CHANCES

Consortium on Health and Ageing: Network of cohorts in Europe and the United States

Final publishable summary report

The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement no. HEALTH – F3-2010-242244.

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Abbreviations

CHANCES Partners

HHF - Hellenic Health Foundation (Greece)

UoA - National and Kapodistrian University of Athens (Greece)

UMU - Umeå University (Sweden)

RIVM - National Institute for Public Health and the Environment (The Netherlands)

WU - Wageningen University (The Netherlands)

DKFZ - The German Cancer Research Center (Germany)

DCS - The Danish Cancer Society (Denmark)

ERASMUS MC - Erasmus University Medical Centre (The Netherlands)

BUW - University of Wuppertal (Germany) **

QUB - Queens University Belfast (United Kingdom)

THL - National Institute for Health and Welfare (Finland)

Uni Mannheim - Universität Mannheim*

MPG - Max-Planck-Gesellschaft München (Germany)**

IARC - International Agency for Research on Cancer (France)

BWH - The Brigham and Women's Hospital, Inc. (United States)

UCL - University College London (United Kingdom)

UIT - University of Tromsø (Norway)

* Month 1 to Month 17

** Month 18 to Month 60

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Executive summary

The challenges associated with the global ageing of populations are among the major concerns of modern-day societies. Mortality, morbidity and disability increase steeply with age. These burdens, which are associated with the ageing of communities, necessitate actions that counteract the negative aspects of demographic ageing by adding meaningful years to life, limit ill health and increase opportunities of social involvement of older people. Good quality data on diverse health outcomes and determinants are fundamental to any such effort and should be valid (based on accurate measurements), precise (based on large populations) and repeatedly measured over time. Towards this direction CHANCES brought together 17 partners (see www.chancesfp7.eu for the partner institutions) and 14 cohorts from Europe and North America (see Annex I for details) in a consortium whose efforts were channelled through 11 Work Packages (WPs). The ultimate goal was to provide new evidence on the health of ageing populations. The project received European-funding for 5 years (1/2/2010 to 31/1/2015).

CHANCES focused on four major groups of chronic conditions and disabilities, typical in the ageing populations: cancer; diabetes and cardiovascular diseases; fractures and osteoporosis and; cognitive function and dementia disorders. Harmonization of the available data across the diverse participating cohorts on outcomes and exposures of interest was successfully undertaken by the THL (National Institute for Health and Welfare, Finland) CHANCES partner and a flexible and dynamic tool for the documentation and update of this procedure was established (*http://www.thl.fi/publications/morgam/chances_d9/index.html*). The project developed an efficient and flexible infrastructure for conducting joint (pooled) analyses to estimate the prevalence, incidence, mortality and economic implications (where appropriate) of the indicated conditions, as well as, to identify/explore socio-economic, environmental, lifestyle, and nutritional determinants. Genetic profiles and biomarkers associated with ageing were also investigated, identified and estimated.

Relevant CHANCES publications cover a wide area of research hypotheses (see Template A1: List of all scientific publications relating to the foreground of the project). The number of publications related to CHANCES is expected to rapidly increase in the near future due to numerous projects which are at their final stage as of the CHANCES termination. In addition, a feasibility study for an intervention

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trial against progression of prostate cancer, based on a low-fat, plant-based low-meat and high-fish diet, and on regular exercise was undertaken in Denmark (Cancer Nurs. 2015 May 15. [Epub ahead of print]).

Moreover, an Alzheimer´s Disease (AD) registry with 372 validated cases of Alzheimer's disease and a set of suitable controls were created in Umeå, Sweden. Each had at least one blood sample available on which certain biomarkers were measured and their role in AD was further explored (Alzheimers Dement. 2014 Oct 7. pii: S1552-5260(14)02770-8). In parallel, a brief, reliable instrument to assess health and ageing-related outcomes (Health Module) in a comparable fashion in European ageing populations was created within CHANCES.

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Project context and main objectives

Context

Data on health of ageing populations are essential for health, social and economic research, policy and management. Such data should be both valid (based on valid measurements) and precise (based on large populations). Furthermore, they should be based on repeated measurements over time, to identify and quantify changes in health-related parameters, their determinants and confounders. No single database in Europe fulfils all these characteristics and establishing such as cohort would represent a very expensive endeavour. An alternative, more efficient approach is however possible. A number of cohorts in Europe and in North America have collected data on the key domains of ageing and risk factors, and combining such cohorts in a consortium represents an efficient and cost effective approach to provide new evidence of the health of ageing populations and its determinants. The CHANCES project consisted of a consortium of 14 cohort studies of health and ageing from Europe and United States, and a few additional key researchers in this area. The project aimed at developing an efficient and flexible infrastructure for conducting pooled or parallel analyses of chronic diseases and disabilities among the elderly, their determinants, and their economic implications, with focus on four groups of determinants and four groups of chronic diseases (please see below), as well as, overall mortality and disability.

In CHANCES, the limit of 60 years of age was selected to define the elderly. However, most cohorts included in the consortium include subjects aged 50 or over, and separate analyses was conducted, if deemed necessary, on health-related characteristics and determinants in subjects aged 50-59, 60-69 and 70+ years.

Methods and Objectives

1) The CHANCES project aimed to combine and integrate on-going studies in order to produce evidence on ageing-related health characteristics and determinants in Europe. Fourteen cohorts and cohort consortia were included in the project: The Cohort of Swedish Men (COSM); The EPIC-Elderly Study; The ESTHER Study; The HAPIEE Study; The MORGAM Study; The NIH-AARP Study; The Northern Sweden Health and Disease Study; The Nurses Health Study; The Rotterdam Elderly Study; The Seneca Study; The SHARE Study; The Swedish Mammography Cohort (SMC); The Tromsø Study; The Zutphen Elderly Study. Selected characteristics of the

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studies included in the consortium can be found in (Eur J Epidemiol; 2014. 29(12):929-36. doi: 10.1007/s10654-014-9977-1. Epub 2014 Dec 13). These studies were: (i) longitudinal (cohort) studies which were primarily established to address health issues related to ageing and ageing-related conditions; (ii) longitudinal (cohort) studies which were established for purposes other than the investigation of ageing-related conditions, but include a sufficiently large number of elderly to justify specific analyses; (iii) cross-sectional studies.

2) CHANCES focused on four major groups of chronic conditions and disabilities which account for a large proportion of the morbidity and mortality burden in the elderly population: (i) cancer; (ii) diabetes and cardiovascular diseases; (iii) fractures and osteoporosis; (iv) cognitive function and Alzheimer disease. Health-related determinants of interest comprised of: (i) socio-economic factors (e.g., education, income), (ii) environmental factors (e.g., occupational exposures), (iii) lifestyle factors (e.g., tobacco smoking, alcohol drinking), and (iv) nutritional factors (e.g., BMI, dietary patterns). Ageing-related determinants included (i) biomarkers and (ii) genetic profiles of ageing.

Using the above-indicated data from CHANCES cohorts the following aims were targeted at:

a) Estimating incidence of the indicated health outcomes and associated cause-specific mortality, b) estimating prevalence of the health conditions indicated above and related disability, c) identifying health- and ageing- related determinants of these conditions and of the resulting disability, and mortality, and d) evaluating the social and economic implications of chronic conditions, disabilities and mortality in the elderly (where applicable).

To achieve the above objectives, each cohort provided relevant data. Combining the different types of studies required *harmonization of data* across the diverse participating cohorts with respect to outcomes and exposures of interest. This major work was carried out by the THL (National Institute for Health and Welfare (Finland), CHANCES partner. Through a web based WIKI space, accessible to CHANCES consortium and collaborators, descriptions of the participating studies, definitions of harmonized variables, conversion rules form the different studies and the characteristics of the harmonized data were fully documented (*http://www.thl.fi/publications/morgam/chances_d9/index.html*). The consortium harmonized 323 variables referring to:

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Outcomes: Health conditions and mortality

The following outcomes were included: lung function; prevalence of hypertension, incidence and family history of coronary heart disease, stroke and diabetes; prevalence and incidence of cancer (by organ of origin); prevalence and incidence of fractures and osteoporosis; prevalence and incidence of depression, cognitive impairment and dementia; multi-morbidity; mortality (by cause); disability and frailty; quality of life; and self-perceived health.

Exposures

Lifestyle: (including tobacco smoking, drinking status, physical activity) ; anthropometry (including weight, height, waist/hip circumference); socioeconomic status (including education, marital status); medical history (including use of drugs; reproductive history) ;dietary factors (including total energy intake, intake of specific macro-and micronutrients, foods and food groups, ethanol intake); and blood biomarkers (including ApoA1, ApoB, CRP, GGT, glucose, glycated haemoglobin, total and HDL cholesterol, triglycerides, vitamin D; oral glucose tolerance test; biomarkers of oxidative stress (hydroperoxides), antioxidant status (biological antioxidant potency) and redox status (total thiols).

3) To assess in particular the role of biomarkers of ageing on the indicated health outcomes, a list of biomarkers to be measured in a common fashion by five CHANCES partners was established and measurements of : electrolytes Ca, Mg, Na, Cl and K, the oxidative stress markers Reactive Oxygen Metabolites, Biological Antioxidant Potential and Total Thiols in Proteins, 25hydroxy-Vitamin D, Gamma Glutamyl Transferase, Creatinine, High Sensitive C-Reactive Protein and the B-vitamins Folate and Vitamin B12, Alanine Aminotransferase, Uric Acid, Urea, ROM, TTL and H-index, I-Index and L-index were undertaken in subsamples of five CHANCES cohorts which agreed to provide blood samples for their participants.

4) To emphasize on the importance of cognitive disorders among the elderly, an Alzheimer´s Disease (AD) registry with validated cases and suitable controls was created in Umeå (Sweden) which enables the investigation of the association between certain biomarkers such as inflammatory markers, protein and metabolic patterns, serological analyses and analysis of specific substances and AD incidence (Alzheimers Dement. 2014 Oct 7. pii: S1552-5260(14)02770-8).

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The achievement of the above-noted objectives is indicated, mainly, by the large number of research proposals which have been developed (70), cutting across various WPs and cohorts (see Table 1 below). So far, 49 projects have been published and many more are expected to appear in the literature in the near future. For the analysis of each research proposal the appropriate epidemiological indices, based on harmonized variables, were combined in pooled analyses or meta-analyses. In addition to the multi-cohort projects, a number of cohort specific scientific papers have been published, including several methodological papers.

A detailed list of all publications is shown in Template A1.

Table 1. Research proposals developed within the CHANCES project by outcome of interest

Outcome of interest	Research topics investigated within proposed projects
Cancer Incidence	Smoking; Vitamin D; food groups/dietary patterns; alcohol consumption; socio-economic position; Disability-Adjusted Life Years (DALY); population attributable fractions for major determinants;
Cardiovascular Diseases and Diabetes	Prediction models and adapted prediction scores; HbA1c levels; smoking; alcohol consumption; education; obesity; dietary patterns; Vitamin D; DALY; population attributable fraction for major determinants;
Fractures and Osteoporosis	Socioeconomic status; weight and weight changes; DALY; population attributable fraction for major determinants; excess mortality following hip fractures;
Cognitive impairment and Alzheimer's Disease	Cardiovascular diseases; lipid intakes; dietary patterns; sedentary behavior; lifetime smoking; DALY
Disabilities and Mortality	Adapted prediction scores; HbA1c levels; smoking; alcohol consumption; education; self-perceived health; physical activity; obesity; dietary patterns; Vitamin D; telomere length; DALY; population attributable fraction for major determinants; predictive value of potential frailty criteria;
Genetic: Telomere length	lifestyle factors; height

5) Related to these objectives, CHANCES also sought to use its emerging epidemiological knowledge, to develop an exemplar public health intervention. A feasibility study for an intervention trial against progression of prostate cancer, based on a low-fat, plant-based low-meat and high-fish diet, and on regular exercise was undertaken in Denmark. Two related

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manuscripts have been published (see Section A, Template A1: List of all scientific publications relating to the foreground of the project). Given the success of the study, the study leaders have expanded the objectives and are proceeding with biochemical and biomarker analyses of the biological samples collected as part of the study.

6) Finally, an important objective of the CHANCES project was the development of the Health Module (HM), i.e. a questionnaire for the assessment of health and ageing-related conditions and outcomes of the elderly in a comparable way across European countries. The development of the HM was based on systematic assessment of previously used measures and was piloted in population samples in Greece, Northern Ireland, Poland and Sweden. Validation analyses of results from these pilot studies have been in general satisfactory and thus HM has been finalised.

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Description of the main S&T results/foregrounds

1) The web-based WIKI area with information on harmonization of available data: A focal point for CHANCES was to harmonize the available data across the diverse participating cohorts with respect to outcomes and exposures of interest and to provide a flexible and dynamic tool for the documentation and update of this procedure. This major work has been successfully carried out by the THL (National Institute for Health and Welfare (Finland), CHANCES partner. A web based WIKI area has been created, where description of participating cohorts and instruments, proposed and approved harmonized variables, availability of harmonized variables in each cohort and conversion rules used to create the harmonized variables in each cohort are contained. The use of WIKI from all CHANCES partners and collaborators comprised a dynamic approach to data harmonization and is considered to have been an valuable experience by the consortium participants. Although the harmonization of data was originally assigned to months 1-42 it turned out that this was rather a continuous process within CHANCES as: a) new cohorts asked for collaboration, and b) new scientific hypotheses were generated, and thus, new harmonised variables were required in order to carry out the respective analysis. This is not regarded as a problem but, on the contrary, as the result of a fruitful and productive collaboration. As a consequence, harmonization procedures were carried out until the termination of the CHANCES programme.

The harmonization procedure can be briefly described through the following steps:

a) A list of exposures and health outcomes of potential interest for the CHANCES project was initially constructed by the Consortium;

b) For each of these a-priori defined exposures/outcomes, relevant variables of similar conceptual construct were selected from each participating cohort and compared between cohorts based on detailed information regarding their assessment methods and coding;

c) Based on the data available from the cohorts, new common variables were proposed by the CHANCES partners with research interests on the specific variables. The proposals were reviewed by all partners prior to acceptance as CHANCES variables.

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d) The CHANCES variables were generated from the available data in each cohort. The algorithms to generate the CHANCES variables varied in complexity, depending on the level of agreement between the locally available data and the proposed CHANCES harmonized variable. For example, there was variation in the smoking questionnaires used in the different cohorts, but it was possible to derive common variables on current daily smoking for all cohorts and the number of years of daily smoking for nearly all cohorts. The algorithms used for generating the variables in each cohort were documented.

e) The availability, comparability and quality of the data for the variables from each cohort were assessed and documented.

A major undertaking was to update the descriptions of the participating studies, definitions of harmonized variables, conversion rules from the different studies and the characteristics of the harmonized data and producing World Wide Web publication (Available from http://www.thl.fi/publications/morgam/chances_d9/ index.html). This e-publication serves as a key methodological reference for the publication of the scientific results of CHANCES. It also makes it possible for any future studies to build on what was already done in CHANCES.

There are currently 323 harmonized variables, and, indicatively, refer to: new cases and history of cancer, CVD and diabetes and fractures; perceived health, nutrition, physical activity, , reproductive history, socio-economic status, cognitive decline, biomarkers and use of drugs.

Moreover, the WIKI proved to be an easy and flexible way of communication among the partners of CHANCES. A network of statisticians was developed and a special area in the WIKI was devoted to the effective communication of statisticians, epidemiologists and analysts in order to better serve the statistical analyses of the various projects. The approach to data harmonization, through dynamic communication among people involved in a large-scale project by means of efficient use of a WIKI server, brings an important advancement to the state of art of large-scale data handling and harmonization.

2) Research proposals and related publications: A large number of research proposals have been developed, cutting across various WPs and cohorts (see Table 1). A total of 70 CHANCES collaborative research proposals have been approved by the Publication Committee throughout the CHANCES lifetime with 49 having been published and 2 accepted for publication in peer

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reviewed journals. The number of publications related to CHANCES is expected to increase rapidly in the near future due to numerous projects which are now at their final stage (i.e., manuscripts under internal review by co-authors). For the analysis of each research proposal, relevant epidemiological indexes, based on harmonized variables were combined using meta-analysis. In addition to the multi-cohort projects, a number of cohort specific scientific papers have been published, and some methodological papers have also appeared.

Indicative results of the above-indicated projects are briefly mentioned below by health outcome and by CHANCES partner responsible for undertaking each project. Notable in this list is the variety in the research hypotheses investigated in CHANCES, as well as the active participation of all CHANCES partners. A list of current publications is shown Template A1 (Section A).

Cardiovascular diseases and type 2 diabetes

- Effects of major lifestyle risk factors, independent and jointly, on life expectancy with and without cardiovascular disease. Adopting a beneficial lifestyle, that includes not smoking, drinking lightly or moderately, taking regular exercise and maintaining a modest excess body mass index, benefits both, life expectancy without cardiovascular disease, and survival after the onset of cardiovascular disease. (Queen's University Belfast)
- Diagnosis, duration and treatment of type 2 diabetes and cancer incidence. There is little evidence to indicate an association between diabetes and the risk of cancer overall, but there is some evidence suggesting such an association for specific types of cancer. (International Agency for Research on Cancer)
- Plasma concentrations of B vitamins and the risk of cardiovascular disease at older age. Folate, but not vitamin B12, may help preventing cardiovascular diseases in older adults, but randomised trials in healthy subjects are necessary to confirm that such intervention is effective. (University College London)
- Smoking and cardiovascular disease in older adults. Smoking is a powerful independent risk factor concerning cardiovascular events and mortality among the elderly - quitting smoking can help reduce the cardiovascular excess risk caused by smoking, even among older adults. (German Cancer Research Centre)
- Obesity and the risk of cardiovascular disease (CVD). Waist circumference, an indicator of abdominal obesity, may be a better measure of overall obesity than body mass index in predicting

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the risk of cardiovascular disease in elderly men and women aged 60-69 but its impact is diminished compared to BMI in older ages (70-79 years old). (Queen's University Belfast)

- The role of socio-economic position in the development of type 2 diabetes in older adults. Lower socio-economic position is associated with an increased risk of type 2 diabetes in older adults. Obesity plays a vital role in the development of type 2 diabetes even amongst well-educated individuals, as 20% of the relationship between socio-economic position and type 2 diabetes appears to be explained by body mass index. (Queen's University Belfast)
- Fruit and vegetable intake and risk of incident type 2 diabetes. Fruit and vegetable intakes, overall, or in terms of single vegetables such as green leafy vegetable or cabbage intakes do not appear to be related to incident type 2 diabetes. (Queen's University Belfast)

Cancer

- Cancer, mortality, morbidity and disability levels of middle-aged and elderly populations. Cancer is a serious cause of mortality, morbidity and disability. Even if the disease burden attributed to cancer is predominantly caused by mortality, some cancers are accompanied by a significant percentage of disability. (Hellenic Health Foundation)
- Cumulative overweight in the elderly and cancer risk. A longer duration of being overweight increases the risk of obesity-related cancers, post-menopausal breast and colorectal cancer, among the elderly. (International Agency for Research on Cancer)
- Obesity and central obesity in relation to cancer risk among the elderly. Body mass index as a measure of obesity, compared to waist circumference, hip circumference or waist-to-hip ratio, appears to be the most appropriate indicator of body fatness with respect to its predictive ability of cancer risk in older adults (International Agency for Research on Cancer)
- Pre-diagnostic vitamin D concentrations and cancer risk in older individuals. There is little evidence to support that vitamin D concentrations in the blood can have a major effect on the development of cancer and cancer prevention among the elderly in Europe. (German Cancer Research Center)
- Quantification of the smoking-associated risk of total and site-specific cancer incidence and mortality. Even in older adults, being a smoker or having been one, considerably increases the risk of developing and dying from cancer, compared to individuals who have never smoked. Nonetheless, even among the elderly, quitting smoking can still have an impact on reducing the risk of cancer. (German Cancer Research Center)
- Alcohol and the risk of cancer. Alcohol use contributes to the development of cancer in the upper aero-digestive tract as well as breast, liver and colorectal cancer. Absolute risks of specific cancer

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types for different levels of exposure at given ages over time can account for the competing force of overall mortality. (International Agency for Research on Cancer)

Osteoporosis and fractures

- Hip fractures affect mortality, morbidity and disability levels of middle-aged and elderly populations. Hip fracture is a serious cause of primary disability and mortality among the elderly. Future interventions should focus not only on shortening recovery and reducing long-term disability after a fracture incident, but also on a better primary prevention of falls. (Hellenic Health Foundation)
- The effects of education and marital status on the risk of hip fracture in older men and women. Higher education level appears to reduce the risk of hip fractures, whereas elders living alone, compared to being married/cohabiting, are more likely to have a hip fracture later in their life. (University of Athens)

Cognitive disorders

- Cognitive decline and cognitive disorders. Alzheimer's disease may be related to virus infection; there are clear indications that the Herpes virus is linked to the development of Alzheimer's disease. Further studies exploring the effects of smoking, dietary patterns, cerebrovascular diseases, physical activity and alcohol consumption on cognitive decline in the elderly are pending. (Umeå University)
- Cognitive performance and decline. Cognitive impairment appears to be an independent risk factor for earlier death. Saturated fats (SFA) and monounsaturated fats (MUFA) do not appear to be associated with cognitive performance, but higher consumption of polyunsaturated fats (PUFA) seems to slightly improve cognitive performance. Close adherence to the Mediterranean diet appears to protect against cognitive decline. (Hellenic Health Foundation; University of Athens)

Overall mortality and other outcomes

- Education inequalities in health among the elderly. There is a consistent disadvantage of low versus higher education among the elderly in Europe, with respect to a number of health indicators. Nonetheless, the degree of education-related inequality in health differs consistently across European countries. (Bergische Universität Wuppertal)

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- Self-perceived health and mortality of the elderly. Elderly people who perceive their health as good/excellent appear to have increased survival rates compared to the elders who feel not healthy, independently of lifestyle and socio-demographic characteristics as well as of diagnosed medical conditions. (Hellenic Health Foundation; University of Athens)
- Educational gradients in the effects of health shocks on early retirement. Health shocks can lead to early retirement, but education has a moderating effect on people's decision to retire early, which differs across sexes. Less educated men are more likely to stop working after experiencing a severe illness compared with higher educated men. The opposite was shown in the case of women. (Bergische Universität Wuppertal)
- Adaptation to adverse health events: The role of education and experience. Individuals' health self-ratings are affected by the onset of a severe disease, such as cancer or stroke, but people are also able to adapt to adverse health shocks over time. Better-educated individuals react more favorably to adverse health events. On the contrary, being diagnosed with a severe illness impairs subjective well-being to a greater extent for individuals that have previous experience of an adverse health event. (Bergische Universität Wuppertal)
- Age at menopause between 40 and 50 lowers a woman's survival. Earlier menopause is associated with increased mortality, Women who went through menopause between 40 and 44 years of age appear to have a 16% higher chance of dying than women experiencing menopause between 50 and 54 years. The chance of dying was 9% higher in women going through menopause between the ages of 45 and 49. (University College London)
- Healthy ageing through a healthy diet - Never too old to eat healthy. The adoption of a healthy diet based on the recommendations of the World Health Organization increases life expectancy by about 2 years and prevents cardiovascular mortality among the elderly populations in Europe and the United States. Following the dietary recommendations of the World Cancer Research Fund/American Institute of Cancer Research prevents the occurrence of diet-related cancers, therefore contributes to a lower burden of cancer later in life. (Wageningen University (WU))
- Vitamin D and mortality: Europeans with vitamin D deficiency die much earlier than Europeans with a sufficient vitamin D concentration in their blood. (German Cancer Research Center)
- Biomarkers and the ageing process. The measurement of suitable biomarkers in the blood that represent nutrition deficiencies and a disturbed oxidation balance in the human body can provide valuable information about the procedures that lead to chronic diseases and the ageing process. (National Institute for Public Health and the Environment)
- Genetic factors are often associated with diseases early in life. Genetic factors are often associated with diseases early in life but there is increasing evidence that common genes may also be

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involved in the disability and mortality among the elderly. In particular there appears to exist a joint effect of common genes on the risk of high cholesterol levels similar to the effect of obesity on blood lipid levels. Similar findings seem to hold for low-risk genes in relation to risk factors of stroke. (Erasmus Universitair Medisch Centrum Rotterdam)

3) Feasibility study for an intervention trial against progression of prostate cancer.

The study was undertaken in Denmark, within the context of "The Nordic Lifestyle Intervention Study among Men with Prostate Cancer (NILS)". Investigators from the CHANCES Partner 'Danish Cancer Society (DCS)' hypothesized that a lifestyle intervention including a health-promoting diet with a high intake of whole grain rye combined with a high level of vigorous activity would: increase insulin sensitivity; reduce insulin secretion; reduce inflammation, and, thereby, delay cancer progression among men with early stage prostate cancer on active surveillance. An additional, hypothesis was that the behavioral lifestyle intervention improves life quality among the participants in the intervention as compared to a control group of patients without this intervention.

The study was implemented successfully recruiting 21 men by October 2011. Preliminary results regarding outcomes as of 6 months post intervention were encouraging. Furthermore, results obtained from interviews with participants of the intervention group in NILS and their spouses gave rise to two related publications (Cancer Nurs. 2015 May 15. [Epub ahead of print]), one of which is still in press.

In one of the manuscripts (in press) the Investigators identified a range of motivation factors and barriers that may be crucial to address in order for elderly men with early stage prostate cancer on active surveillance to implement, adjust to and maintain a health promoting lifestyle change during active surveillance.

Based on the results of this work, the authors suggested that a NILS framework, in combination with active surveillance, motivates early stage prostate cancer patients to change their lifestyle and cope constructively with the physical, social and psychological implications of their disease.

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In the second manuscript (Cancer Nurs. 2015 May 15. [Epub ahead of print]) the authors identified three phases that the spouses of men with early stage prostate cancer go through. The phases are:

- insecurity about their situation
- coping with the above mentioned insecurities by focusing on scientific facts on the disease,
- pushing their worries about the diagnosis to the background, but actively supporting the husband in the lifestyle changes prescribed in the lifestyle intervention
- finding a sense of reassurance by being able to actively support the husband with practical
- concerns, such as the need for further information and attending doctor´s appointments.

Moreover, the framework of combining active surveillance and the lifestyle intervention seemed to give the spouses confidence in their own role of supporting the husband. Based on these results, the framework of combining active surveillance with the behavioral lifestyle intervention in NILS, that include the prostate cancer patient´s spouses in the intervention, mobilizes spouse empowerment, in that they can take on an active and meaningful role in relation to their husband's disease.

Given the success of the study, the study leaders have expanded the objectives and are proceeding with biochemical and biomarker analyses of the biological samples collected as part of the study.

4) Measurements of biomarkers which are potential markers of the ageing process

Within CHANCES a set of biomarkers related to the ageing process, as based from current evidence, such as, electrolytes Ca, Mg, Na, Cl and K, the oxidative stress markers Reactive Oxygen Metabolites, Biological Antioxidant Potential and Total Thiols in Proteins, 25hydroxy-Vitamin D, Gamma Glutamyl Transferase, Creatinine, High Sensitive C-Reactive Protein and the B-vitamins Folate and Vitamin B12, Alanine Aminotransferase, Uric Acid, Urea, ROM, TTL and H-index, I-Index and L-index was pre-defined and measurements were undertaken in blood samples from the ESTHER, the HAPIEE-Prague, HAPIEE-Kaunas, HAPIEE-Krakow and EPIC Elderly Greece cohorts.

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The advantage of this set of biomarkers is the insurance of homogeneity and quality across centres with respect to laboratory analyses. Certain CHANCES research projects are investigating the association of the above-indicated biomarkers, implicated in biological pathways of ageing, with certain health outcomes typical among the elderly. Results of this work have appeared in the CHANCES dissemination workshop, some have already been published (see Template A1: List of all scientific publications relating to the foreground of the project) and others are expected to be published in peer reviewed journals.

5) Establishment of an Alzheimer´s Disease (AD) registry.

Today´s research in Alzheimer´s disease (AD) indicates that, within a few years, the medical community will have access to interventions on the pathological protein metabolism behind cognitive decline. The pathophysiological process of Alzheimer's disease is thought to begin many years before the diagnosis of AD dementia. This long "preclinical" phase of AD would provide a critical opportunity for therapeutic intervention. Therefore, preclinical markers are crucial in order to detect and intervene in preclinical phase of cognitive decline. Among possible candidates for preclinical biomarkers are inflammatory markers, protein and metabolic patterns, serological analyses and analyses of specific substances.

An Alzheimer Registry consisting of 372 Alzheimer´s disease cases, as confirmed by a number of pre-specified methods, together with suitable controls, all with at least one available blood sample as identified from the corresponding biobanks, was created in Umeå. For all subjects contained in the case-control dataset, general health status and life style factors have been documented in a specific database, but through future database linkage extensive information on other factors (e.g. socio- economic) can also be added.

Serological analyses and analysis of specific substances, including inflammatory markers, protein and metabolic patterns, have been undertaken in all samples. The established AD registry comprises a very important endeavor since it will enable the examination of patterns of change in clinical markers in early life which are associated with the incidence of cognitive decline and, thus, will offer new and better opportunities for therapeutic regimens for the indicated disease which lack as of today. Analyses of data from the AD have been initiated with promising results and will advance more in 2015.

6) The development of the Health Module (HM) to assess healthy ageing

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One work package (WP11) was devoted this Deliverable, since one of the primary aims of the CHANCES project was to to develop a brief, reliable and standardized instrument for assessing the health of the elderly residing in Europe in a comparable fashion. The module consists of a set of tools to assess the most important domains of ageing, combining both subjective and objective measurements commonly used in the research on healthy ageing. It provides a comprehensive yet (relatively) brief and versatile instrument that can be easily added to existing or newly designed studies of older adults, particularly studies that have not been explicitly designed to study healthy ageing.

The module includes assessment of key domains of healthy ageing, identified through a literature review, assessment of study protocols of within CHANCES cohorts and other major ageing studies (e.g. the English Longitudinal Study of Ageing (ELSA), the Study of Health, Ageing and Retirement in Europe (SHARE), and the US Health and Retirement Study (HRS)), and analyses of several datasets from ageing studies. Special attention was paid to making the module comparable with the European Health Examination Survey (EHES) and the European Health Interview Survey (EHIS); although so far EHES/EHIS have included younger populations, it is envisaged that in the future the age range will be expanded to include older persons, and the health module would be an ideal addition to such European survey where cross-national comparability is a priority.

In order to produce a versatile and short instrument, the module has two levels: a shorter “minimum” component, and an extended component with additional assessments. The minimum health module incorporates domains of self-reported health, health problems and limitations due to health problems, disability (ADL/AIDL), weight loss and depressive symptoms; and objective assessments of cognitive and physical functions. Since the comparability of measurements across countries, languages and cultures is essential in international studies, the objective measures of physical functioning (grip strength, chair rise and walk speed) and cognitive functions (mini-mental state examination (MMSE), immediate and delayed memory and verbal speed) are crucially important to complement the subjective measures. The extended module includes question on eyesight, hearing, oral health, sleep or quality of life, and studies may choose all or some of them, depending on feasibility, practicalities and timing. The health module protocol also suggests for additional variables (such as common risk factors for chronic diseases or socioeconomic factors) which many studies collect anyway and which provide the necessary context.

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The health module has been primarily designed to be administered by an interviewer, either using a computer aided personal interviewing (CAPI) software or by using a paper copy of the questionnaire. With some changes, however, it may be possible to administer the interview over the telephone (of course, except most of the objective assessments). The health module can be used in cross-sectional and longitudinal studies which include older adults, even when the main focus of the study is not on healthy ageing. The intended target population are individuals aged 50 years or over. Most sections of the health module can also be applied to younger populations. However, because the selected measures are particularly relevant to older populations, it would be important to check for reliability and validity of these measures when used with younger populations.

This instrument was piloted in population samples from selected CHANCES cohorts (Greece, Northern Ireland, Poland) and in a comparable external study (Sweden). The analyses of the pilot study results suggested a good validity; all associations between variables were in the expected direction and strength. The mean duration of the health module was around 45 minutes (slightly shorter when the module was administered in a clinic). All parts of the module have been found to be practical and logistically feasible, both in a clinic and at participants' homes, and all parts of the module were acceptable to study participants. Based on the results of the pilot studies, the health module was finalised and submitted as a CHANCES Achievement to the European Commission.

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Potential impact

The CHANCES project produced novel and strong scientific evidence on the determinants of healthy ageing in Europe, including modifiable behaviors, nutritional factors, and/or other exposures. Projects developed within CHANCES also touch on the socioeconomic inequalities and consequent implications for society regarding the continuously increasing elderly populations. This evidence provides valuable information, necessary for the development of health strategies that can contribute to the prevention and better treatment of major diseases affecting the elderly, hence also improving their quality of life. In addition, CHANCES has provided a brief, validated and standardized instrument to assess health and ageing-related outcomes (Health Module) in a comparable fashion across European ageing populations.

Taken together, these results can be used to shape the agenda of European public health policy in order to help society to meet one of its greatest challenges: to treat elderly persons as equal, active partners yet, at the same time, recognize their special needs and offer them a good quality of life.

In addition the CHANCES project produced a platform of a well established network of ageing cohorts which can be used for further collaborative projects investigating the role of various health determinants and outcomes in the elderly.

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Main dissemination activities and exploitation of results

- Dissemination Workshop: Parallel session on CHANCES at the **IUNS 20th International Congress of Nutrition**, Granada, entitled "The role of nutrition in healthy ageing: insight from the CHANCES Project" Spain, 17 September 2013 (Presentations made by DKFZ, Erasmus MC, RIVM, UoA)
- Round Table on CHANCES at the **4th Pan-Hellenic Congress of Public Health and Social Medicine Forum**, entitled "CHANCES: Investigation of risk factors affecting morbidity and mortality in the elderly - An international study in Europe and the United States", Athens, Greece, 23 November 23 (Presentations made by HHF and UoA)
- **Dissemination and Networking Workshop** (Networking and forging working relationships with other existing or planned ageing cohorts and the CHANCES Consortium), Paris, France, 12th February 2014
- Satellite Symposium on CHANCES, entitled "Risk factors for healthy aging: Insight from the CHANCES Project", at the **III World Congress of Public Health Nutrition**, Las Palmas, Gran Canaria, 10th November 2014 (Presentations made by HHF, DKFZ, UCL, QUB, RIVM)
- **Dissemination Workshop**: "Healthy Ageing: definition, risk factors and implications for Public Health: the CHANCES Project experience" (Communication of Project Outcomes and Results), Athens, Greece, 23rd January 2015
- Poster session included in the CHANCES Dissemination Workshop, on which results from finalized, as well as from ongoing projects, were presented
- Press kit containing summaries of oral and poster presentations distributed to attendees, TV and radio producers, as well as to newspapers (including web-based)
- Press Releases on the CHANCES Dissemination Workshop, as well as on the results presented during the Workshop
- Press Release entitled "Vitamin D levels may have a role in cancer prognosis, study shows" (DKFZ) on the BMJ page of EurekAlert, 18th June 2014
- Presentation of the CHANCES Project in The Parliament Magazine (feature on 'Active and Healthy Ageing'), 9th June 2014

More information on the CHANCES dissemination activities:

http://www.chancesfp7.eu/presentations.html

http://www.chancesfp7.eu/media.html

http://www.chancesfp7.eu/congress.html

A detailed list of all dissemination activities is shown in Template A2: list of all dissemination activities.

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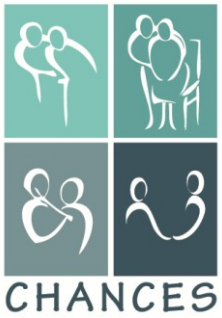
The CHANCES Project's LOGO



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