Call: H2020-SFS-2015-2 Topic: SFS-16-2015

Title of Proposal: **TackIIng MaInutrition in the ELderlY through holistic dietary and lifestyle strategies within a community-centered and personalised framework (Acronym: *TIMELY*)**

List of Participants

Participant No	Participant organisation name	Country
1 (Coordinator)	Alma Mater Studiorum-Università di Bologna (**UNIBO**)	IT
2	Ulster University (**ULSTER**)	UK
3	Region of Southern Denmark (**RSD**)	DK
4	University of Groningen (**UMCG**)	NL
5	Netherlands Organisation for Applied Scientific Research (**TNO**)	NL
6	Consejo Superior de Investigaciones Científicas (**CSIC**)	ES
7	Natural Resources Institute Finland (**LUKE**)	FI
8	University College Dublin, National University of Ireland (**UCD**)	IE
9	University of Birmingham (**UoB**)	UK
10	University of Cambridge (**UCAM**)	UK
11	Technical University of Cluj-Napoca (**TUC**)	RO
12	European Commission – Directorate General Joint Research Centre (**JRC**)	BE
13	European Food Information Council (**EUFIC**)	BE
14	AGE Platform Europe (**AGE**)	BE
15	Hellenic Health Foundation (**HHF**)	EL
16	Ingeniería y Soluciones informáticas del sur, S.L. (**ISOIN**)	ES
17	Electrolux (**ELUX**)	IT
18	Glanbia Foods Ireland Ltd & Glanbia Nutritionals Ltd (**GLANBIA**)	IE
19	Karde AS (**KARDE**)	NO
20	CogVis Software und Consulting GmbH (**CogVIS**)	AT
21	Geoimaging Ltd (**GEO**)	CY
22	LB Lyopharm srl (**LB**)	IT
23	Nestlè Institute of Health Sciences (**NIHS**)	CH
24	Centiv GmbH (**CENTIV**)	DE
25	AKGIDA SAN.VE T□C.A.□. (**AKGIDA**)	TR
26	Sabri Ulker Food Research Foundation (**SUF**)	TR
27	Orogel S.p.A. (**OROGEL**)	IT
28	University of Montreal (**UdeM**)	CA
29	University of Otago (**OTAGO**)	NZ
30	Pennsylvania State University (**PSU**)	USA
31	Commonwealth Scientific and Industrial Research Organisation (**CSIRO**)	AU

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1. EXCELLENCE

1.1 Objectives

In the EU framework of promoting healthy ageing, malnutrition (MN) in older people represents a big socio-economic issue: more than 32% of older people in community and 47% in hospital (DG SANCO) are at risk of MN due to un-healthy lifestyles resulting from a reduced nutrient intake and/or impaired absorption and metabolism. MN contributes significantly to the functional decline associated with unsuccessful ageing, since it is linked to comorbidities, chronic diseases and mortality. Moreover, MN represents a real problem to older adults with mild cognitive impairment who need an easy-to-use solution based on their dietary preferences and habits. Current health policies have been largely inadequate in combating the rising prevalence of MN in the ageing EU population, and new and innovative approaches putting a stronger emphasis to the role of diet and nutrition are urgently needed (WHO; JRC Science and Policy Report "The Role of Nutrition in Active and Healthy Ageing", 2014). Indeed, in a continental scenario in which life expectancy is rising, the option of spending more years in ill health not only affects the quality of life of individuals and their families, but also puts pressures on the global public health and care services. Therefore, being crucial to identify appropriate holistic strategies to help the population age healthier, the TIMELY project aims to meet the challenge of preventing and treating MN in the elderly by integrating expertise from all requested disciplines and sectors that represent. Notably, TIMELY will develop a comprehensive set of research and innovation actions addressing the following key objectives and associated activities:

OBJECTIVE A - DISCOVERY PHASE: Development of a systems model of MN including all biological/non-biological (bio/non-bio) components of MN in the elderly

- **To exploit existing large nutrition-focused cohorts** of older adults (65+yrs old) from different EU countries and worldwide (NZ, CA and US), as well as from the most relevant different settings in which MN is likely to develop (free-living, nursing homes and hospitals) to identify malnourished (MNed) and at risk of MN (MNrisk) subjects and collect data about their bio/non-bio conditions (socio-economic, cultural, lifestyle, food preferences, among others).
- **To perform a *de novo* recruitment of MNed and MNrisk subjects** to maximise the understanding of the mechanisms of the ageing process in relation to MN, with the aim to integrate and expand the already available biological dataset by in-depth omics analyses.
- **To develop a Systems AGEing and Nutrition mODEl (SAGENODE)** to evaluate the interaction between bio/non-bio components, find out the major determinants of MN, and stratify MNed and MNrisk subjects into subgroups according to the different combination of major MN determinants.
- **To select the major MN determinants and risk factors** identified by SAGENODE to **be included in a personal Biopassport**.

OBJECTIVE B - TRANSLATION PHASE: Development of evidence-based dietary and lifestyle strategies for tackling MN in the elderly

- **To develop and deliver evidence-based practical dietary and lifestyle SUBGROUP-SPECIFIC RECOMMENDATIONS** for the different types of end users.
- **To develop NEW FOODS, meals and dietary plans for the elderly**. TIMELY will also implement the emerging 3D food printing technology for personalised nutritional intervention.
- **To develop NEW ICT TOOLS**, **SERVICES** and **DEVICES** in order to compute and adapt MNed and MNrisk subgroup-specific diets, empower seniors to remain physically and socially active, and respond to the needs of having a more reliable and elderly-specific automatic food intake monitoring.
- **To develop a personal BIOPASSPORT as a new screening tool** to identify MNed and MNrisk subjects, allocate them into the best representative subgroup and subsequently **select the best-fitting combination of dietary and lifestyle strategies** (recommendations, food products, ICT tools).

OBJECTIVE C - VALIDATION PHASE: Validation of recommendations, food products and ICT tools in holistic community-based interventions

- **To validate the TIMELY developed strategies and services in the real world**. Two small twinned cities located in the North and South of EU will be designed as Silver Ecosystem and will participate as open-field labs in community-based validation studies. This will allow to fine-tune the intervention strategies to derive dietary and lifestyle strategies to tackle MN in the elderly in EU.

The main expected results of TIMELY are:

In relation to Objective A:

- A **large harmonized bio/non-bio DATASET** derived from the existing ageing cohorts and *de novo* recruitment, representing the largest and most valuable EU-funded knowledge base for building up actions and strategies in the Active and Healthy Ageing domain.
- The **setup of SAGENODE** to identify a list of **major MN determinants, risk factors and their combinations**, allowing the stratification of MNed and MNrisk subjects into subgroups.

In relation to Objective B:

- **DIETARY AND LIFESTYLE RECOMMENDATIONS:** *i)* evidence-based practical dietary and lifestyle recommendations specific for **MNed and MNrisk subgroups**; *ii)* recommendations for **training** of care-givers, nurses, medical doctors and other **relevant healthcare workers**; *iii)* recommendations to **industrial stakeholders** for the design of new elderly MN-tailored food products and ICT tools, services and devices; and, *iv)* recommendations for strengthening the role of diet and nutrition in **policy-making** to protect older citizens from the burden of age and lifestyle-related diseases.
- **FOOD PRODUCTS:** *i)* **novel nutritionally dense, fortified and soft eating FOODS** (e.g. soups, drinks, dairy products, snacks and finger foods) for the elderly; *ii)* **new MEALS and DIETARY PLANS** targeting MNed and MNrisk subgroups; *iii)* **new 3D FOOD PRINTER SETUPS** with a suitable user interface, to print defined food products, including meal components and whole meals, to be consumed at nursing homes or hospitals; and, *iv)* a **PROTOCOL** to improve the 3D printing speed to meet the use case requirements.
- **BIOPASSPORT:** *i)* a **FORMAT** for the personal Biopassport, based on the major MN determinants and risk factors, **ELDERLY-TAILORED INSTRUCTIONS** to use the personal Biopassport, which will be provided through a web-based interface (new age-friendly ICT tools dedicated to fill in, update and consult the personal Biopassport) and/or a personal booklet; and, *ii)* **INTEGRATED WEB-BASED INTERFACES** to exploit the Biopassport for the selection of the best-fitting dietary and lifestyle strategies.
- **ICT PRODUCTS:** *i)* age-friendly **MULTI-DEVICE APPS** services supporting and motivating the elderly to comply with the recommendations; *ii)* an innovative **DEVICE for food intake monitoring**; *iii)* ICT **SERVICES** to empower seniors to remain physically and socially active; and, *iv)* **SMART KITCHEN APPLIANCES** interconnected with the developed services, to facilitate the food preparation and good hygiene at home.

In relation to Objective C:

A set of VALIDATED, PRACTICAL and EFFECTIVE DIETARY and LIFESTYLE STRATEGIES for tailored treatment and prevention of MN in the elderly in EU.

1.2 Relation to the work programme

The following Table 1 describes how TIMELY will coherently tackle the challenges and generate the expected impact addressed by the **H2020 Topic "SFS-16-2015: Tackling malnutrition in the elderly"**.

From SFS-16-2015 *Specific Challenge*	**TIMELY actions**
Population ageing in Europe poses major demographic and socioeconomic challenges which are expected to increase over the coming decades. […] Changes in body composition and organ function, the ability to eat or access food, inadequate dietary intake and the partial loss of taste and smell are associated with ageing and may contribute to malnutrition.	Through a better comprehension of the overall complexity of MN, in terms of mechanisms involved and connection and interaction of bio/non-bio determinants, TIMELY will develop new evidence-based dietary strategies, to deal with the inherent heterogeneity of elderly MN. In the context of the current EU demographic scenario, TIMELY wants to impact on reverting this dramatic tendency, by **achieving early recognition of MN** (through the development of a personal Biopassport as a new screening tool) and **increasing the efficacy of MN treatment through integrated dietary and lifestyle strategies**.
Providing an adequate diet with all essential nutrients, and promoting physical activity are essential for healthy ageing.	TIMELY will develop **new practical dietary and lifestyle recommendations**, **elderly-tailored food products**, as well as **ICT tools and devices** to monitor food intake, motivate the elderly to remain physically and socially active, and comply with recommendations.
From SFS-16-2015 *Scope*	**TIMELY actions**
Based on a better understanding of the mechanisms of the ageing process, dietary strategies, dietary recommendations and new food products to prevent and treat malnutrition in the elderly (living at home, in nursing homes, hospitals, and/or emergencies) should be developed with the aim of preventing functional decline and improving appetite, health and quality of life of the elderly	In the light of a better understanding of the mechanisms of ageing process, age-related specific nutritional requirements, dietary behaviours and preferences, and settings, **elderly-tailored dietary recommendations and new foods** (such as soups, drinks and dairy products) will be developed. 3D food printing technology will be used to address both functional decline and personal food preferences, improving appetite.
A holistic strategy to prevent malnutrition should be developed, and could include research on the role of, amongst others, nutrients in the human organism (their bioavailability and interactions), the gut microbiome, food preparation at home, the physical and social environment (such as social network).	Through the SAGENODE model, TIMELY accepts the challenge of a holistic approach to prevent MN in seniors by **integrating bio** (including gut microbiome and other nutritional and omics profiles) **and non-bio** (socio-economic, cultural, lifestyle, food preferences) **determinants**. MNed and MNrisk subjects will be stratified according to these determinants and **holistic dietary and lifestyle strategies** will be specifically designed for the resulting subgroups.

Proposals should address responsible research and innovation aspects by taking account of specific nutritional requirements, dietary behaviours and preferences, sensory aspects, the gender dimension, ethical factors, socio-economic factors and/or cultural aspects.	The broad range of elderly cohorts available to TIMELY ensures that **all the individual drivers** specified in the call are taken into account in the stratification of MNed and MNrisk subjects, and in generating innovative tailored recommendations. Integrated strategies (dietary recommendations, new foods, ICT tools and devices) will be tuned to address the heterogeneity of MN in older adults, aiming at creating a healthy nutrition/lifestyle environment.
Proposals could include the development of smarter and more intelligent devices for the monitoring of food intake	**New age-friendly ICT tools, services and devices** will be developed to support and motivate seniors to adopt the personalised diet, monitor their food intake, and empower them to be physically and socially active.
Proposals are encouraged to include third country participants, especially those established in Australia, Canada, Japan, New Zealand and/or the United States.	In the frame of the cooperation of the International KBBE forum, for which the Coordinator co-organised with the EC and hosted in Bologna the **2014 Workshop "Health for all: understanding the ageing process"**, TIMELY includes partners from **Canada**, **New Zealand**, **Australia** and **USA**. This will not only allow to strengthen international cooperation with relevant third countries, but will ensure the access to valuable cohorts from the selected partners, as well as to provide important tools such as an oral digestion and swallowing mouth model and a sensory diet database.
Relevant stakeholders, including industry and SMEs, should be involved.	Out of 31 members, 15 partners of TIMELY are food and ICT SMEs, large companies and stakeholder groups, involved in the design and production of new food products, ICT tools and devices.

1.3 Concept and approach

1.3.1 Overall Concept

MN in the elderly is considered a true geriatric syndrome which leads to a disruption of homeostasis in body weight, body composition and physical function, accompanied by frailty, severe disability and poor outcome (Russell and Elia, Proc Nutr Soc, 2010). Indeed, MN has severe clinical consequences, including weight loss, functional impairments (impaired immune response, reduced resistance to infections, weakness, impaired muscle strength, poor cough pressure), impaired quality of life (apathy, depression, immobility, disability, loss of independence), increased complications, higher morbidity and mortality (Schilp et al., Br J Nutr, 2011). **MN in the elderly is widespread** with an estimated prevalence of 2-9% in free living, 10-14% in residents in sheltered housing, 16-20% in outpatients, 37-82% in hospital patients, 19-65% in residents in care homes.

The critical causal factor for developing MN is dietary intake, which is insufficient to meet individual nutritional requirements and can be related to a number of different and interacting **biological and non-biological determinants**. Indeed, one of the most relevant aspects of **elderly MN** is its complexity and **heterogeneity. MN is driven by the ageing process,** which is itself a complex and heterogeneous phenotype, characterized by the decline of organ and system functions (cognitive, mobility, intestinal functionality, absorption, taste, chewing, swallowing, etc.) (Kennedy et al., Cell, 2014), impinging upon the capability of the elderly to have a healthy nutrition and diet. Among these biological determinants, psychological factors largely associated with ageing (depression, mood, anxiety, anorexia, sleep disorders and alteration of circadian rhythms) play a major role (de Boe et al., Ageing Res Rev, 2013). To this complex biological scenario a large body of knowledge identified a set of non-biological, largely socio-economical and educational factors (poverty, poor food choices, self-neglect, loneliness) as major determinants of MN in the elderly (Irz et al., J Health Econ, 2015). A further complexity is represented by the major **settings** where MN occurs and can be recognized. Indeed, the yet inadequate available data suggest that MN can be different (severity, combination of determinants) in free-living, residents in nursing homes and hospital patients, thus leading to the striking need of identifying specific approaches and interventions to be put in action in order to counteract the rise in MN prevalence across EU.

In the last decade, a growing body of evidence demonstrated the **benefits of nutritional intervention** for improving the nutritional status and reducing adverse health outcomes in older adults, also as a result of a research funding policy of EU aimed at better understanding the nutritional needs for a better quality of life in the 65+yrs old population (Tsz and Caldeira, JRC Science and policy reports, 2014). However, **intervention strategies proposed to date, principally based on the administration of specific micro- and macronutrients without taking into account the inherently complex and heterogeneous MN phenotype**, have largely failed in combating and preventing MN in the elderly population. Furthermore, oral nutritional supplements, whose expenditure is enormously rising yearly, are less accessible to older people with low income.

In order to overcome such a fragmented scenario, urgent is the need to develop a holistic model, which disentangles the complexity of MN in the elderly, identifying the major determinants and their combinations, moving towards personalised strategies to treat and prevent MN.

TIMELY will consider MN as a multifactorial process driven by ageing, integrating bio-psycho-social components, and will adopt a holistic strategy and a multidisciplinary approach to tackle MN in the elderly. This will allow to treat and prevent MN as an integral part of the ageing scenario, dissecting how mechanisms of ageing process contribute to MN. A strong conceptual basis of TIMELY is the integration of bio and non-bio determinants that are critical in leading to MN, thus developing the SAGENODE model. SAGENODE will stratify MNed and MNrisk subjects into subgroups according to the different combination of major MN determinants. Based on MNed and MNrisk subgroups, new specific evidence-based dietary and lifestyle recommendations, new elderly-targeted food products, ICT tools, services and devices will be developed for the benefit of the general population. The individual allocation into the subgroups will be performed by computing a personal Biopassport, which will be a unique instrument delivered by TIMELY to ensure an early recognition of MN status or risk and select the best-fitting combination of dietary and lifestyle strategies (Fig. 1), ultimately leading to a reduction of healthcare costs at individual and community level.

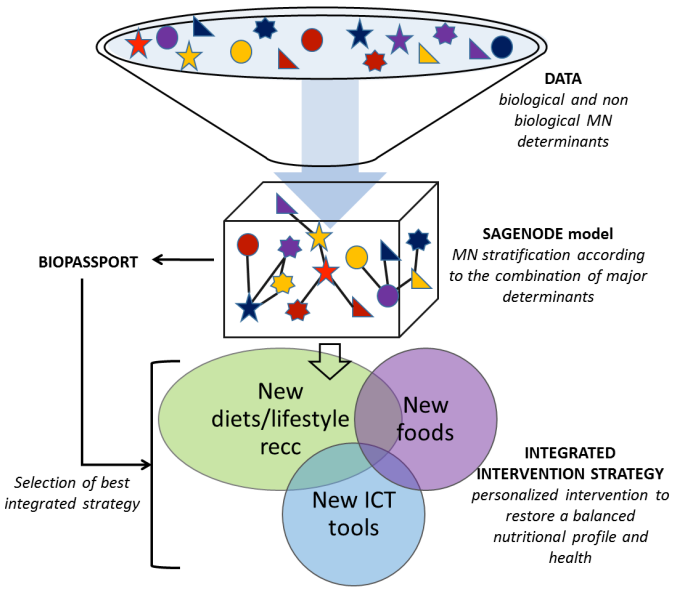


***Fig. 1**: The TIMELY holistic approach to provide a better understanding of MN in the elderly and the integrated intervention strategy proposed by TIMELY.*

One of the main reasons for the failure of conventional intervention studies can reside in the lack of **contextualization of MN within the global, social, economic and biological changes**, which have led to pervasive and consistent changes of habits and maladaptive nutrition behaviours in the elderly. For this reason, TIMELY acknowledges the importance of the engagement of the end users of the proposed innovations to help bridging the gap between research and practice. In particular, a holistic approach which takes into account all these determinants is mandatory to tackle MN in the elderly.

A pillar of TIMELY is the recognition of the fundamental value of the so-called Silver Ecosystems, the real-life condition environments characterised by a growing share of ageing population, that will represent a test-bed for the uptake and efficacy of the proposed innovative products, services and measures. In particular, TIMELY will validate the Biopassport function and the proposed intervention strategies, including dietary and lifestyle recommendations, new foods, ICT tools, services and devices, in the real world involving open-field labs represented by two twinning cities located in the Netherlands and Italy.

1.3.2 Project Strategy

The overall project strategy will involve three phases: DISCOVERY, TRANSLATION, VALIDATION (Fig. 2).

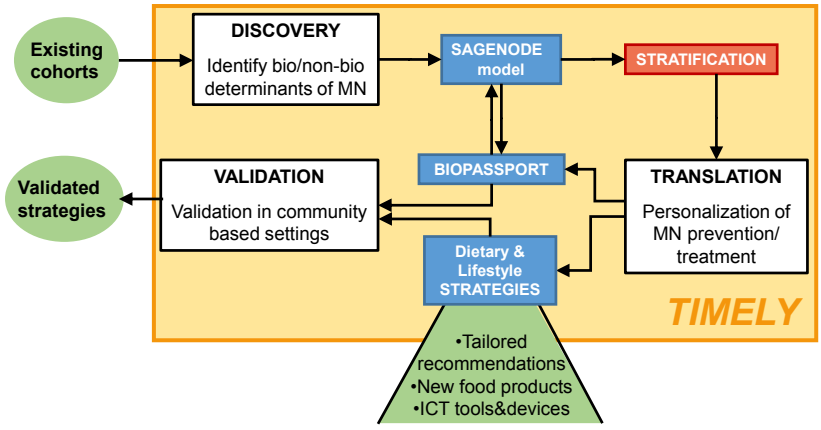


***Fig. 2:** Interplay among the three main phases of TIMELY.*

DISCOVERY PHASE

1. Database screening

TIMELY will have access to several **large nutrition-focused cohorts of elderly subjects** (more than 150,000 subjects, 65+yrs old) in different settings (free-living, nursing homes and hospitals) in EU countries and worldwide (NZ, CA, US) (Table 2), mostly followed **longitudinally** and all thoroughly characterized for a variety of domains and parameters (age, gender, ethnicity, geographical, clinical, socio-economic, anthropometric, diet and lifestyle, physical activity, medical history and medication used, mobility, cognitive function, depression and anxiety, blood pressure, cardiovascular health, bone health, biochemical/haematological and in some cases also genetic data). Biological samples from these subjects have been previously collected and stored, and are available to be further analysed in TIMELY.

Using a combination of accepted screening tools to evaluate MN and the risk of MN (SGA, MNA-SF, MUST, NRS2002, SNAQ, EVS, vitamin status, etc.), the above-mentioned cohorts will be employed to: *i)* estimate the prevalence of MN across countries

and settings; *ii)* identify MNed and MNrisk subjects; *iii)* collect bio/non-bio data from the identified MNed and MNrisk subjects; and, *iv)* recover their stored biological samples for in-depth omics analysis.

***Table 2**: Large nutrition-focused cohorts of elderly subjects available to TIMELY.*

Cohort name	Cohort location	Subject number	Subject age in 2015 (yrs)
TUDA	UK, IE	5,186	60-102
SHARE	18 EU countries (AT, BE, CH, DE, DK, ES, FR, EL, IT, NL, SE, CZ, IE, PL, EE, HU, PT, SI) + ISR	85,000	60+
NANS	IE	226	65-90
Life lines	NL	12,706	65-93
Embrace	NL	1,084	75+
EPIC-NORFOLK	UK	25,631	59-98
EPIC-GREECE	EL	6,315	65+
GRAS	US	22,000	65+
NuAGE	CA	1,793	78-92
NZ-NAP	NZ	310	65-107

2. Dissection of the bio/non-bio complexity and heterogeneity of MN in the elderly and development of a MN systems model

To evaluate the impact of and the interaction between bio/non-bio determinants of MN, the complex phenotype and heterogeneity of MN in the elderly will be dissected by means of a **multidimensional approach**. Bio/non-bio data from the MNed and MNrisk subjects identified within the existing cohorts (DISCOVERY phase, step 1) will be integrated in a multidimensional space to develop the SAGENODE model. SAGENODE will stratify MNed and MNrisk subjects into subgroups according to the different combination of major MN determinants, thus **paving the way to an approach for prevention and treatment of MN in the elderly that is holistic in relation to the variety of determinants and personalized in scope and recipient**. The identified MN determinants will be utilized for the development of the personal Biopassport (TRANSLATION phase, step 1). The available biological dataset will be integrated and expanded through the ***de novo* recruitment of 400-500 MNed and MNrisk subjects in different settings**. The newly enrolled MNed and MNrisk subjects will be fully characterized regarding age-related specific functional parameters (taste, dentition and chewing, swallowing, strength, physical activity/ability, cognitive function, among others) and by using a combination of cutting-edge methodologies and techniques (metabolomics and lipidomics, gut and oral microbiomes, genetics, epigenetics, glycomics, qualitative and quantitative analysis of micronutrients) for a **better understanding of the age-related mechanisms**.

TRANSLATION PHASE

1. Development of a personal Biopassport

TIMELY will develop a personal Biopassport, based on a not costly and not invasive practical biomarker strategy, which will take into account the major individual bio/non-bio MN determinants (DISCOVERY phase, step 2), as well as the major MN-associated impairments (musculoskeletal problems, insulin resistance, hypertension, atherosclerosis, metabolic disorders, immobility) and socio-economic factors that, even if not identified as MN determinants by SAGENODE, are important to evaluate health and socio-economic condition of the elderly, based on the current literature. The Biopassport will be used as an **advanced screening tool for the identification of MNed and MNrisk subjects** and their allocation into the subgroups, according to the specific combination of MN determinants. In order to deal with the rapid socio-economic changes in the EU society, the Biopassport will be designed to allow the continuous update of SAGENODE, eventually finding new connections among the MN determinants or even new MN determinants, in a sort of machine-learning approach. This in turn will allow the continuous implementation of MNed and MNrisk subgroups, the corresponding interventions strategies and the Biopassport itself.

2. Development of recommendations, food products, ICT tools, services and devices

Based on the identified MNed/MNrisk subgroups, which will allow a better comprehension of the interactions between nutrition and ageing, TIMELY will develop:

(i) **evidence-based practical dietary and lifestyle recommendations**, capable of addressing the complexity and the heterogeneity (countries, cultures, ethnicity, settings) of MN in the elderly. Specific attention will be devoted to the **training** of relatives, care-givers, nurses, medical doctors, nutritionists, dieticians and other healthcare professionals.

(ii) **new food products** (e.g. soups, drinks, dairy products, finger foods, snacks, 3D printed foods) and meals/dietary plans, which will take into account specific elderly nutritional requirements (in the different settings), the role, bioavailability and interactions of nutrients, as well as dietary behaviours and preferences, including sensory and texture aspects. Enrichment in soluble proteins with high digestibility (>95%), an improved nutritional balance of amino acids, micronutrients (vitamins and minerals), fibres, anti-oxidants and bioactive compounds will be considered. TIMELY will employ an advanced oral digestion and swallowing mouth model to optimize the development of new soft eating foods. TIMELY will exploit the **emerging 3D food printing technology** to promote personalised diets, particularly in nursing home and hospital settings,

to address individual nutritional and food preferences, as well as age-related alterations in taste, chewing and swallowing, among others.

(iii) **new ICT tools, services and devices**. TIMELY will develop an age-friendly integrated web-based interface to fill in, update and consult the personal Biopassport (TRANSLATION phase, step 1), and exploit the SAGENODE algorithm for the allocation in the best-fitting MNed and MNrisk subgroup. New tools will be designed to compute and adapt subgroup-specific diets, and **empower elderly** subjects to remain physically and socially active, as well as new intelligent devices for automatic monitoring of food intake. TIMELY will create **age-friendly multi-device apps** services supporting the elderly in compliance with recommendations. Devices to facilitate nutritional literacy and training of the elderly and their care-givers will be also developed. ICT tools will be integrated with newly developed kitchen appliances to facilitate **food preparation and good hygiene at home**.

VALIDATION PHASE

The final validation of the TIMELY outcomes in the real world constitutes a major strength of the proposal. Two twinned cities, Kerkrade (NL) and Castel S. Pietro (IT), belonging to the South Holland and Emilia Romagna Regions, which are both acknowledge as 2-stars Reference Sites in the European Innovation Partnership on Active and Healthy Ageing, will participate as open-field labs (instead of conventional small scale intervention studies), to test the feasibility, compliance and efficacy of the personalised integrated strategies based on the newly developed dietary/lifestyle recommendations, food products (also 3D printed) and ICT tools. These open-field labs will allow TIMELY to **validate, fine-tune and implement foods, tools and recommendations**, in order to produce effective strategies to tackle MN in the elderly in EU. The silver ecosystem approach will benefit of the **support of municipalities**, with the **involvement of senior social clubs, family homes, sheltered housing, nursing homes and hospitals in the territory**, as well as all the players associated with community care.

Enrolled elderly will be asked to fill in their personal Biopassports through the dedicated ICT tool, allowing the identification of the individual MN status or risk. A 6-month lifestyle personalised intervention will be carried out by using the previously developed dietary and lifestyle recommendations, the new food prototypes and dietary strategies, the new ICT tools, services and devices, in a way to make the older person more active, involved in the society and "co-creator" of her/his health status. The efficacy of the holistic and personalised interventions in improving health and nutritional status will be evaluated by updating the personal Biopassports. In particular, TIMELY fully recognises that older people are a totally heterogeneous group and, in order to deliver acceptable solutions to the challenges of ageing, it is essential to involve the target group into each research and innovation phase, to establish an ongoing dialogue with researchers and developers. Besides helping to overcome acceptability gaps (e.g. privacy, safety), the validation in real world will ensure TIMELY to respond to a range of key issues, such as ethical concerns, affordability and costs of the proposed innovations, as well as their interoperability, technical reliability, and support. Moreover, engaging with users supports the identification of issues that need further study and allows the refinement of the recommendations towards more effective ones, thus leading to a greater impact of the TIMELY results.

1.3.3 Trans-disciplinary consideration

TIMELY is highly interdisciplinary and intersectorial and gathers a strong set of industrial partners from the sectors of food, ICT and kitchen appliances (5 large, 6 SMEs from 9 countries), and research centres of excellence (12 from 9 countries) who have a specific and well documented expertise in: *i)* studying the healthy ageing process in the elderly in a range of communities, ethnic groups and settings (Partner number 1,2,3,4,9,15,28,29,30,31); *ii)* pioneering the assessment of the nutritional and metabolic status of the elderly by omics analyses (1,5,6,8,23); *iii)* characterizing the compositional and functional profile of the gut microbiome in the elderly (1,6); *iv)* studying the nutrient/s role, bioavailability and interactions (2,8); *v)* studying socio-economic variables and food choices of the elderly (1,7,10); *vi)* pioneering a systems biology approach to the ageing process (1,5); *vii)* performing nutritional intervention in the elderly (1,2,3,4,9); *viii)* producing ICT tools and services to address the specific elderly needs (11,16,17,19,20,21); *ix)* producing new elderly-tailored food products (18,22,24,25,27); *x)* disseminating dietary and lifestyle elderly-specific recommendations and strategies (12,13,14,26).

1.3.4 Positioning of the project in the spectrum from "idea to application"

Taking into account by analogy the provisions of HORIZON 2020 – WORK PROGRAMME 2014-2015 Annexes G. Technology readiness levels (TRL), the innovation component of TIMELY is ambitious and will focus on most innovative and promising solutions for empowering the elderly and their carers with an array of knowledge, tools and instruments that will ultimately combat the upsurge of MN. The following Table 3 shows the TRL levels that TIMELY aims at reaching for each main innovation.

Partners interested	Proposed innovation	Starting TRL	Arrival TRL
1,2,3,4,5,6,7,8,9,10,16,23	ICT tools for the Biopassport	3	7
16,20,21	Web-based interface to exploit the Biopassport	4	8
16,19,20,21	Innovative ICT tools, services and devices	4	7
5	New 3D food printer setups	6	7
16,17	Interoperable multimedia user-interface kitchen appliance	4	6
1,2,3,4,6,7,8,9,10,18,24,25,27	New food prototypes	4	7
1,2,3,9,22	Foods for special medical purpose	4	7

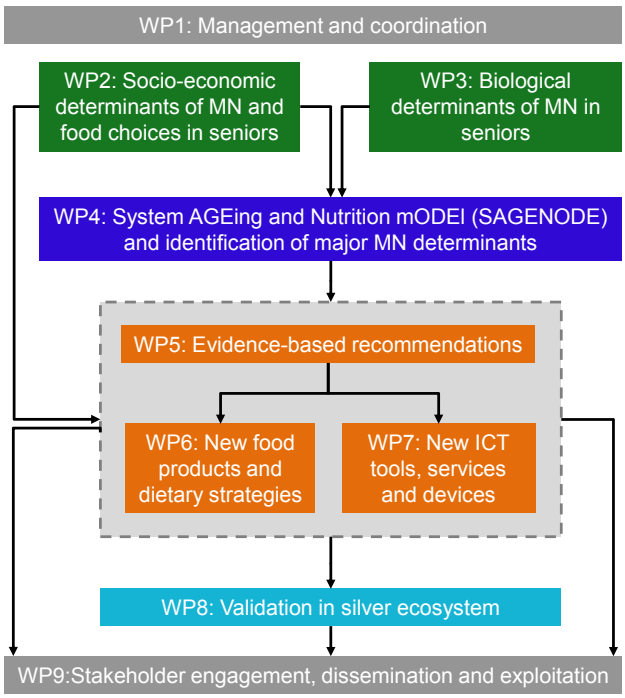
The proposed activities are expected to start from TRL3 (experimental proof of concept) and TRL4 (technology validated in lab). In relation to the 3D food printing technology, which is a rather consolidated technology for which TIMELY is planning an incremental innovation, the starting TRL is 6 (technology demonstrated in relevant environment-industrial). With its array of demand-driven market oriented research and innovation actions, TIMELY will reach TRL6, TRL7 (system prototype demonstration in operational environment) and TRL8 (system complete and qualified).

1.3.5 Current know-how covered by National and International Projects

The TIMELY partnership links a wide range of recent and ongoing projects. The following Table 4 summarizes only the most relevant EU projects in the field of nutrition, lifestyle and healthy ageing, besides the cohort studies of Table 2.

Project (Funding scheme, duration)	**Partners involved**	**Expected synergies and value added for TIMELY**
NutriTech (FP7-KBBE, 2012-2015)	TNO	Use of cutting-edge analytical technologies and methods to study the diet-health relationship
Food4Me (FP7-KBBE, 2011-2015)	UCD, TNO, EUFIC	Development of tools for personalised nutrition
PERFORMANCE (FP7-KBBE, 2012-2014)	TNO	Development of fully personalised food by means of 3D printing technology for the elderly
NU-AGE (FP7-KBBE, 2011-2016)	UNIBO, LUKE, NIHS, TNO, EUFIC	Effect of specific nutrients on the elderly health status; omics profiles of heathy subjects useful as controls
SUSDIET (ERANET Sus-food, 2014-2017)	LUKE	Analysis of socio-economic variables to implement sustainable diets in EU
OPTIFEL (FP7-KBBE, 2013-2017)	CENTIV	Development of personalised food and packaging for elderly people
MyNewGut (FP7-KBBE, 2013-2018)	CSIC, UNIBO, TNO	A better comprehension of the microbiome influence on health status of the host and prevention of diet-related diseases
ELDERSUP (AAL JP, 2014-2016)	ISOIN, GEO	Development of a web and mobile platform bringing together senior adults and companies
Fearless (AAL JP, 2011-2014)	CogVIS	Research and development of computer vision and video analytics algorithms using 3D sensors
SMARTCARE (CIP-ICT-PSP, 2013-2016)	RSD	An open ICT platform enabling the delivery of integrated care to older EU citizens
CLYMBOL (FP7-KBBE, 2012-2016)	EUFIC	A better understanding of the effects of health claims and symbols on food labels, and their impact on purchase and consumption behaviour
CREDITS4HEALTH (FP7-HEALTH, 2013-2016)	HHF	Favouring healthy lifestyles and balanced diet in the elderly

1.3.6 Project approach and methodology



TIMELY foresees activities with a multidisciplinary approach that integrates different expertise to deal with the challenge of preventing and treating elderly MN. The TIMELY strategy is developed in 5 years and organized in 9 Work Packages. The WP interconnection is depicted in the PERT scheme of Fig. 3.

WP1: Management and coordination (WP Leader: Patrizia Brigidi, UNIBO) - *Main Objectives and tasks*: 1) to coordinate and supervise research and innovation activities; 2) to provide administrative and financial management.

WP2: Socio-economic determinants of MN and food choices in seniors (WP Leader: Xavier Irz, LUKE) - *Main Objectives and tasks:* 1) to investigate associations between elderly MN and socio-economic variables by exploiting high-quality datasets from former EU projects; 2) to econometrically analyse food preferences in elderly and the determinants of their demand for food and nutrition, from secondary datasets on expenditure and consumption; 3) to investigate the causal relationship between social ties and social participation, as well as diet and health/wellbeing; 4) to inform the development of recommendations (WP5), new food products, including those to be produced by means of 3D food printing

(WP6), and new ICT tools, services and devices (WP7); 5) to standardize data collection and sharing in order to establish valuable synergies with the Joint Programming Initiative "A Healthy Diet for an Healthy Life" (JPI HDHL).

WP3: Biological determinants of MN in seniors (WP Leader: Sean Strain, ULSTER) - *Main Objectives and tasks:* 1) to identify MNed and MNrisk subjects in existing ageing cohorts using accepted MN screening tools in hospital and nursing home settings and accepted cut-offs for vitamin biomarker status in free-living setting; 2) to provide stored biological samples available from the existing cohorts for in-depth omics analysis (WP4); 3) to integrate the existing cohorts with *de novo* recruitment of MNed and MNrisk elderly (400-500), including ethnically diverse subjects, to be fully characterized; 4) to standardize data collection and sharing in order to establish valuable synergies with the JPI HDHL.

WP4: Systems AGEing and Nutrition mODEl and identification of major MN determinants (WP Leader: Ben Van Ommen, TNO) - *Main Objectives and tasks:* 1) to perform in-depth omics analyses (metabolomics, lipidomics, gut and oral microbiomes, epigenetics, glycomics, genetics of candidate genes) of samples collected in WP3; 2) to harmonize and combine bio/non-bio datasets of MNed and MNrisk subjects, provided by WP2 and WP3; 3) to multi-dimensionally analyse bio/non-bio data; 4) to develop a Systems AGEing and Nutrition mODEl (SAGENODE) for identifying the major interconnected MN determinants; 5) to select the major MN determinants and risk factors to be included in the personal Biopassport (WP5).

WP5: Evidence-based recommendations (WP Leader: Andrea de Winter, UMCG) - *Main Objectives and tasks:* 1) to develop an age-friendly format and instructions for the personal Biopassport; 2) to evaluate the potential of the personal Biopassport as new screening tool in comparison to available MN screening; 3) to develop evidence-based MNed and MNrisk subgroup-specific dietary and lifestyle recommendations exploiting SAGENODE (WP4); 4) to develop recommendations targeting care-givers, nurses, medical doctors and other relevant healthcare workers; 5) to develop recommendations to stakeholders for elderly-targeted foods (WP6) and ICT tools, services and devices (WP7); 6) to develop recommendations for crisis and disaster situations, conditions in which elderly subjects are particularly prone to develop MN; 7) to share methodologies and best practices addressing Reference Sites and relevant players within the EIP AHA.

WP6: New food products and dietary strategies (WP Leader: Christian Rebière, LB) - *Main Objectives and tasks:* 1) to develop new nutritionally dense food prototypes (soups, dairy products, drinks, snacks, finger foods) and/or foods enriched in functional ingredients; 2) to optimize food texture and structure through oral digestion and swallowing mouth model; 3) to select and test ingredients and formulations for 3D food printing, and validate easy-to-eat food products (meal components, whole meals, finger foods and snacks) having attractive and/or familiar shapes; 4) to design dedicated 3D printer setup and user interface for hospital and nursing home settings, and improve the 3D printing speed to meet the industrial requirements; 5) to develop new oral nutritional supplements and nutritionally dense lyophilized products for crisis and disaster situations.

WP7: New ICT tools, services and devices (WP Leader: Victor Sanchez Martin, ISOIN) - *Main Objectives and tasks:* to develop 1) an age-friendly integrated web-based interface to use the personal Biopassport for allocation into the best-fitting MNed and MNrisk subgroup and computing the dietary and lifestyle strategy (WP5, WP6); 2) intelligent devices for food intake and lifestyle monitoring; 3) tools/services for assessment of compliance and detection of MN-leading behaviours; 4) tools/services for care-givers, nurses, medical doctors, nutritionists, dieticians for diet adaptation; 5) age-friendly services accessible through smartphone, tablet, PC, to provide nutrition literacy and promote social and physical activity; 6) smart kitchen appliances (refrigerators and robots) interconnected with the developed services.

WP8: Validation of strategies to tackle MN in silver ecosystem (WP Leader: Patrizia Brigidi, UNIBO) - *Main Objectives and tasks*: 1) to enrol men and women 65+yrs old in free-living, nursing home and hospital settings in Kerkrade and Castel S. Pietro cities, and draw up the personal Biopassport to screen for MN risk; 2) to perform randomized, controlled 6-month personalized interventions, based on dietary and lifestyle recommendations (WP5), new foods and dietary strategies (WP6), new ICT tools, services and devices (WP7), including on site trials with dedicated 3D food printers producing personalized food products, all developed within the project; 3) to characterize MNed and MNrisk subjects through in-depth omics analyses before and after intervention; 4) to evaluate the efficacy of these interventions in improving health and nutritional status by updating the personal Biopassports.

WP9: Stakeholder engagement, dissemination and exploitation of the results (WP Leader: Laura Fernandez, EUFIC) - *Main Objectives and tasks*: 1) to produce and disseminate information about the project, its objectives, approaches and results to stakeholders relevant to healthy ageing: care-givers, nurses, medical doctors, nutritionists and dieticians; food and drink industries and other businesses promoting innovation towards healthy ageing; policy makers/public health authorities, elderly and consumer organisations, the scientific community, the media, and the general public; 2) to facilitate collaboration and information exchange between organisations involved in healthy ageing; 3) to promote the use of results among specific target groups, i.e. food industry, care-givers, nurses, medical doctors, seniors and policy-makers.

1.3.7 Gender equality and people involved

Women live longer than men but spend less of their later life in good health. Indeed, with respect to males, older females are more prone to frailty, suffering higher loss of muscle and osteopenia (partly due to calcium, vitamin D and estrogen deficiency), that lead to fractures. Moreover, older females have a higher body mass index, showing a less marked tendency to reduce food intake and being less physically active (Myint et al., Age Ageing, 2011). Gender must be taken into account in determining the factors underlying MN in the elderly to overcome the current situation in which nutritional advice is potentially inappropriate for half of the population. By considering both males and females we will deliver a step change by providing health policy-makers

and industry with information to ensure lifestyle advice to prevent or reduce MN is gender appropriate. TIMELY will ensure that new food products meet men and women's needs, interest and tastes. The elaboration of tailor-made nutritional and lifestyle strategies will consider the gender perspective to respond to different socio-psychological needs.
The TIMELY partners adopt equal opportunities for women and men, encouraging women to participate as researchers in the different areas within the technical scope. Women are covering key roles, i.e. project coordinator and WP leader for 4 out of 9 WPs. Recruitments and appointments of new positions will be based on quality and experience: when equally qualified, TIMELY will aim at a 1:1 ratio between female and male. Recruitment procedures will be conforming to national and EU guidelines. TIMELY will take decision to guarantee an equitable access to natural and economic resources, education and other social and welfare services to women involved.

1.4 Ambition

1.4.1. TIMELY advancement on the state-of-the-art

WP2: Socio-economic determinants of MN and food choices in seniors

State of the art: Progresses have been made to understand the biology of MN, but nutrition issues cannot be understood without considering the socio-economic environment. Indeed, economic variables influence the choice of more or less healthy foods, and weaker social ties (e.g. lone-living) are associated with significantly lower diet quality. Socio-economic influences are likely to be particularly important among the elderly since ageing often brings social isolation, greater risk of poverty, difficulties in accessing shops and changes in preferences.
Advances by the proposal: TIMELY will apply the tools of demand analysis to characterize specifically the preferences and drivers of demand (e.g. price, income, taste shifters) for food of the elderly, using econometric methods (e.g. EASI demand system; cohort effects). Through this, TIMELY will tackle for the first time whether/how preferences of the elderly, as revealed by their food purchases, differ from preferences of other adults, and whether they change over time (i.e. independently of the ageing effect). TIMELY will apply to the specific case of the elderly the considerable expertise of the consortium in analysing the relationship among structural factors, i.e. social ties, diet costs, and food choices/nutrition.

WP3: Biological determinants of MN in seniors

State of the art: MN is often unrecognised and untreated and can occur in the elderly living at home in the community, in nursing homes and in hospitals. Although the biological and other determinants of MN are complex, the adverse effects of MN usually respond to nutritional treatment and there is evidence that detecting and correcting MN has many benefits.
Advances by the proposal: TIMELY will focus on MN and risk of MN in ageing using innovative multidisciplinary approaches that will bring together areas of research that have been developed separately for many years. New methodologies for enhancing nutritional, metabolic, clinical and behavioural data with secondary area-based socio-economic information will be introduced, to improve our understanding of the complex inter-relationships between MN associated age-related health issues and the physical and social environments.

WP4: Systems AGEing and Nutrition mODEl and identification of major MN determinants

State of the art: Even if MN is characterized by multifactorial causalities which lead to the disruption of homeostasis in body weight, until now studies on MN suffer from a fragmented approach. This has failed in providing a systems level view of the process, exploring connections between nutritional, physiological and socio-economic factors in determining MN. Moreover, as far as we know, the study of MN in the elderly did not exploit the most advanced omics technologies, which can be useful to shed light on such a complex phenotype and identify new mechanisms and potential biomarkers.
Advances by the proposal: TIMELY will develop the first systems model of MN (SAGENODE), where ageing, nutritional and socio-economic factors are merged in a multidimensional space. SAGENODE will explore the connection between bio and non-bio determinants as causative agents of MN. The model will be implemented with cutting-edge data obtained with the most advanced omics technologies, for the first time applied to the study of MN. This holistic approach will allow a better comprehension on how the mechanisms of the human ageing process, including bio and non-bio factors, determine MN and MN risk, allowing in turn the design of new evidence-based integrated intervention strategies to treat and prevent MN in the elderly.

WP5: Evidence-based recommendations

State of the art: Multifaceted or comprehensive interventions that combine different approaches and targeting different barriers have shown to be more successful than single or isolated interventions. Important elements of comprehensive approaches are nutrition or dietary recommendations, empowerment of individuals, capacity building of professionals and improving health communication. Interventions that are tailored to the individual needs have shown to be more effective making clear that interventions should be adapted to the needs of older adults.
Advances by the proposal: In WP5 scientific knowledge is translated into tried-and-tested, evidence-based recommendations to prevent and treat MN in the elderly, and will be available to the public, key stakeholders concerning the health and wellbeing of older adults, food industry, and services targeting the elderly population. Furthermore, the evidence-based recommendations will move beyond the generic advice on MN prevention, but will be personalised according to the Biopassport (taking into account biological, social, cultural and lifestyle differences).

WP6: New food products and dietary strategies

State of the art: It has been unquestionably assessed in many studies the efficacy of diet enrichment with energy and protein dense foods in elderly at risk of MN. On the other hand, the risk of MN and frailty in aged subjects are not a criteria per se for oral nutritional supplementation coverage by the healthcare systems. Therefore, it is urgent the need to develop and deliver on the market small servings of economically affordable foods specifically targeting the nutritional, sensorial and texturing requirements of older people. 3D food printing technology offers great possibilities for the production of innovative foods but at present commercial activities and applications are limited and research is needed to tap the full potential of this field.

Advances by the proposal: TIMELY will exploit the synergy between research excellence and international food companies to design innovative and promptly applicable dietary solutions (i.e. ingredients, food products, meals, dietary plans). To achieve this goal, TIMELY will benefit not only of the most recent nutritional knowledge, but also of advanced competences and tools, such as a oral digestion and swallowing mouth model to overcome typical age-related digestive problems, a sensory diet database to tackle the elderly increased threshold for taste and sensitivity to texture, and the 3D food printing technology to address individual preferences. Strategies and products to meet the needs of MNed or MNrisk subjects will be specifically developed for the subgroups of older people with different bio/non-bio MN-leading determinants identified within TIMELY. Additionally, the TIMELY food printer will be developed for on-site, rather than centralized printing, thus posing new requirements with respect to issues such as speed and scale, but also ease of use (user interface), complexity, cleanability.

WP7: New ICT tools, services and devices

State of the art: Currently, there are lots of mobile and web applications providing calories and nutrition information using rather non-scientific approach based on the nutritional values taken from food composition tables and not considering the actual food intake. The nutritional assessment performed by nutritionists using questioners implies a great memory effort from older adults. There is a need for using advanced ICT techniques for better collecting the older adult food intake, to assess un-healthy behaviours and provide qualified recommendations. In particular, monitoring the real food intake is a key issue for all researchers within the nutrition field, because the most common techniques, basic on statistics, are not able to individualize personalized intake or even they doesn't take into account if the person himself is eating the entire dish or not.

Advances by the proposal: TIMELY will carry out cutting-edge research to originally combine latest advances in smart sensing, image processing, semantic modelling, fusion and reasoning with the goal of proactive and early prediction of un-healthy self-feeding behaviours which may lead to MN. TIMELY will develop ICT tools for automatic assessing short- and long-term self-feeding behaviour and adherence to a prescribed dietary plan, allowing continuous and nutrition conscious adaptation of the dietary plan using bio-inspired meta-heuristics. A new smart device will be developed to automatically monitor the users' food intake in an intuitive and non-intrusive way, easing their interaction with smart house appliances.

WP8: Validation of strategies to tackle MN in silver ecosystem

State of the art: Until now, the validation of intervention strategies has been mainly carried out in conventional nutrition intervention trials, generally in a controlled environment. However, these conventional approaches do not allow the measurement and tuning of the efficacy of the tested intervention in response to the unpredictable complexity and heterogeneity of the real life, factors that are strategic in tackling MN.

Advances by the proposal: TIMELY will validate the developed intervention strategies in open-field labs in two small twinned cities located in NL and IT. This will allow us to test, fine-tune and implement TIMELY intervention strategies and tools in the real world, in order to deal with the whole complexity and heterogeneity of the elderly MN in EU.

1.4.2. TIMELY innovation potential

The main focus of TIMELY is to impact on **strengthening the EU´s key global market position in innovative products and services for the elderly**. In particular, the products and services that TIMELY defines as critical and puts as a basis for its research and innovation activities are clustered among three major pillars: i) new food products/meals/diets and dietary strategies; ii) new ICT tools and devices; iii) new advanced kitchen appliances. The expected TIMELY innovations, belonging to these three pillars, encompass a number of different end users. These three pillars are the core of the so-called Silver Economy, the economy of longevity, which brings together a variety of actors around the objective of bringing to the market innovative products and services for the elderly. Fig. 4 shows how the strong industrial component of the TIMELY consortium addresses the need of delivering innovation along the entire value chain of the Silver Economy.

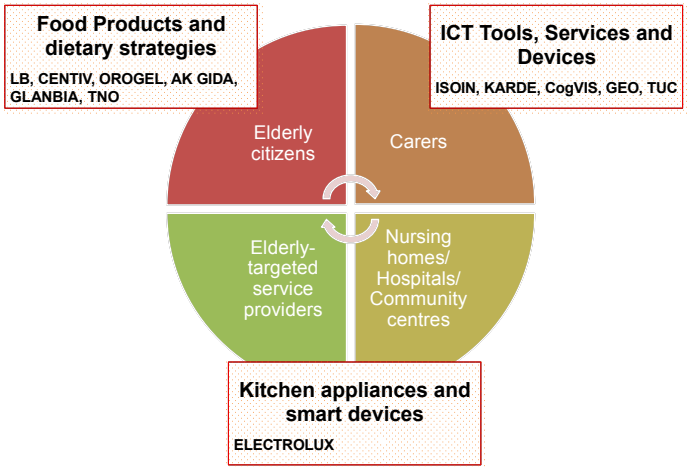


Fig. 4: *The innovation potential of TIMELY distributed around the major pillars and end users of the Silver Economy, and main industrial partners involved.*

To provide the strongest innovation potential, the TIMELY consortium is composed by partners that are either applicant/inventors in National and International patents and national/multi-national market leaders in their specific sector. Being the innovation potential critical for the success, an

extensive patent search has been carried out and a **dedicated strategy for delivering innovation** has been incepted. **The results achieved within TIMELY will be subjected to appropriate IPR protection and some of them to patent application**. In particular:

i) **New food products/meals/diets and dietary strategies.** Partners involved: LB, OROGEL, CENTIV, AKGIDA, GLANBIA, TNO. A number of patents are available among the partnership in different sector of activities. As an example, CENTIV owns Patent DE 102012107400.3. "Development of personalized nutrition and corresponding calculator for specialized beverage powders", which will be used as a background for developing a TIMELY-brand new nutrition-calculator for caterers to help in tackling malnutrition. Similarly, LB owns different patents (RM2012A000418, RM2012A000412/WO2014/027305A, EP2444083) on the purification of food elements and components and nutritional enrichment, to be used as background for the development of new fortified food products enriched in functional ingredients and with correct nutritional balance of amino acids ultimately needed for ensuring an appropriate dietary regime of the elderly. TIMELY will advance the current state of innovation in relation to 3D food printing (for which patents are currently registered, e.g. WO2014190168), by going beyond the printing of "mere" gel products and developing new, more complex food products as well as the technology required to print them. The envisioned products will comprise a wider range of ingredients, shapes and, most importantly, textures. Additionally, TIMELY will develop a printer for on-site, rather than centralized printing, addressing issues, such as speed and scale, ease of use (user interface), complexity, cleanability, etc.

ii) **New ICT tools and devices**; this range of innovations will be achieved by the cooperative work of innovation intensive ICT SMEs (ISOIN, KARDE, CogVIS, GEO). Apps, software and similar web-based products are generally non-patentable. The partners have an extensive track record in delivering innovative products for assistive technologies and e-health. TIMELY innovations will be subjected to appropriate protection based on the specificities of the software domains. Differently, a number of patents about food intake monitoring devices are currently registered (as a non-exhaustive example, US2014255883 , WO2013086372, US2014347491). TIMELY will develop an intelligent device for food intake and lifestyle monitoring, taking advantage of the solid and cutting-edge knowledge base of the project consortium, that will be patented during the project, followed by an appropriate exploitation strategy as an integral part of the TIMELY outreach activities.

iii) **New advanced kitchen appliances**: the development of new kitchen appliances is in charge of Electrolux Italia S.p.A., which belongs to the Electrolux Group, a global Leader in home appliances, based on deep consumer insight and developed in close collaboration with professional user. Electrolux Italia has more than 80 registered patents currently active on kitchen appliances. Based on these strengths, a working prototype of smart refrigerator capable to facilitate elderly people in the preparation of food at home, able to receive information from the TIMELY Biopassport and eventual «wearable sensors» will be developed, protected and exploited according to the strategies that will be identified during the TIMELY lifecycle.

2. IMPACT

2.1 Expected impacts

Europe is facing a huge demographic challenge, being by far the oldest continent. Countries like Germany and Italy have the 2nd and 3rd highest median ages in the world, and by 2050 a significant share of EU countries will have a median ages of 50+ (The Silver Dollar – Longevity Revolution, BofA Merril Lynch, 2014). This unprecedented phenomenon, together with the rise of the prevalence in MN reported by the DG SANCO, poses **serious implications at public health, socio-economic and industrial levels**, thus requiring a likewise unprecedented response from the science, policy-making, civil society and industrial world. For this reason, TIMELY provides an ambitious work plan that aims at timely and significantly address the most critical challenges of the greying EU. TIMELY relies on an integrated strategy, which takes advantage of the strong and established expertise of the TIMELY consortium in the study of nutrition and healthy ageing, and is rooted into a wide and consolidated knowledge base consisting of the largest and most significant existing nutrition-focused cohorts of older adults (more than 150,000 subjects). TIMELY will **generate innovative solutions**, strategies, ideas, foods, ICT tools, which will have a concrete low-to-mid term impact for the main categories of project end users, such as i) the elderly population of today and tomorrow, ii) their care-takers (nursing homes and hospitals, health professionals, nutritionists and dieticians, among others), iii) the EU industry working in the field of products and services for the elderly (from the EU food industry to the ICT and personal- or home-devices), iv) the policy makers of the EU and national public health sectors. Fig. 5 shows how the innovation potential of TIMELY will impact on these end user categories, as well as the interplay among the generated sectorial impacts.

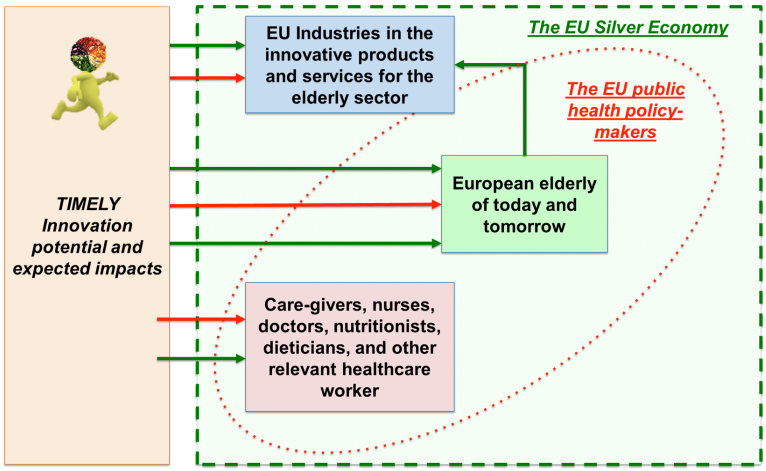


***Fig. 5**: Impacts of TIMELY on end user categories.*

In the context of this scenario, which encompasses a

rise in the prevalence of MN in each setting up to 82% in hospital, TIMELY wants to specifically impact on three aspects that will allow EU to revert this dramatic tendency: i) **achieving early recognition of MN** by developing a personal Biopassport as a new screening tool to assess the individual MN status or risk, associated with dedicated strategies of training and dissemination to make it readily adoptable by a broad number of older adults; ii) **increasing the efficacy of MN treatment** through the development of tailored recommendations, based on integrated dietary and lifestyle strategies; iii) **reducing MN prevalence**, through the early recognition and the implementation of evidence-based strategies. This will provide meaningful benefit on public health costs of MN. TIMELY also accepts the broader challenge of impacting on the promotion of active and healthy ageing, with the final goal of sensibly increasing healthy life years.

Expected impact 1: ***Design and development of evidence-based dietary strategies, dietary recommendations and new food products that support active and healthy ageing and help prevent malnutrition in the elderly.***

SHORT- and MID-TERM IMPACT (which will be delivered by the end of the TIMELY project): TIMELY recognises the **inherent heterogeneity of MN in the elderly**, and through a better comprehension of its overall complexity and array of bio/non-bio determinants, new evidence-based dietary strategies and recommendations will be designed, validated and disseminated to the relevant stakeholders and policy-makers (Fig. 5). TIMELY will face the problem of treating and preventing the elderly MN by using a semi-personalized approach: **different subgroups** will be identified according to the peculiar combination of major bio/non-bio determinants and **subgroup-specific dietary and lifestyle strategies** will be provided, including recommendations, new foods, dietary plans, ICT tools, services and devices. This strategic approach will respond to the critical need of overcoming the imperfection and inefficacy of existing prevention programmes, especially in poorest countries or in countries undergoing an emergency crisis, as reported by WHO. In particular, providing the basis for new evidence-based public health policies based on a better understanding of the mechanisms of the ageing process will impact on the ability of EU to support healthy ageing and prevent elderly MN. The development of **dietary strategies, recommendations and new food products** is the core of TIMELY, that thanks to its strong and diverse food industry partnership will ensure the technological feasibility of developing new food prototypes able to **cope not only with the nutritional impairment, but also with the peculiar sensory and texture requirements of MNed and MNrisk elders**. TIMELY will impact on the EU capabilities of providing new health-promoting products, strategies and services based on food enrichment, food reformulation, a better understanding of the consumers' behaviour and preferences and a full exploitation of the most-advanced technologies, e.g. 3D food printing. The ability to develop new preventive food formulations and to 3D print nutritious, attractive and personalized food products, meal components or whole meals can not only contribute to a decrease in MN and the related cost, but will also create new business potential for EU-based food industries and food equipment providers. In the domain of dietary and lifestyle strategies, the development of new ICT tools, services and devices to compute and adapt personalised diet regimens, motivate and monitor food intake, and empower the elderly to be socially and physically active, as well as kitchen appliances to facilitate the elderly food preparation at home, will be supported by the involved SMEs and large companies. The food and technology companies will facilitate access to market of new foods and devices, increasing the immediate impact of the industrial advancement achieved within the collaborative project. By specifically targeting MNed and MNrisk subjects as problematic subgroups of the ever-growing ageing population, TIMELY **will indirectly impact on the accomplishment of important broader goals, such as the improvement of general dietary recommendations for seniors, as well as the most effective strategies to deliver them to the older population while ensuring compliance**. Indeed, other intervention studies focused on the promotion of healthy ageing, health care structures and, later on, the whole ageing population might benefit of the food products and age-friendly ICT tools and devices that will be developed in TIMELY, helping food intake monitoring, nutritional counselling and personalisation of the diet. From the **users'** perspective, **awareness** will be raised among the older population in EU, via **dedicated webinars, workshops and communications**. Besides, attention will be also paid to the involvement of decision-makers at various level, to inform and provide concrete tools to be implemented for improving the quality of life of people aged 65+.

LONG-TERM IMPACT:

The dissemination of the holistic intervention strategies developed within TIMELY, their adoption by relevant care-givers and public health relevant stakeholders, as well as their user-focused utilisation by EU food and services industries will contribute to the **reduction of MN prevalence in the elderly in EU**. Moreover, TIMELY will promote the utilisation of the personal Biopassport, applying the most promising prognostic biomarkers of MN, in clinical practice and among the GPs through the links developed at regional level and via user-platforms (e.g. AGE Platform EU), will stimulate a close collaboration between clinicians and industrial partnership, in order to continuously update and improve the functionality and age-friendliness of the Biopassport-related tools, devices and services. The utilization of the Biopassport and the SAGENODE web-based interface in the EU population will also allow to continuously explore new MN determinants or connection between them, increasing the efficacy of the intervention strategies put in place in response to demographical and socio-economic changes, as well as opening the opportunity to design new or implemented integrated intervention strategies based on new recommendations and new foods. This will stimulate the development of innovative foods by SMEs and food industries.

Even more importantly, the scientific knowledge produced, in terms of a better comprehension of the biology of MN and ageing, will encourage the adoption and further implementation of a holistic approach in the treatment of age-related diseases. TIMELY will stimulate innovation in the field of age-friendly, functional food ingredients, by providing adequate knowledge and end-points

(i.e. bio/non-bio determinants) that enable the scientific substantiation of health claims. The potential of discovering new biomarkers and risk factors and their validation in the real world (silver ecosystems) will boost further nutritional investigations for the development of age-friendly, functional foods in food and beverage industry, specifically tailored to **prevent MN even before the MN risk is perceived/detected**. Future research based on TIMELY achievements and outcomes may have enormous commercial significance (new foods, new ICT tools and devices), that will be fully acknowledged during the project lifecycle and will be at the basis of specific exploitation strategies consisting of core activities of TIMELY work plan. The consortium will devote effort in the dissemination and exploitation activity to ensure an adequate follow up of TIMELY outcomes to the food industries and technological companies. **The consortium will also pay attention to the users' perspective**: awareness will be raised among the elderly, via dedicated webinars, workshops and communications. Besides, attention will be also paid to the **involvement of policy- and decision-makers at various levels**, to inform and provide concrete tools to be implemented for improving the quality of life of people aged 65+. Indeed, this is a very critical point because, as highlighted by the JRC Science and Policy Report "The Role of Nutrition in Active and Healthy Ageing", it is mandatory to raise awareness that more attention should be given to diet and nutrition in policy-making to protect our older citizens.

Expected impact 2: ***Complementary support to the research and innovation activities carried out in the European Innovation Partnership on Active and Healthy Ageing and to the development of the European Research Area through the Joint Programming Initiative 'A Healthy Diet for a Healthy Life'. European Innovation Partnership on Active and Healthy Ageing and to the development of the European Research Area through the Joint Programming Initiative 'A Healthy Diet for a Healthy Life***

Achieving a greater impact at pan-EU level in the field of healthy ageing requires a thorough **mobilisation at regional and national leve**l. In doing so, the two main routes identified by the EC are the European Innovation Partnership on Active and Healthy Ageing (EIP-AHA) and the JPI "A Healthy diet for a Healthy Life (JPI-HDHL) that have a mutual interest in the prevention of frailty with a specific focus on malnutrition and in the promotion of healthy ageing. TIMELY will develop dedicated strategies fully recognising the specificities of these two instruments and their valuable inter-relations.

TIMELY and the EIP AHA: In the frame of the EIP AHA, the **Action Group A3** has tested and developed an integrated approach with personalised interventions. Now the initiative is looking for complementary case for further cooperation and TIMELY is in the right position for offering its support and planned finding. Such an approach is welcome also by DG SANCO, in the frame of the EU efforts to tackle MN. TIMELY will reinforce the holistic vision to healthy ageing, towards which AGE Platform Europe campaigns in the frame of the EIP AHA Steering Group, seeing active and healthy ageing as being "the process of optimizing opportunities for physical, social and mental health to enable older people to take an active part in society without discrimination and to enjoy an independent and good quality of life". By **combining the medical and scientific approach to the direct involvement of older people in research**, working for tools designed-for-all and adapted to the varying needs of ageing, TIMELY contributes to complement and reinforce a more comprehensive vision of ageing.

Furthermore, TIMELY recognises the relevance of regions in the frame of EIP AHA. The implementation of real world validation studies at ecosystem level in two twinned cities in the regions of South Holland (NL) and Emilia Romagna (IT) as well as the relevant role of Southern Denmark Region (DK) in the recruitment of MNed and MNrisk subjects and in the development of recommendations sees its rationale in the importance of mobilising **EIP AHA Reference Sites**. Indeed, these are three out of the 32 currently acknowledged Reference Sites for the EIP AHA, awarded with 2 (IT and NL) and 3 stars (DK) in 2013. The role of Regions is very important for the implementation of demand-driven ecosystem-based innovations and TIMELY will take advantage of the strong working relationship sought by the EIP AHA management structure to develop mutual learning and support innovation across the regions. Starting from the TIMELY experience, and fully exploiting the **co-development process of users engagement** promoted by AGE Platform EU and the **mobilisation of networks of regions such as EUREGHA, ERRIN, AER and CORAL**, specific methodologies for the **replication of Good Practices across the EU** will be put in place to achieve the broadest impact possible in preventing MN and supporting healthy ageing.

TIMELY and the JPI HDHL: The overall aim of the Joint Programming process is to pool national research efforts in order to make better use of EU's research funds and to tackle common EU challenges in some few key areas. Currently, most of the TIMELY partners are fully engaged in promoting the scope of the JPI HDHL, being involved in a number of Joint Actions currently funded (among others, UNIBO is national coordinator in the DEDIPAC action, and partner of the ENPADASI and FOODBALL actions). Notably JPI HDHL identified the topic of MN as a possible new joint action to be launched during the next years. For this reason, acknowledging the importance of a coherent and harmonised IPR, Open Access and Knowledge Sharing framework, **TIMELY will develop protocols for data sharing**, **standardising data collection** for country-to country or pan-EU comparisons, as well as for **linking the project with on-going and future joint actions** and knowledge platforms implemented within the JPI HDHL context. This will ultimately generate a strongest array of meaningful results and will positively impact on the EU Research Area by **increasing the synergies among the funded research, avoiding the duplication of funding or the development of activities not aimed at a common goal** and thus allowing Members States to fund specific actions that are giving a real added value both at local and international level.

Expected impact 3: ***A strengthening of the EU´s key global market position in innovative products and services for the elderly.***

This great demographic challenge currently faced by the EU represents not only a serious threat for international public health if not properly managed, but also an untapped opportunity from an economic point of view for the innovative elderly-targeted products and service industries. According to The Silver Dollar – Longevity Revolution (BofA Merril Lynch, 2014), in EU2020, consumer spending power in 60+ will reach $15tn. This trend is associated with **large changes in consumer preferences** that ultimately impacts on the products/services themselves, their design and marketing strategies, as well as the relationship with the Silver Economy relevant players (Fig. 5) Older people want good products and services in the same way anyone else does, and in this perspective some industrial sectors most likely will benefit from the ageing marketplace, in particular those in which companies are focused on products and services designed to enhance the quality of life, health, wellbeing and independence of older people. Recently, some EU countries, as France, adopted a strategy to foster a dedicated "silver" industrial sector and bring together a variety of actors around the objective of bringing to the market innovative products and services for the elderly, which are expected to generate new jobs. In this perspective, consumer goods, food and beverages, retail and technology have been singled out as being particularly attractive to older consumers. Food and ICT SMEs as well as bigger companies are recognizing these opportunities for business growth in the ageing market niche. However, not enough marketing is currently addressing MNed and MNrisk older people. ***TIMELY consortium will impact on the overall positioning of the EU industries:*** the current key position as global leader of EU industries will be further strengthened by the understanding of real needs and real requirements of MNed and MNrisk elderly, supporting them to achieve more healthy lifestyles. TIMELY takes advantage of **transforming users into partners**, ensuring relevance and adequacy of new approaches, goods and services, and thus guaranteeing that the developed solutions are tailored to their needs and meet their real requirements, and works towards greater acceptability. Finally, dedicated dissemination and exploitation strategies will allow not only the TIMELY consortium to expand their relevance and positioning, but will also ensure - through dedicated workshop and public events - to **identify the major opportunities for achieving a greater economic impact for the market players**. In particular, according to a recent report by The Economist Intelligence Unit, which looked at the risks and opportunities faced by businesses as they start to grapple with changing demographics, smaller companies seem more responsive than their larger peers in seeing this as a new market area with opportunities for them. For this reason, TIMELY will not only ensure the greater exploitation opportunities for the 6 SME partners of the consortium, but will also **identify appropriate marketplace and business networks** for dissemination and exploitation purposes.

Expected impact 4: ***A better understanding of the interaction between nutrition and the ageing process through international collaboration and exchange of knowledge/best practice.***

The DISCOVERY phase of TIMELY will be entirely devoted to seek a better understanding of the interaction between nutrition and ageing, the latter being a multifactorial process driving to MN. Indeed, TIMELY involves a unique and consolidated partnership, which joins international centres of excellence with a well-documented expertise in studying the ageing process with a holistic and multidisciplinary-based approach. TIMELY will embed MN in the process of human ageing, allowing the consortium to identify the major MN risks factors which force the deviation from the trajectory of healthy ageing. The international consortium will **share and elaborate data from several EU and non-EU funded aging-focused studies**, sensibly impacting on the knowledge exchange in this field. The access to large cohorts including bio/non-bio data from more than 150,000 subjects, 65+yrs old, in different EU countries and worldwide, and different settings, as well as biological samples to be fully characterized with omics approaches, will allow TIMELY to develop the first multidimensional model of MN that will dissect the heterogeneity of MN into discrete subgroups, according to the peculiar interaction of major bio/non-bio determinants. Also, TIMELY will expand the knowledge on the phenotype of MN by applying an advanced set of omics and multidimensional analysis also encompassing non-biological factors, in order to better understand the mechanism underlying MN in the elderly and allow an early detection of MN.

The knowledge generated by TIMELY will have a **significant impact on the international collaborations and best practices exchange**, also through relevant EU initiatives, as well as through international cooperation initiatives like the International KBBE Forum which includes EU, CA, AU and NZ and that have been a valuable platform for developing cooperation, such as the **2014 KBBE Workshop "Health for all: understanding the ageing process"** hosted by UNIBO (see Section 1.2 and Expected Impact 2). In particular, it will be of great benefit at several levels for a variety of possible users, such as patients, geriatricians, nutritionists, public health authorities, etc. Target groups for the TIMELY dissemination activity will not only address the scientific domain as major generator of meaningful evidences for public health purposes, but will include secondary disseminators (educators, journalists, national and internationals patients groups, decision makers and health policy-makers (e.g. health protection agency, ministry of health, medical associations), health care providers (e.g. hospitals, nursing homes, etc.), and other relevant stakeholders of the food and innovative services/products for the elderly industry. The new knowledge will also open **new opportunities to develop innovative products** by EU food SMEs and large industries, as well as ICT and elderly-targeted service industries dealing with nutritional practices in the ageing, thus strengthening the competitiveness and the capability to grow.