

Nr. of Words	Range
From 1 to 24	0
From 25 to 29	1
From 30 to 34	2
From 35 to 38	3
From 39 to over	4

Table 13. Score scale for semantic fluency test.

	Schooling (in years)				
	0-3	4-5	6-8	9-13	14-17
Age					
25-34	6	2	-2	-6	-8
35-44	7	3	-1	-5	-7

45-54	9	4	1	-3	-6
55-64	10	6	2	-2	-4
65-74	12	8	4	0	-2
>75	14	10	6	2	0

Table 14. Correction table for semantic fluency test.

Cut-off: 25 (n. of word), after DOREMI we expect to reach a value >32.

6.3.5 Attentional Matrices

This is also referred to as: evaluation of selective visual attention [264]. Three matrices of numbers were administered; each is constituted by 13 rows of 10 numbers from 0 to 9 randomly arranged. The subject must cross out as fast as possible target numbers. The maximum time for each matrix is 45 seconds. It's possible to complete the task after the time (45 sec), scoring the numbers crossed and recording the actual time of completion. If the subject takes less than 45 sec., you write down the time.

Score range 0-60, cut-off :31

Instruction:

Show the 1st matrix and say: "Now you'll have to mark with a pencil all the numbers corresponding to those shown in the top of the matrix." The line A is used as an example. If the person proves that he understood the task, go on. The function of line B is run-in. You must start to count the time only from the line I. You are not allowed to correct dams already made.

7. DEFINITION OF SAMPLE POPULATION AND SCENARIOS OF USE

7.1 Malnutrition, Sedentariness and Cognitive Decline: Inclusion criteria

In the selection of DOREMI participants several parameters will be take in account for final inclusion in the project, in particular linked to the three main pillars of this study: Sedentariness, Malnutrition and Cognitive Decline. User characteristics will be:

- **Age**. People between 65 and 80 years will be enrolled.
- **Sex**. A balanced male/female ratio will take in account in the composition of DOREMI population.
- **Physical Activity**: PASE test. This score can identify two groups of elderly people for DOREMI project, one with reduced physical activity (43 – 105), and one with marked impairment of physical activity or inactivity (< 42). People which values included in these two groups will be object of our study
- **Malnutrition**: MNA and BMI. The MNA test is able to determine the low food intake population. For DOREMI project users that express values between 17 and 23.5 will be selected for our research program. BMI, on the other hand, is helpful to define the subject with a high food intake (overweight and obese population). For the project will be accepted users in the range 18.5-30 of BMI (18.5-25 normal range, 25-30 overweight), with a possible tolerance until 32.5.
- **Cognitive Decline**: MMSE. The aim of this test is the screening of mental impairment. In the project, users with a value between 22 and 24 (mild cognitive impairment) will be enrolled.
  Furthermore, eligible participants will be able to:
- Live alone on their own at home or in nursing homes
- Possess basic computer skills (they should know what is internet, what are games)
- Have chance of actively choosing diet

7.2 Exclusion criteria

During ambulatory medical evaluation, the following criteria/pathologies will be considered as exclusion criteria:

- MMSE score < 22
- Advanced cancer
- Speech, hearing and vision problems which may interfere with physical activity
- Severe neurological disorders (epilepsy, multiple sclerosis, Parkinson disease, Alzheimer disease)
- History of head injury and substance abuse
- Moderate to severe aortic stenosis
- Hypertrophic cardiomyopathy
- NYHA III/IV heart failure
- Patients with an implanted ICD or CRT-D
- Severe chronic renal failure (glomerular filtration rate GFR<30 ml/min, or blood creatinine >2.4 mg/dl for males, >1.9 mg/dl for females)
- Severe hepatic failure
- Chronic obstructive pulmonary disease
- Uncompensated diabetes mellitus
- Chronic hematologic disorders
- Peripheral arteriopathy (Leriche-Fontaine Class III)
- Severe disabilities due to osteoarticular pathologies.
- Severe mobility impairment

7.3 Scenario of use: Rowland

Rowland is a 69 years old business man, divorced with two sons. He was living alone after the end of a long relationship in a nice little house with a beautiful garden where he loved to spend time. He lived far away from the centre of the town, but each morning he walked for a few miles for buying newspapers, milk and fresh vegetables.

He was a dynamic sport man: he used play tennis and golf twice a week, he loved visiting museums and each year during Christmas time, he organized with his sons a charity show to raise funds for abandoned children, in which they starred as comedians.

Four years ago, something changed in Rowland's life: he started feeling tired playing tennis, distracted playing golf, closed and reserved in public life.

For fear of getting tired he immediately reduced the physical activity and he began to gain weight; he stopped going out for dinner with friends and spent day after day locked up at home watching news on television, crunching on peanuts. All the flowers in his garden, began to die.

The day the doctor told him he suffered from hypertension and probably of CVD, he sold his company because he didn't feel more able to participate in active working life. In the last two year, he complained loss of memory, attention and concentration, which were related by the consulted neurologist to "Mild Cognitive Impairment" (MCI).

After a consultation, doctor proposed to Rowland to participate to DOREMI training. The specialist started to describe the related activities playing, in particular, on his feeling for past active lifestyle and pointing out him the possibility of its recovery. Doctor explained the technological, social and gamified approach for a new elderly lifestyle. Rowland was subjected to different tests as PASE (to categorize his physical activity), MMSE (to evaluate the impairments related to MCI), the quantification of his BMI (with standard formula) and the impedeziometric analysis (useful for calculation of lean mass, metabolic rate and hydration). The results showed how Rowland was the ideal user for DOREMI environment.

Rowland accepted to participate to the trial. His house was prepared by DOREMI technicians. A wireless sensor network was installed in the most frequented rooms of the apartment, as living room, kitchen, bedroom. This system, in an unobtrusive manner, saw to the user during the day, recognizing his activities and interacting with the bracelet given to Rowland. This last device, worn during the all the training period, was one the "silent" doctors of the DOREMI environment. In fact, it was useful to evaluate physical activity, thanks to integrated accelerometer/pedometer, heart rate, kcal consumption, both indoor and outdoor. Rowland was stimulated by the Virtual Companion, developed by DOREMI, to perform a series of outdoor activities (walking, light running, etc.) to do alone or with other DOREMI users.

In house, another support was the Intelligent carpet balance furnished to Rowland. Placed at the side of bed, every morning and evening, this device, in a natural manner for Rowland, measured his weight and stability: few seconds of attention to perform the measure and Rowland can continued his daily activity routine. Rowland had also a "personal" virtual dietician during the DOREMI training, thanks to a specifically designed software for DOREMI participants. On the tablet, he selected every day the picture of food and the relative quantity taken, thanks to user-friendly interface. He started to fill his food diary in a simple and funny manner, while the DOREMI system collected all this data to evaluate his food intake and quality. Also in this case, Virtual Companion suggested to improve healthy food intake, avoiding, for example, to eat an handful of his loved peanuts and crunching an healthy carrot.

To stimulate Rowland, DOREMI proposed also a gamified environment, composed of Cognitive, social and exergames. The cognitive games were projected and personalized on the Rowland cognitive capabilities: in this case, from his anamnestic analysis, games were focused on memory and attention. Exergames were developed to improve physical activity, stimulating Rowland with a series of exercises useful to recovery his leaved out passion for golf. His score increased during the training and thanks to Social games, designed to help the socialization between users, he was motivated to start once again to play golf with other users fan of this sport too.

All the collected data were continuously sent to WSN and analysed by the Reasoning system. As results he received feedback thanks to the Virtual Companion developed by the project.

After two months of DOREMI treatment, Rowland went back to his doctor with a different spirit. Respect to the baseline evaluation, the tests showed a general improvement of his cognitive functions, a decreased BMI, thanks to a more equilibrate diet, and a better physical and psychological state.

8. RELEVANT INPUTS NEEDED IN WP5 TO DEVELOP SPECIFIC FEATURES OF THE GAME ENVIRONMENT

The main aspect that should be taken into account to develop the game environment is the motivation. The focus of any persuasive system must be a technology-mediated transformation of either attitudes or behaviours, including a transformation by bolstering or reinforcing existing attitudes or behaviours.

Individuals who are highly motivated are more likely to engage in, devote effort to, and persist longer at a particular activity. Motivation refers to an individual's choice to engage in an activity and the intensity of effort or persistence in that activity [265,266]. Most models have emphasized intrinsic motivation, focusing on the motives to perform a task that is derived from the participation itself. This could be reached by challenging factors, curiosity, fantasy and sense of control in the game environment [267-269]. Although instructional games are primarily seen as a means to enhance intrinsic motivation, extrinsic motivation is also important. The goal is to develop learners who are self-directed and self-motivated, both because the activity is interesting in itself and because achieving the outcome is important.

Looking at the 'effort' expelled during the learning process will help determine whether learners are motivated. However, for 'effort' to even occur, two necessary prerequisites are required: the person must value the task [270] and the users must believe they can succeed in the task [271]. In any given instructional situation, the learning task needs to be presented in a way that is engaging and meaningful to the learner, and in a way that promotes positive expectations for the successful achievement of learning objectives [272].

More specifically, in the game design phase, a feedback system which provides information about progress towards the goal should be considered. In fact, performance-related immediate feedback is a central mechanism for motivation:

a) Players are likely to be motivated if gamification provides immediate feedback in form of positive and negative reinforcement.

b) Players are likely to be motivated if gamification offers rewards.

For games development, it is important to determine an appropriate number of steps for the challenge. Each challenge should be completed in a correct number of steps. A high enough number of steps would correctly train the cognitive abilities of the patients. However, too many steps could overload them and lower the benefits of the game.

The feedback system should also keep track of the patient's abilities, producing an in-game estimation of these. This would allow the clinician, caregiver and patient to assess the impact of the game on cognitive performance, and could be used to adapt the level of game difficulty to the actual performance achieved.

Furthermore, social aspects and interactions should be considered in the game environment design. Both cooperative and competitive mechanisms could be used to improve the engagement and to better challenge users. Take into account the social and cultural background of the user will promote ecological (2) interactions, favouring the setting of the game in the correct physical place (e.g., a city well known to the user) and cultural environment. For the same reason, the game scenarios should be adaptive to the users' preferences. Also communication processes, between users, should be supported in the system. Promoting a naturalistic interaction, this should allow a significant reduction of the learning time, and thus optimize the effects of the game experience. Connected to this point is to take advantage of the multimodal aspect. In fact, it is important to train sensory and motor modalities at the same time. When possible, multi-sensory interactions should be introduced both as input and output.

Finally, for the game environment design and development it is important to consider all the instruments that will be used to assess different diseases. These tests can help to extract the right categories that will be gamified. This gamification will represent the first step for the gamification of the entire active ageing protocol and will help the development of the single 'atomic' games.

All these described inputs, necessary for development of gamification environment, must be taken in account to furnish an immediate feedback in form of positive reinforcement as well as to offer rewards, useful for players' motivation. The serious games (exergames, social and cognitive games) integrated with DOREMI wearable sensors (accelerometer, heart rate measure), hardware (intelligent carpet) and dietetic support (METADIETA), will give a continuous feedback to users, helping their physical parameters control with a beneficial effect on the cognitive abilities. This approach will be the key for users' acceptability of DOREMI platform.

(2) Ecology = The branch of sociology that is concerned with studying the relationships between human groups and their physical and social environments

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