



SELF-EVALUATION

Center for Healthy Aging

CEHA facts in brief	
External grants	>DKK 420m (EUR 56m) in addition to the Nordea-fonden grant
Publications	791 (CEHA I); 504 (CEHA II)
Scientific presentations:	142 engagements by group leaders nationally and internationally between September 2015 and September 2016
PhD projects	81 (CEHA I) and 50 (CEHA II)
Post-doctoral projects	54 (CEHA I) and 33 (CEHA II)
Visiting professors	Five (2010); nine (2011); nine (2012); eight (2013); seven (2014); six (2015), and six (2016)
Recruitment	Seven nationally and internationally recognized senior researchers and six new group leaders
International summer schools	<ul style="list-style-type: none"> • IARU Summer School <i>Interdisciplinary Aspects of Healthy Aging</i> (2011-2016) • EIT Health <i>Alive and KICKing</i> – innovative solutions to aging related challenges, including Massive Online Open Course (MOOC)
International networks	IARU, EIT Health and ABRAHAM (selected)
Communication and outreach	People's Political Festival in 2016, Science Slams, Life on the Line game, and other events and activities
Awards	Center of Excellence Grant (Danish Research Council/ Grundforskningsfonden); four University of Copenhagen Excellence projects; two Global Excellence Awards; and an ERC Advanced Grant

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4	EXECUTIVE SUMMARY
6	CEHA: TACKLING CHALLENGES IN AGING RESEARCH
8	CEHA'S UNIQUE APPROACH
10	ORGANIZATION, MANAGEMENT, AND RECRUITMENT
14	RESEARCH COLLABORATIONS AND NETWORKING
18	RESEARCH THEMES AND PROGRAMS
	CEHA I: A brief retrospective
22	CEHA II
	Overview
	Theme I: Community innovation for healthy aging
	Theme II: Lifecourse aging processes
	Theme III: Community innovation for healthy aging
30	RESEARCH OUTPUT, MULTIDISCIPLINARITY, AND DISSEMINATION
32	RESEARCH TRAINING
34	SOCIETAL IMPACT: ENGAGEMENT, OUTREACH, AND COMMUNICATION
38	FINANCIAL OVERVIEW (2009-2016)
40	SWOT ANALYSIS
42	APPENDICES
	A1: CEHA II management structure
43	A2: CEHA I (2009-2013): Overview and achievements of the research programs
45	A3: CEHA II (2014-2016): Overview of the key research achievements
46	A4: Selected publications: 2009-Sept 2016
51	A5: Financial breakdown (2014-2015)





EXECUTIVE SUMMARY

On 1 January 2009, the Faculty of Health and Medical Sciences, University of Copenhagen, established the Center for Healthy Aging (CEHA) to undertake cutting-edge interdisciplinary research on aging. By 2018, the Danish foundation Nordea-fonden will have invested a total of DKK 300m (EUR 40m) to enable the Center to address one of the most pressing societal challenges. As part of its governance, international peers evaluated the Center's performance in 2012 and applauded CEHA for the quality of its research and for its potential to change and improve the "everyday life of many people." They strongly recommended continuing support of CEHA because the scope of the research program was unique in Denmark and ambitious. It was, and remains, one of the few programs worldwide to study human aging in such breadth and depth.

As part of the site visit review 2017, we present the results of our internal evaluation of the Center's performance from January 2009 to September 2016 that follows a structure that has been set out by Nordea-fonden. It provides a clear and concise picture of what has been achieved to date and includes an analysis of our strengths, weaknesses, opportunities, and threats. It is complemented by an updated strategy of CEHA for the foreseeable future.

Understanding aging

The ongoing increase in life expectancy has radically changed the lifecourse of individuals and the demographic structure of our populations. This development raises key questions including how to live longer in better health and how to be active in society despite the aging process taking its toll. Research on aging must therefore consider and account for diverse biological, social, and economic factors, as well as accounting for lifestyle choices, all of which influence the length (lifespan), the functionality (healthspan), and the satisfaction (well-being) of an individual's life. A growing body of knowledge indicates that the interaction of endogenous stressors (cellular/biological) and exogenous stressors (social/interpersonal) markedly influence our lifespan, healthspan, and well-being. Furthermore, while early life experiences can have delayed negative consequences in later life, the converse is also true, in that conditions in adult life can (at least partially) compensate for damaging early life experiences. The goals of understanding aging at a cellular,

individual, and societal level, together with translating this knowledge into effective interventions that enable healthy aging, are therefore of paramount importance. CEHA aims to be at the forefront of this effort by performing state-of-the-art research, applying innovative approaches, and building sophisticated multidisciplinary networks.

Research within CEHA is of a very high international standing, reflected in the way the Center is organized around a common conceptual framework, the complementary disciplinary research, and an impressive scientific output (almost 1300 articles in peer-reviewed journals). The first phase of the Center (2009-2013) built up the core relational network and systems, and six research programs emerged from smaller pre-existing research groups that were transferred to our Center. During the second phase (2014-2018) the six programs were merged into three themes, and a communication platform was established. The incremental integration of different expertises – biological, psycho-social, cultural, public health policy, and clinical – at CEHA enhances a productive exchange of knowledge and promotes synergy between the participating groups. This cohesive and holistic approach not only leads to a more profound understanding of the mechanisms that underlie human aging, but also stimulates designing experiments that upon positive evaluation will ensure practical and effective interventions to extend our healthy lifespan.

At the forefront of aging research

A key strength of CEHA is its vibrant infrastructure, particularly being embedded in the University of Copenhagen, which is among the top-ranked universities in continental Europe. This is complemented by strong ties with three university hospitals (Rigshospitalet/Glostrup, Hvidovre hospital, and Bispebjerg hospital) in the Copenhagen area, all of which make substantial investments in CEHA. Our leadership ensures a common vision and focus on priorities and has made the Center a significant player in the international research community. CEHA occupies key positions in collaborative ventures, such as the aging initiative of the International Alliance of Research Universities, Aging, Longevity and Health. Furthermore, CEHA has close partnerships with the National Institutes of Health and National Institute on Aging which are among the world's leading research



Professor Lene Juel Rasmussen,
Managing Director

centers. There is a widespread misconception that human aging only leads to decrepitude and is not amenable to intervention, which has led to ageism and an innovation arrest. CEHA takes a positive attitude to growing older and strives to translate aging research into action. In this vein CEHA has been instrumental in setting up the EIT Health consortium, which aims to promote entrepreneurship and innovations in healthy living and active aging, to improve the healthcare and quality of life of citizens across Europe.

An important defining feature of CEHA is our citizen-centric approach. Much of CEHA's research is done in dialog with key stakeholders, particularly citizens themselves, and also professionals who are working to create a good framework for citizens' healthy aging. CEHA has, therefore, embarked on a series of interaction projects in local communities promoting health at old age. Interaction with the municipalities is an essential element in the innovation cycle because the local politicians and civil servants have the responsibility for many of the areas that affect healthy aging. An illustrative example of active engagement with citizens and relevant stakeholders are the successful activities created by CEHA at the annual Danish People's Political Festival.

Impact beyond research

Education of graduate students to fully fledged professionals, and from citizens to entrepreneurs, is a priority of CEHA. The Center was instrumental in building the educational campus within the European EIT Health initiative of healthy living and active aging, and it actively participates in the Copenhagen Health and Innovation Platform, a joint venture of three universities, the municipality, and the Health Region. CEHA has built up a rich portfolio of educational offerings amongst which there are (post) graduate programs, PhD schools, international summer schools, and Massive Open Online Courses offered on the Coursera platform.

The Center is already making its mark on the global landscape of research and innovation into human aging, as evidenced by the progress described in this report. CEHA has received a Center of Excellence Grant (Danish Research Council/ Grundforskningsfonden), four University of Copenhagen Excellence projects, two Global Excellence Awards, and an



Dean Ulla Wewer,
Faculty of Health and Medical Sciences, Nordea-fonden Grant Holder

ERC Advanced Grant. Apart from the strategic investments of Nordea-fonden, we have been successful in obtaining external funds to the tune of DKK 421m (EUR 56.6m). We have also been able to attract several internationally recognized experts in aging such as Ian Hickson (Oxford University) and Rudi Westendorp (Leiden University) as well as a number of talented young group leaders. Furthermore, Ken Arnold of the Wellcome Trust (London), who was appointed as Creative Director of the Medical Museion (University of Copenhagen), is now heading the Communication and Outreach Platform.

We have achieved much so far; the experience we have harvested since establishing CEHA in 2009 has been invaluable, and, importantly, practicable. We look forward to building on these strong foundations in the years to come, working toward the goal of healthy aging for our society and making a real difference to older citizens.



Lene Juel Rasmussen

Ulla Wewer

CEHA: TACKLING CHALLENGES IN AGING RESEARCH

Major demographic changes across the globe are causing a rapid increase of elderly people in virtually all societies: by 2050, 20 percent of the global population will be older than 60 years of age and the number of people over the age of 80 will have tripled¹. The developed countries of the world have seen an unprecedented doubling of average lifespan over the 20th century, and it is estimated that average life expectancy of newborns will gradually increase to about 100 years during the 21st century. These trends impose economic, cultural, medical, social, and public-health challenges that will affect individuals, communities, and economies, and whose full implications are only just beginning to be fully understood and appreciated.

Aging is a leading risk factor for nearly all major chronic diseases, which increase morbidity and significantly drive healthcare costs². In Denmark, the latest population projection predicts that the proportion of those over the age of 65 will increase from 16 percent today to 25 percent in 2042, after which it will decline slightly (source: Statistics Denmark; Fig. 1). Consequently, aging is one of the most broadly recognized societal challenges that we will face in the coming decades, and the goal of 'healthy aging' is thus an urgent priority.

Active and healthy aging has been proposed as a keystone for a sustainable Europe. Danish policies and priorities reflect this approach to aging. Danish welfare policies outline a range of intersectoral strategies focusing on individual and structural factors affecting the ability to maintain health and live actively and independently into old age. This includes, for example, the law on preventive home visits that is now targeted on groups of elderly at risk of functional decline; reablement to help people regain the ability to look after themselves; increased focus on elderly patients in coordinated care policies across primary care, hospitals, and municipal services; housing developments; and the so-called 'dignity policy' with associated funding seeking to ensure improved innovative and holistic care for elderly at the local community level.

From an individual perspective a longer life can be seen as progress. Especially, if there is an increase in the high-quality years of life. Therefore, the growing number of elderly people will not necessarily become the burden that many fear. Rather, a growing number of functional elderly will become a new resource, both regarding general labor as well as civil society.

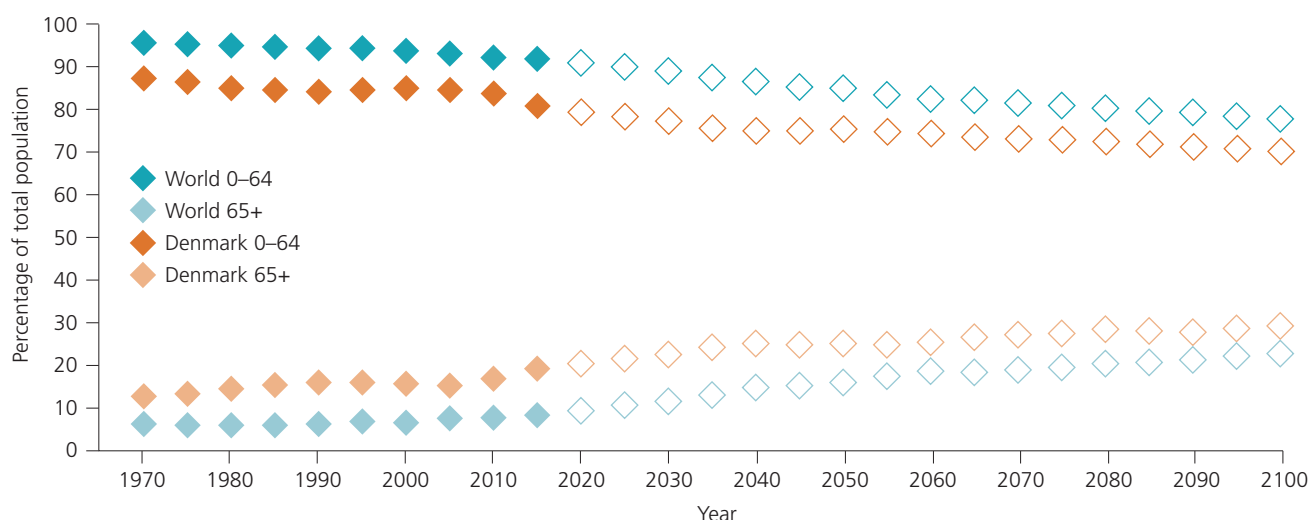


Figure 1. Historical and forecasted demographic changes in Denmark and globally.

Challenges in aging research

There are several overarching issues that urgently need addressing in order to achieve healthy aging:

1. Despite the critical relevance of human aging to European society, we have limited understanding of the basic biological mechanisms that contribute to and influence it, and how these mechanisms relate to disease development.
2. We do not fully understand how the environment contributes to human aging and, more importantly, how the biological and environmental factors interact. This knowledge is essential to defining strategies that extend 'healthspan' – the period of years lived without disabilities, during which people can live active lives.
3. The effect of genetic and lifestyle factors on health parameters must be analyzed extensively in population studies. This knowledge will be fundamental to addressing the unsustainable burden of the aging population on healthcare systems, where a dramatic shift in approach is needed.
4. Drugs and other interventions that target basic aging processes have been discovered that, in the laboratory setting, not only enhance healthy lifespans but also delay age-related chronic diseases and disabilities. Furthermore, a number of biomarkers for early detection of age-related pathologies have been identified. Translation of these and other emerging interventions into clinical applications will transform healthcare and, consequently, society as we know it.
5. The community – our neighborhood – plays a major role in our health; therefore, it is crucial to understand how the heterogeneity of local communities influences the promotion of health and energy of aging citizens. Thus the active collaboration and dialog with partner municipalities will constitute interventions based on research activities and generate insights into the organization and implementation of care for the elderly.

Clearly, aging is a complex process that can be understood fully only by using multiple perspectives – biological, social, psychological, and cultural. It is thus crucial to employ a multidisciplinary, holistic, cell-to-society research approach when developing interventions and policies aimed at promoting the healthy aging of individuals and societies. With this in mind, the Center for Healthy Aging (CEHA) was set up in 2009.

CEHA's vision and mission

Since its inception, CEHA has consistently improved our understanding of aging at the cellular, individual and societal level, brought together researchers with diverse disciplinary backgrounds, trained many doctoral and post-doctoral students, and promoted healthy aging by engaging with a wide range of stakeholders. Extensive epidemiological, imaging, and physical-exercise studies have made it possible for researchers at CEHA to identify health-promoting interventions. Furthermore, through communication studies we have shown how people can be

CEHA'S VISION AND MISSION

The Center's vision is to take a leading role in discovering biological, social, psychological, and cultural mechanisms in aging and learning how these can be translated into preventive action.

Our mission is to produce research to a high international standard on major aspects of aging, to contribute substantially to training young researchers interested in aging and related fields, and to investigate how research findings can be used in health promotion efforts aimed at preventing unnecessary age-related decline and disease and at improving the conditions of the middle-aged and the elderly.

engaged in and made aware of healthy lifestyles.

CEHA is embedded within the University of Copenhagen, an arrangement that brings numerous mutual benefits. The university provides substantial financial support including salaries of senior faculty and staff, co-financing of PhD scholarships, and state-of-the-art research facilities and environment for the Center's interdisciplinary research at the Faculty of Health and Medical Sciences.

CEHA's strategic goals are:

- to undertake cutting-edge, multidisciplinary research to better understand the aging process;
- to devise a new understanding of aging that encompasses both the individual and societal levels;
- to challenge the negative discourse of aging, frailty, and dependency by focusing instead on energy, resilience, intrinsic capacities, and (psychosocial) functional abilities;
- to communicate policy-relevant research and concrete recommendations to the relevant stakeholders in government and other sectors in Denmark and beyond;
- to contribute to the public discourse on aging by undertaking innovative outreach activities.

Furthermore, the location of the Center within the University of Copenhagen enables exploitation of the synergies between units of the faculties of Health and Medical Sciences, Humanities, and Social Sciences. Examples include the Novo Nordisk Foundation Center for Protein Research (<http://www.cpr.ku.dk/>) and the Novo Nordisk Foundation Center for Basic Metabolic Research (<http://metabol.ku.dk/>); the Copenhagen Center for Health Research in the Humanities (CoRe); and the Center for Health Economics and Policy (CHEP). Furthermore, CEHA contributes to the University with educational and training activities within the fields of aging research (e.g. innovative Masters level summer schools, PhD courses and postdoctoral projects; see "Research training"). There are thus continuous multiple synergies between the Center and larger research and strategic initiatives at the University of Copenhagen.

1. Population Division, DESA, United Nations: <http://www.un.org/esa/population/publications/worldaging19502050/pdf/81chapteriii.pdf>
2. Global status report on non-communicable diseases 2010, WHO (http://www.who.int/nmh/publications/ncd_report_full_en.pdf)
3. Horizon 2020 Societal Challenge 1: Health, Demographic Change and Wellbeing and Strategic Foresight which acknowledges the demographic trend of aging is reiterated as putting increased pressure on health systems

CEHA'S UNIQUE APPROACH

The following characteristics (see Fig. 2) highlight the uniqueness of this Center:

Multiple disciplines

We are committed to an interdisciplinary research approach to understand aging: our researchers are drawn from multiple disciplines, encompassing biology; health, medical, and social sciences; and humanities from universities around the world. The vibrant infrastructure of CEHA embedded in the University of Copenhagen, together with a strong leadership team and many established international collaborations, ensures that the multidisciplinary approach is effective and synergistic.

Holistic approach

We seek to understand all dimensions of aging – biological, social, psychological, and cultural – and at all scales, ranging from the cell through individuals to society. This approach to understanding aging is quite unique and only a few institutions around the world take this type of approach.

Scientific excellence

We promote rigorous and innovative research on aging by bringing together top international scientists to address important questions from multiple perspectives. A common conceptual framework for all researchers at the Center, regardless of discipline, ensures that we stay focused on our main priorities and remain successful in translating our findings into innovative health-promotion interventions to aid healthy aging.

Capacity building

We train the next generation of aging researchers via our high-quality educational programs, with an emphasis on the holistic approach and ensuring excellent communication skills when interacting with the media, citizens, and stakeholders.

Engagement

We engage with a wide range of stakeholders including the Danish public, policymakers, municipalities, and businesses to communicate our research so as to inform concrete interventions and policies to promote healthy aging.

Constant evolution and challenging stereotypes

We are a dynamic center that tunes our research and adapts our engagement to respond to changing scientific and social issues. We are committed to contributing to the education of citizens by challenging ageism in our society and the habitual thinking about lifecourse that postulates that becoming dependent and disabled is inevitable with aging.

CEHA is emphasizing multidisciplinary collaborations among CEHA scientists and between CEHA scientists and their national and international colleagues, because we understand that collaboration stimulates creativity and growth, leading to synergy between the participating groups. We hope that this

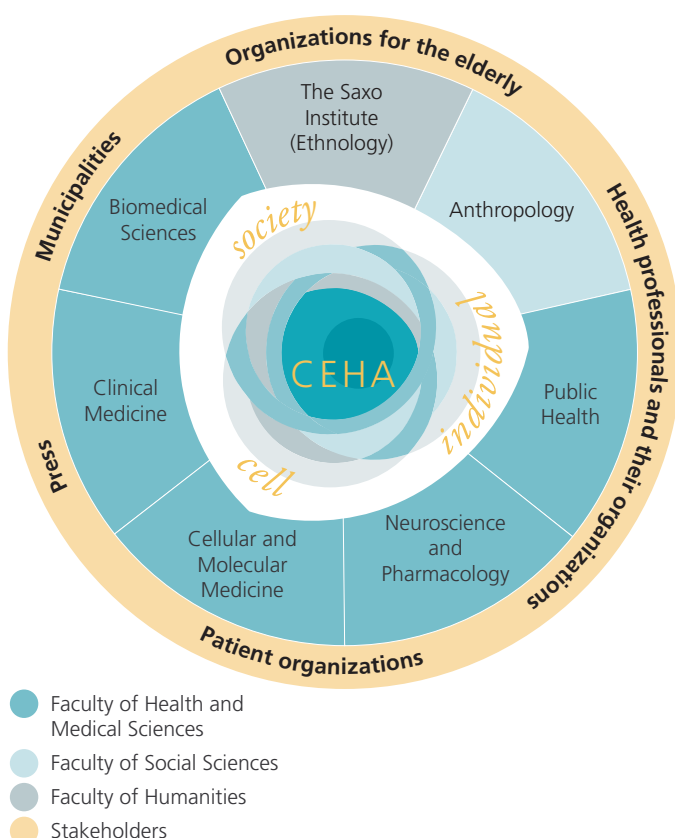


Figure 2. CEHA's approach is interdisciplinary and holistic, and focuses on engaging with multiple stakeholders through impactful communications and outreach.

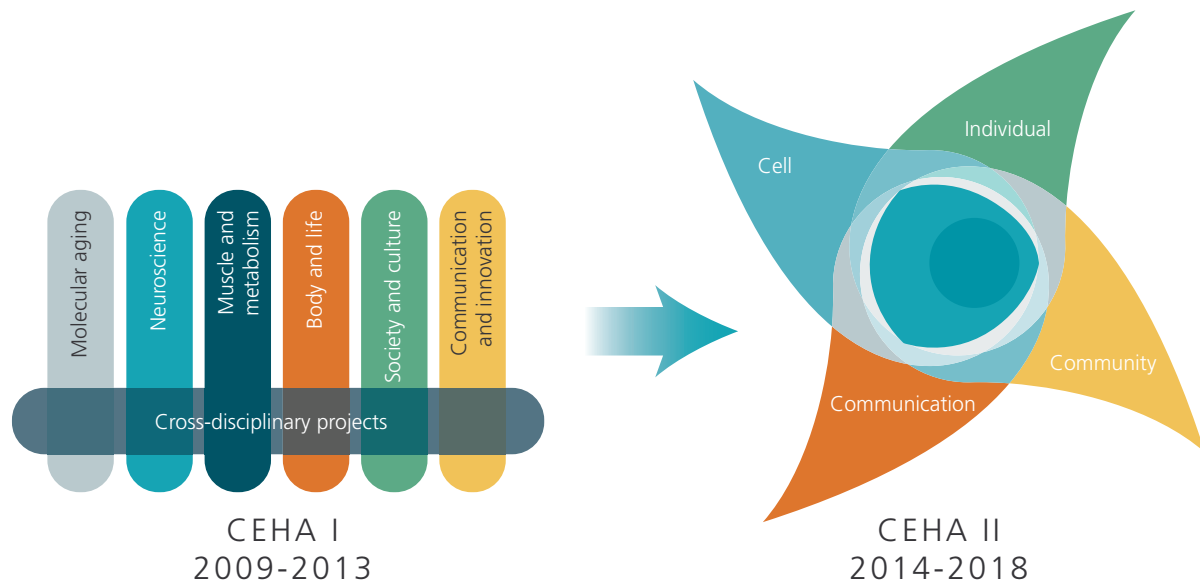


Figure 3. Development of CEHA 2009-2018.

approach will hasten progress and allow each researcher to accomplish more than he or she could accomplish working independently.

CEHA coming of age

Since its emergence in 2009 by a generous donation from Nordea-fonden, CEHA has championed interdisciplinary research on aging that has often had a medical and scientific interest in disease and frailty but in recent years CEHA research has also focused on prevention and health promotion. Simultaneously, CEHA has consistently addressed the societal and cultural dimensions of aging, which has developed into interaction projects in Danish municipalities to improve health and well-being.

Since its launch, CEHA has gone from consisting of high-level monodisciplinary researchers primarily from the University of Copenhagen to consisting of high-level multidisciplinary aging researchers from the University of Copenhagen as well as international colleges. The Center, which began with 110 employees in 2009, now boasts 231 employees in 2016. This has resulted in a steadily growing number of individual research collaborations (see publications) and participation in prestigious international collaborations and networks such as IARU, ABRAHAM and EIT Health.

CEHA I (2009-2013)

CEHA I was set up to promote leading-edge research on human health and aging, with an emphasis on understanding how human behavior and lifestyle choices modulate life trajectories and health outcomes from a cell-individual-society perspective. During this initial period, the Center established a solid research platform that has provided new knowledge and insights into the mechanisms of aging at the societal and individual levels. For example, our research showed that endogenous (cellular/biological) stress and exogenous (social, interpersonal) stress influence both lifespan and healthspan.

Furthermore, while early life experiences can have delayed negative consequences in later life, the converse is also true. Conditions in adult life can (at least partially) compensate for damaging early life experiences, and genetic and social factors

in early life can protect against strains and stress in late life. Knowledge about such early signs of aging in midlife is important to identify vulnerable individuals and prevent frailty, disability, and comorbidity becoming manifest. This was carried out by a set of jointly programmed projects that emerged from various disciplines within the field of aging (Fig. 3).

CEHA II (2014-2018)

CEHA II (Fig. 3) was launched to contribute to basic knowledge of aging and to lay critical and valuable ground for promoting healthy aging in the Danish population through intervention and social innovation projects. Research during CEHA II is building on knowledge gained from CEHA I and the large number of interdisciplinary collaborations that have been facilitated by the establishment of the Center.

A unifying theme in CEHA II has proved to be the strong significance of 'energy' in aging. One of the key findings is that people's ability to maintain active lifestyles (active aging) promotes a specific version of good old age based on a strong body and an active physical and social existence to improve the quality of life of older people. CEHA II is delivering a series of multidisciplinary devised, and collaboratively executed, interventions on how people can age more healthily (see later sections).

Developing an engagement strategy

Outreach and stakeholder engagement has grown in importance as CEHA has evolved. In 2014, CEHA strengthened this area to expand the focus beyond citizens. It developed a stakeholder strategy for the 2014-2018 period that targeted decision-makers, organizations for the elderly, healthcare professionals, and selected patient organizations. The Center now regularly undertakes joint events with organizations, arranges stakeholder meetings for selected stakeholders, and contributes with columns in municipal healthcare newsletters and Danish newspapers.

In the next phase (beyond 2018), CEHA will further transform itself toward an integrated group of researchers and innovators that will use their unique skills to implement intervention collaborations based on a shared conceptual framework.

ORGANIZATION, MANAGEMENT, AND RECRUITMENT

Organization

CEHA is organized as a network of research units located in seven different departments within three University of Copenhagen Faculties (Humanities, Social Sciences as well as Health and Medical Sciences) and in three hospitals in the Greater Copenhagen Area (Hvidovre, Glostrup, Bispebjerg) (Fig. 4). Since 2014, the research units have been organized in three multidisciplinary research themes (I-III).

Although CEHA laboratories are currently distributed at multiple sites on the University of Copenhagen campus, in January-February 2017 the laboratories will be 'centralized' on the 2nd and 3rd floors of a newly constructed research building, called the Mærsk building. This 14-storey building with state-of-the-art facilities designed for interdisciplinary research will enhance CEHA's ability to conduct cutting-edge research and will provide renewed opportunities for interaction and collaborations among CEHA researchers. Here CEHA will complement the bench-to-bedside translational model with a human-to-mechanism back-translational type of research. The Mærsk building will also bring greater coherence within the neighborhood that will increase citizen involvement. In the new facility, CEHA faculty and staff will also have the opportunity to interact with non-CEHA faculty and staff working in aging-related fields, such as biology, applied physiology, neuroscience, behavior, anthropology, economics, and ethnography.

Management and advisory boards

The administrative duties of the Center are carried out by the Managing Director, a Steering Group, an International Scientific Advisory Board, and Administrative Staff. The Managing Director Lene Juel Rasmussen and Co-Director Rudi Westendorp (appointed October 2016) report to the Dean of the Faculty of Health and Medical Sciences, Dr Ulla Wewer, who is ultimately responsible for all CEHA activities. CEHA management staff are located within the Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences.

Operational tasks at CEHA, including strategic planning and development, and coordination between themes, are agreed upon by the directors and executed by the Managing Director. The administrative staff manage logistics and help coordinate

research activities and programs, working closely together with the Communication and Outreach Platform. The Secretariat is centrally located in the Faculty of Health and Medical Sciences and consists of the Head of Administration, the Academic Officer, and a secretary. Moreover, the Secretariat houses some of the employees from the Communication and Outreach Platform team (see below).

The main oversight committee for CEHA is the Steering Group. The group members include leaders of each of the three CEHA themes (Fig. 4), as well as the leader of the Communication and Outreach Platform (see Appendix A.1 for the list of members). The Steering Group provides oversight for research activities, financial issues, recruitment, strategic planning, and outreach. The Chair of the Steering Group is the Managing Director and the Co-Chair is the Co-Director.

CEHA is supported by an International Scientific Advisory Board (SAB), which reports to the Dean. It includes eight distinguished scientists, representing broad scientific expertise relevant to CEHA research.

The role of the SAB is to provide advice about strategic planning, recruitment, feasibility, progress, and development of the research themes. The Board proposes criteria for evaluating scientific progress and success, assists in establishing suitable external national and international collaborations, and advises on scientific goals. Finally, the SAB helps CEHA leadership ensure that its research programs meet the highest international standards and achieve optimal scientific impact.

Internally, CEHA is supported by an Internal Advisory Committee, which includes the Dean, the Co-Director, the Managing Director, and two internationally renowned researchers, Professor Vilhelm Bohr (National Institutes of Health, USA) and Professor Carlos Mendes de Leon (University of Michigan School of Public Health, USA). The heads of departments and Deans of the Faculties of Humanities and Social Sciences are also involved through coordinated meetings.

The Managing Director, Co-Director, and Head of Administration meet the Dean twice every month. The Steering Group meets approximately eight times a year, while CEHA management and staff meet with the SAB once a year in connection with CEHA's annual retreat. Support from the Internal Advisory Committee is requested on an ad hoc basis.

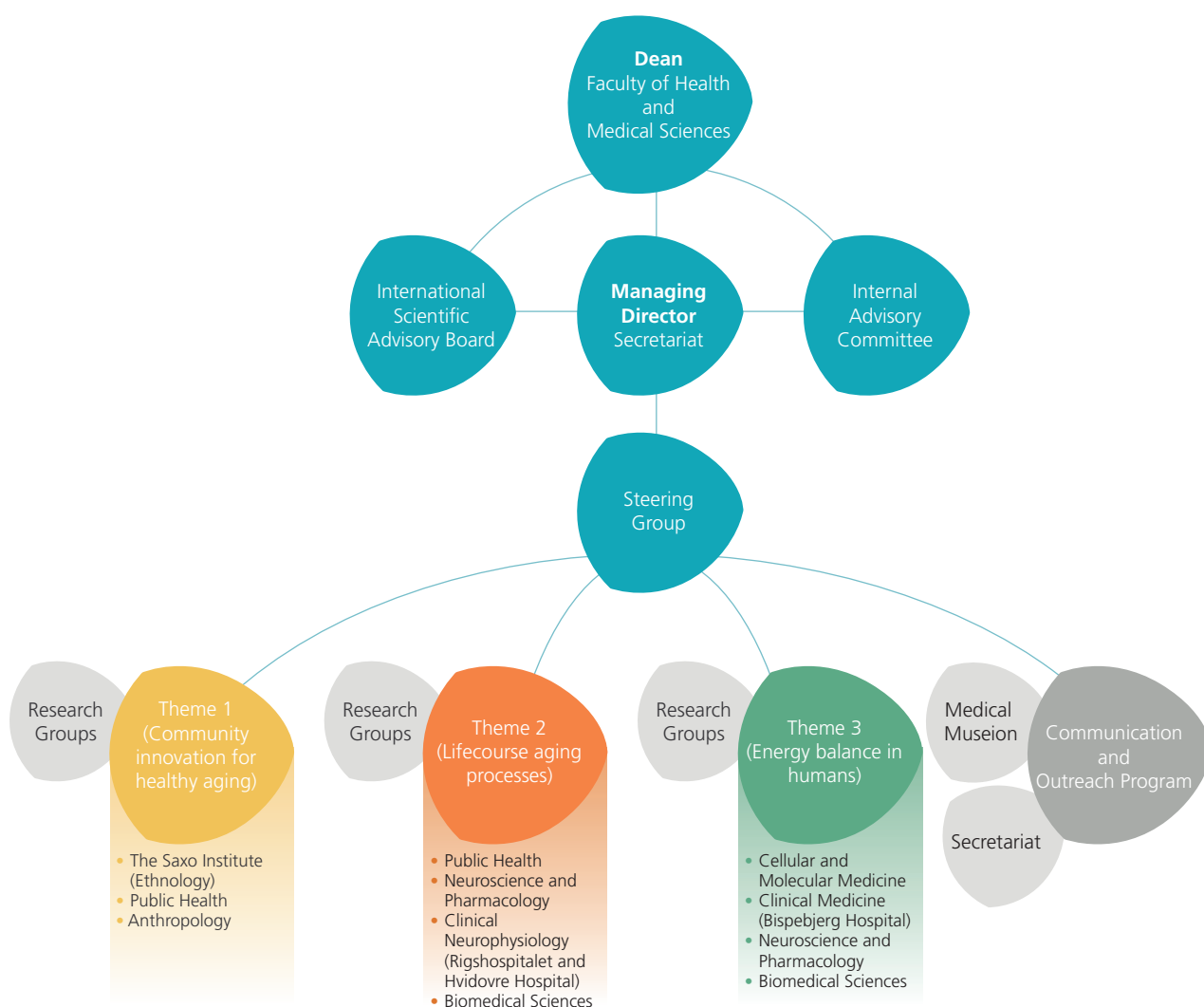


Figure 4. CEHA's organization. Departments associated with a theme are listed below the respective theme.

Staff

As of 1 September 2016, CEHA had 81 full and part-time employees (funded by the Nordea-fonden grant) plus 150 employees paid by external funding (non-Nordea-fonden funding), including staff paid by the University of Copenhagen. Of these staff, there are 56 senior researchers; 38 postdocs; 6 guest researchers; 64 PhD students; 11 research assistants; 22 bachelor/master/pregraduate research students; and 9 lab technicians. In CEHA II, 48 PhD projects have been completed so far. Among the research and research support staff (PhD students apart), 23 are from Theme I, 70 are from Theme II, and 34 are from Theme III. Figure 5 shows how the staff composition has changed through time.

The Communication and Outreach Platform includes four employees: an Event Coordinator (who works at the Medical Museion), a Social Media Curator (who works both in the CEHA Secretariat and at the Medical Museion), and a Communication Consultant and an Event Coordinator within the CEHA Secretariat who focus on press, mass communication, stakeholder relations, and events (see "Societal impact: engagement, outreach, and communication" for details).

During 2009-2016, CEHA established a strong Visiting Professor Program, which has led to CEHA hosting many guest professors for stays of a few weeks to several years. For each year the number of guest professors at the CEHA were: five (2010), nine (2011), nine (2012), eight (2013), seven (2014), six (2015), and six (2016).

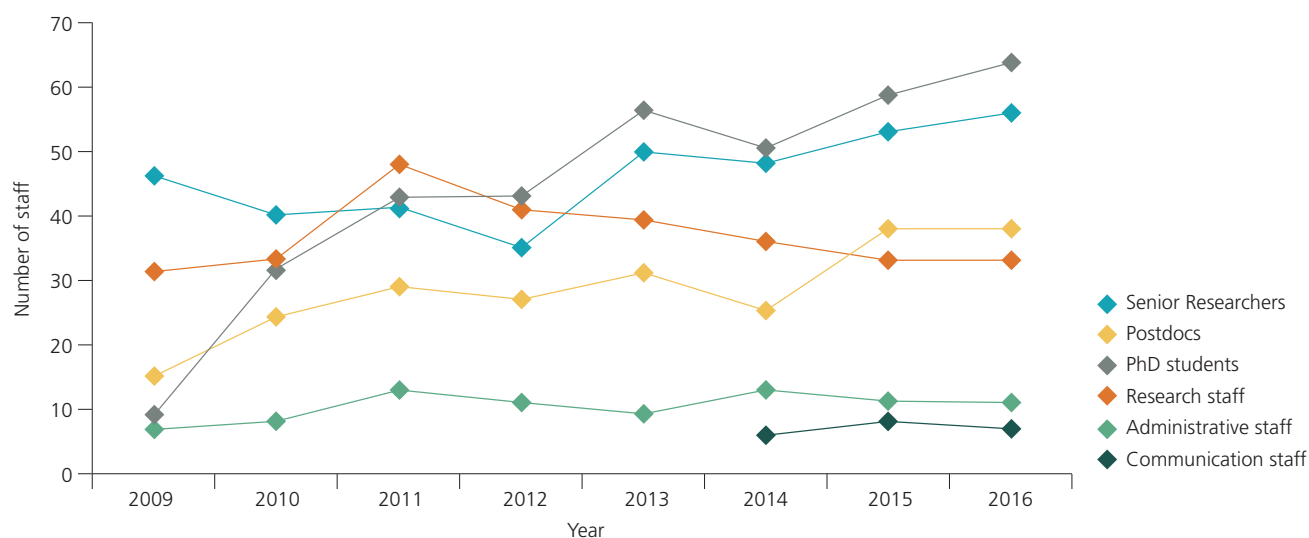


Figure 5. Staff composition over time.

Recruitment and researcher support

CEHA II's recruitment strategy 2014-2018 is to 1) recruit at least one or two internationally recognized researchers, and 2) create career opportunities for top young scientists by appointing a number of junior group leaders. The Visiting Professor Program is one of the tools we have used to achieve these goals. CEHA has already exceeded this ambition, having recruited seven nationally and internationally recognized senior researchers and six new group leaders (named and described below).

Top recruits

In 2010, Ian Hickson (Oxford University, UK), a leading expert in genome maintenance systems, was recruited as Professor in Genome Stability and Aging in CEHA's Molecular Aging Unit (Theme III). The same year, he received the Fellow of The Royal Society award. In 2013, Professor Hickson received an ERC Advanced Grant, and in 2015 he obtained a Center of Excellence Grant to establish the Center for Chromosome Stability.

Karsten Vrangbæk started as Theme I leader in 2015. He is Professor at the Political Science and Public Health Department and Director of Center for Health Economics and Policy, University of Copenhagen. Vrangbæk is involved in international research and educational activities focusing on health policy, health systems analysis, economic consequences of aging populations, and public-private collaboration in health- and elderly care.

In 2015, Rudi Westendorp, Leiden University Centre, Netherlands, joined CEHA's Theme II as Professor of Medicine at Old Age. At CEHA, he is investigating innovative solutions for promoting the length and the quality of life of older people. Professor Westendorp has since 2016 been responsible for CEHA's two summer schools, and he also played a key role in the joint proposal for a Knowledge and Innovation Community (KIC; an EU Horizon 2020 initiative; see "Research collaborations and networking").

In 2016, Tom Kirkwood was employed as Professor of Biogerontology (Theme III) in a strategic role in interdisciplinarity and development of the research and training environment. Over the last 12 years, he led the growth of the Newcastle University Institute for Aging, UK, to become one of the leading centers for aging research worldwide. He has made notable contributions

in the fields of evolutionary genetics of aging and longevity, molecular mechanisms of cellular aging, and in the relationship between intrinsic aging and age-related diseases and frailty.

Ken Arnold was appointed Creative Director of Medical Museion and Professor at Copenhagen University in June 2016. He also holds a position as Creative Director at the Wellcome Trust, London, where he focuses on developing international opportunities for cultural collaboration and exchange. He holds a PhD in the History of Science from Princeton University and a BA in Natural Sciences from Cambridge University. He regularly speaks and writes on museums and the relations between the arts and sciences.

As a result of the Visiting Professor Program, Professor Linda Bergersen and Dr Tiago Moreira were recruited on a part-time basis to CEHA. After her visiting professorship Bergersen (Professor of Physiology at the University of Oslo, Norway) started as part-time Professor of Neurobiology of Aging at CEHA in 2013. Her main research area is brain energy production and neurotransmission. Bergersen bridged the Program Ia and Ib in CEHA I and she has ongoing collaborative projects within Theme II-III in CEHA II. Dr Tiago Moreira (Durham University, UK) has also joined CEHA in 2016 as an Adjunct Professor following several years as a guest professor in Theme I. His research explores the interaction between knowledge and healthcare, especially the role and use of health technology.

Young group leaders

Associate Professors Maria Kristiansen (Department of Public Health) and Bjarke Oxlund (Department of Anthropology) have been recruited as group leaders in Theme I. They are engaged in community-based interventions. Kristiansen is involved in health-services research, social and ethnic inequality in health, and access to healthcare among older people. Oxlund is specialized in medical anthropology, aging, gender, population issues, and quantitative surveys.

At a junior level (assistant professors), CEHA has recruited: Javier Peña-Díaz from the Federal Institute of Technology in Zurich, Switzerland (Theme III; focus on DNA repair in aging-related disease); Andrés López-Contreras from the Spanish National Cancer Center, Spain (Theme III; focus on impact of genomic instability on aging); Morten Scheibye-Knudsen from



NYS in the public event "Drawing Science" at the Medical Museion, 2014.

the National Institutes of Health, USA (Theme III; focus on aging interventions, DNA damage, mitochondria, metabolism, neurodegeneration); and Simon Bekker-Jensen (Associate Professor) from the Center for Protein Research, Denmark (Theme III; focus on cell biology, cell stress, aging). Bekker-Jensen will be inaugurated as professor in January 2017.

Network of Young Scholars (NYS)

The NYS was established in 2010 by CEHA undergraduate and postdoctoral fellows to promote interdisciplinary research training and educational activities, and improve social interactions among young CEHA researchers. Activities are coordinated by the NYS Steering Group, which is made up of CEHA PhD and postdoctoral students. In CEHA II, NYS began actively working to enhance the PhD experience and provide support for multidisciplinary research activities. Since 2015, focus has been on developing a catalog of courses on aging and/or interdisciplinarity that are available to primarily PhD students

within CEHA. In 2015, NYS launched its first PhD course: *Interdisciplinary Research: Aging as a field of study*. NYS is a very valuable asset to CEHA.

Support from the Communication and Outreach Platform

CEHA is giving high priority to communicating its research and knowledge – not only within the scientific community, but also to a wide range of stakeholders and the general public. The Communication and Outreach Platform was established to support and train the researchers to communicate via mass media, social media, and events to disseminate results and knowledge efficiently. In addition to scientific journals as a means of publishing findings, CEHA uses a broad cross-media form of communication and reaches its target audience via many channels of communication. The Platform is also prepared to blaze new trails (see "Societal impact: engagement, outreach, and communication" for details).

RESEARCH COLLABORATIONS AND NETWORKING

CEHA collaborates actively with several institutions and networks, both within Denmark and around the world (see Fig. 6). Apart from scientific and outreach advantages, these collaborations enforce the mobility of researchers and students and play a key role in CEHA's recruitment strategies at all levels. Below we describe some of these collaborations.

Selected international collaborations

CEHA and the University of Copenhagen participate in and interact regularly with the 10 other leading research universities in the International Alliance of Research Universities (IARU, <http://www.iaruni.org/>). IARU's Aging, Longevity and Health (ALH) project is an important network within the international aging research community, and its goals – including promoting institutional joint working – align well with CEHA's research goals. The 11 international research-intensive universities involved have a shared global vision and a commitment to educating future world leaders and to examining aging as a 21st-century issue with a multidisciplinary approach.

IARU network

CEHA has from the beginning been the driving force within the ALH network. This work has led to permanent activities such as CEHA's annual international IARU Summer School *Interdisciplinary Aspects of Healthy Aging* in 2011-2016, a biannual IARU Graduate Student Conference (on rotation between IARU partners; 2012/2014/2016) and ongoing research collaborations, such as the IHan and the Walkability projects.

IHan is an International Healthy Aging Network (part of IARU) which focuses on molecular and cognitive biomarkers of healthy aging and age-related diseases, including type-2 diabetes and Alzheimer's disease. Walkability investigates whether the existence of perceived community assets and/or specific characteristics of the built environment, including streetscape

design, and/or characteristics of the social environment, influence the propensity of older adults to walk, exercise and/or practise other healthy behaviors.

CEHA has also hosted highly successful events, conferences, and workshops for IARU members and other interested scientists such as: the international congress on ALH, which included a press conference, in 2010; and two international congresses (*Cultures of Health and Aging?* and *Biology of Aging*) as well as an IARU Graduate Student Conference in 2014 (*Aging Research and Scientific Careers*). These activities have attracted attention to CEHA and strengthened relations between researchers and their students.

The close association between CEHA and IARU is a cornerstone in the efforts to internationalize CEHA. In 2014, CEHA empowered the IARU network further by forming (and chairing) the ALH Steering Committee, whose *raison d'être* is to increase engagement across IARU campuses and to promote joint activities and funding opportunities for IARU ALH participants. The Steering Committee meets approximately once a year.

Network on basic and translational aging research

In 2011, CEHA joined forces with major research centers in Groningen (The Netherlands), Cologne (Germany), and Newcastle (UK) to form a research network for basic and translational science in healthy aging. CEHA also has an active collaboration with the National Institutes of Health/National Institute on Aging (NIH/NIA, USA) via Vilhelm A Bohr, who is associated with CEHA as a group leader in Theme III. Professor Bohr has been instrumental in the establishment of CEHA. The close collaboration with Bohr has been fundamental in securing excellent recruitments to CEHA such as the professors Ian Hickson and Linda Bergersen and Assistant Professor Morten Scheibye-Knudsen and in the sharing of infrastructure with NIH/NIA.

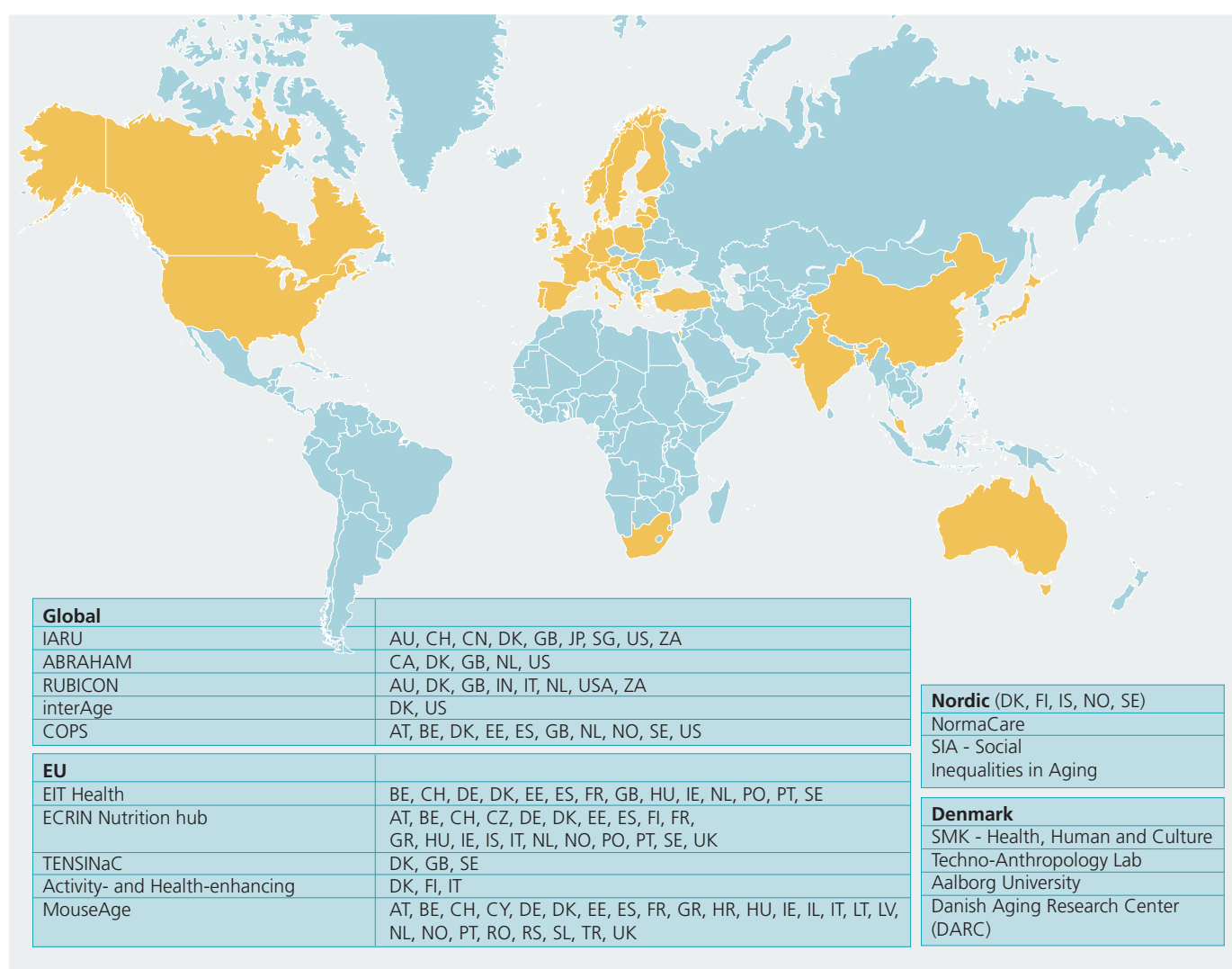


Figure 6. Overview of CEHA's collaborations.

EIT Health

In early 2014, the European Institute of Innovation and Technology (EIT) launched a call for Knowledge and Innovation Communities (KICs), as part of the larger European Union (EU) initiative, Horizon 2020. The goal of the KIC initiative is to tackle the grand challenges facing the EU by providing innovative solutions to societal problems through highly integrated, creative, and excellence-driven partnerships among stakeholders in education, technology, research, business, and entrepreneurship. More than 50 core partners (and their 90 associate organizations), including leading businesses, public partners, research centers, and universities from nine EU countries (including University of Copenhagen), responded to the 2014 call for KICs by submitting a proposal for the project InnoLife – Healthy living and active aging. InnoLife was the winning KIC, to be renamed EIT Health, and was awarded a business value of approximately 395 million euros over 7-10 years.

The goal of EIT Health is to promote entrepreneurship and develop innovations in healthy living and active aging, providing Europe with new opportunities and resources to improve quality of life and healthcare. This will be achieved by delivering products, services, and concepts designed to improve quality of life and contribute to the sustainability of healthcare across the EU. The partners represent the top tier in excellence in healthcare and research, and the outreach activities of EIT Health are expected to spread throughout the EU (<https://www.eit-health.eu/>).

EIT Health provides opportunities for new and strengthened collaborations between CEHA, the University of Copenhagen, IARU universities and beyond. A fine example of this is CEHA's first activity within the EIT Health, which was the development of a new summer course on health innovation for the elderly population. The course, called *Alive and KICKing – innovative solutions to aging related challenges*, was developed together with the Copenhagen Business School, the pharmaceutical company Novo Nordisk A/S, and the innovation and entrepreneurship hub SUND Vækst – the latter a collaboration between CopenRehab/Faculty of Health and Medical Sciences and the Municipality of Copenhagen. In connection with the EIT Health work, Novo Nordisk A/S Vice-President and Head of R&D External Relations Søren Bregenholt was appointed as Honorary Industrial Ambassador at the Faculty of Health and Medical

Sciences 2014. The role of the Ambassador is to generate innovative ideas and work with students and researchers to create concrete solutions and products, thereby bringing industry, CEHA, and the University closer together.

ABRAHAM network

CEHA is also active in the network Alliance for Biology of ageing Research And Healthy Ageing Multidisciplinary biobanking approaches (ABRAHAM), which was created in 2010 and includes researchers, companies, governmental institutions, and patients/citizens. ABRAHAM aims to create a transatlantic network with partners from the EU, the USA, and Canada to enhance integration in the field of biobanking and basic aging research in order to contribute to the goal set by the European Commission to add two extra healthy years to life by 2020. This collaborative effort harmonizes, standardizes and exchanges data and materials from biobank and cohort studies, facilitates shared use of infrastructures, facilities and expertise, and enables exchange visits of personnel to participating institutes exploring options for new projects and/or pilot studies.

This network builds on several existing projects, some of which involve transatlantic partnerships that focus on aging-related issues, such as genome stability and metabolism, and systems biology. The founding partners are: the University Medical Center Groningen (The Netherlands), University of Copenhagen (Denmark), University of Newcastle upon Tyne (United Kingdom), Mayo Clinic (Minnesota, USA), and McGill University (Montreal, Canada), all of which have extensive collaborations with industries in the food, pharmaceutical and medical technology sectors as well as experience in human clinical trials. Since 2013 CEHA has, together with the ABRAHAM network, co-organized the 3rd-7th Annual Alliance for Healthy Aging Conference series, the EU Marie Curie ITN MARRIAGE, as well as several EU research and infrastructure applications.

National collaborations

Within Denmark, Themes II and III in CEHA actively collaborate with the Danish Aging Research Center (DARC) at the University of Southern Denmark. This collaboration has resulted in several scientific publications, as well as education of PhD students that have been co-supervised by CEHA and DARC researchers.



Stakeholder event with municipalities in 2014.

Theme III CEHA researchers also collaborate closely with research groups at the Novo Nordisk Foundation Center for Protein Research, University of Copenhagen. These collaborations have also resulted in high-level scientific publications as well as in the recruitment of Assistant Professor Simon Bekker-Jensen to Theme III. CEHA Theme I-III researchers have multiple ongoing collaborations with clinical departments at several Danish hospitals in the Greater Copenhagen area that are crucial for several successful CEHA projects such as LISA, COLOSMA, and LIFESTAT. See “CEHA II overview” for details.

Collaborating with municipalities

Much of CEHA's research is done in dialog with citizens as well as all the professionals who are working to create a good framework for citizens' healthy aging. Municipalities are one of the natural collaborative partners for our research because they have political responsibility for many of the areas that affect healthy aging. CEHA is therefore participating in a series of intervention projects in municipalities, especially under the aegis of the “health promotional innovations.”

The *Transferring healthy aging* is an umbrella study in Theme I exploring implementation of diverse interventions and the tension between context-dependency and efficacy on the one hand, and transferability of healthy aging interventions on the other. The study includes:

- community-based loneliness intervention targeting elderly community-dwelling adults to be followed longitudinally and

compared with loneliness interventions in other municipalities;

- transferability of healthy aging interventions across contexts, target groups, and organizational settings;
- community-based intervention for ethnic minority elderly women conducted in a private-public partnership;
- register-based study focusing on healthcare utilization across diverse ethnic and socioeconomic groups adding further to the focus on healthy aging, and in particular inequalities in health and disease in older age;
- series of user-involvement activities with the participation of experts, health professionals, interest organizations, private business, and elderly people focusing on diet, physical activity, and social relations.

Stakeholder strategy

Furthermore, CEHA drew up a stakeholder strategy in 2014 (further described in “Societal impact: engagement, outreach, and communication”). The primary target groups are elderly organizations, municipal decision-makers, healthcare professionals, and selected patient organizations. The aim is to highlight and discuss healthy aging with stakeholders through events, workshops, seminars and lectures organized by CEHA, and by engagement during joints projects and events. One very successful example of this collaboration is the work at the People's Political Festival in 2016, which strengthened CEHA's stakeholder relations. This event has showcased CEHA research to attract future collaborations and funding.

RESEARCH THEMES AND PROGRAMS

CEHA I: A brief retrospective

From 2009 to 2013, the goal of CEHA I was to conduct leading-edge research on human health and aging, with an emphasis on understanding how human behavior and lifestyle choices modulate life trajectories and health outcomes. We also aimed to identify mechanisms to develop and implement diagnostic and/or preventive interventions that minimize health burdens associated with normal and accelerated aging and aging-related chronic disease. The common thread running through this research period was ‘frailty’ and the research was centered on five research programs. Below is a brief description of each program, followed by a description of the major cross-disciplinary projects conducted during CEHA I – more details in the Appendix A.2.

Programs

1a. Molecular Aging – focus on oxidative stress, lactate signaling, calcium homeostasis, neuroenergetics, mitochondrial dysfunction, and neurodegenerative diseases.

Program leader: Ian Hickson

The Molecular Aging Program studied the role of DNA repair in conserving genome instability and counteracting aging. We demonstrated how defects in DNA repair can cause premature aging. We also demonstrated that mitochondrial dysfunction can lead to an array of physiological changes in cells and tissues that manifest as progressive age-related pathologies. Furthermore, we investigated how extrinsic sources of cellular stress contribute to cellular and tissue aging. For example, we characterized cellular responses to inflammatory cytokines and pathogenic infections, and demonstrated that they can exacerbate cellular aging.

1b. Neuroscience – focus on oxidative stress, genomic instability, calcium homeostasis, neuroenergetics, mitochondrial dysfunction, and neurodegenerative diseases.

Program leader: Martin Lauritzen

The Neuroscience Program explored how aging influences brain function in the context of animal model systems and a cohort of Danish men born in 1953. We showed that cognitive decline is associated with decreased un-stimulated salivary secretion and a bad subjective sleep experience. Importantly, the functional

magnetic resonance imaging studies suggested that cognitive decline was associated with a disrupted ability to produce network activity and the default mode network that the brain uses when preparing for a task was severely affected – similar to the pattern that is observed in patients with Alzheimer’s disease (AD). This suggests that our test-persons may be at risk of developing AD and that an intervention should be carried out. The predictive value of this finding is being assessed in the project carried out in CEHA II from 2014 to 2018.

2. Muscle and Matrix – focus on understanding metabolic, genetic, and lifestyle factors that influence skeletal muscle function throughout the lifecourse.

Program leaders: Michael Kjær and Flemming Dela

The Muscle and Matrix Program studied how regular physical activity improves inflammatory status, and maintains muscle mass and function especially in old age. We showed that morbidly obese subjects can demonstrate improved glucose tolerance after an intensive lifestyle intervention, while the abundance of muscle ceramide and triacylglycerol remain unchanged. We also demonstrated that consumption of a fat-rich diet does not influence muscle ceramide content. In addition, we showed that high-intensity interval training promotes reversal of insulin resistance in patients with type-2 diabetes.

3. Body and Life – focus on lifecourse perspective on aging.

Program leaders: Kirsten Avlund and Erik Lykke Mortensen

In the Body and Life Program we studied the influence of lifecourse processes on frailty and specific signs of early aging. The largest project and the most significant accomplishment of the Program was the Copenhagen Aging and Midlife Biobank (CAMB). The completion of the CAMB database is a milestone not only for Program 3 researchers, but for CEHA and Danish aging research in general. CAMB has provided unique possibilities for collaborations among CEHA researchers on how multiple exposures and adversities across the lifespan influence aging processes and age-related changes in health and in physical, social, and cognitive function across the lifespan. Program 3 researchers also used other cohorts such as the

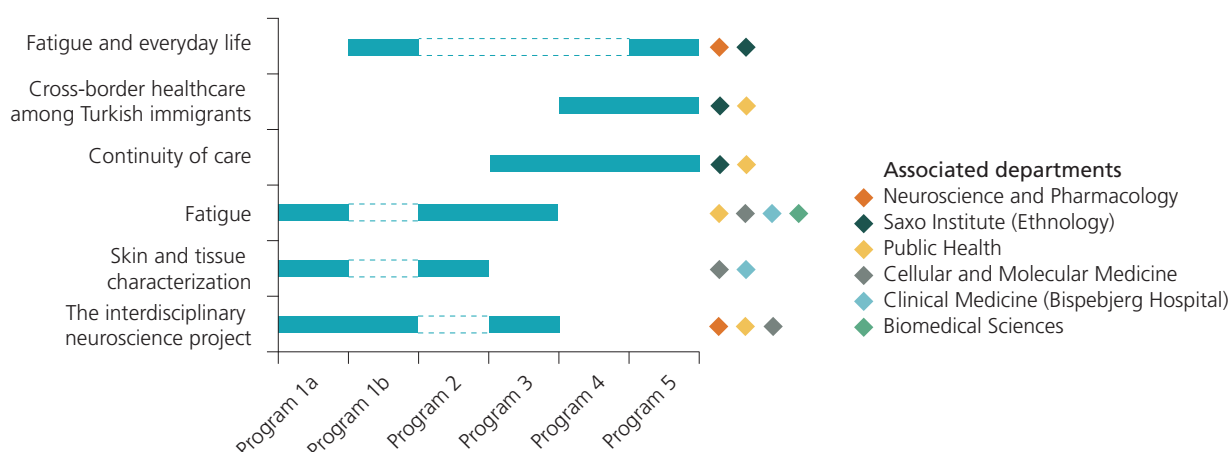


Figure 7. Overview of multidisciplinary projects in CEHA I.

Glostrup 1914 cohort and register data to identify important determinants of age-related changes across the lifespan.

4. Society, Culture and Healthcare Policy – focus on preventive medication, health services, and health of an aging population.

Program leader: Allan Krasnik

The research in Program 4 applied a cross-disciplinary approach to the role of preventive medication as a major intervention with strong implications for society, health services, and the health of an aging population. We developed tools for functional monitoring to support decision-making in general healthcare practice, and study results identified and analyzed successes and failures of different initiatives for better coordination of care. Aging populations are at risk of multiple chronic diseases, for which new therapeutic and/or preventive care options may be available. International comparative studies were initiated to study the continuity and quality in preventive care for aging populations in health organizations using integrated and comprehensive mechanisms. If they receive well-coordinated high-quality care, the aging population could experience both a better quality of health along with increased lifespan.

5. Health in Everyday Life – focus on how people deal with aging in their everyday lives to maintain or increase their quality of life.

Program leaders: Lene Otto, Astrid Jespersen, and Thomas Söderqvist

Program 5 made significant progress towards establishing humanistic aging research and cultural gerontology as an important and central field of study in Denmark. Through extensive ethnographic fieldwork, a large body of qualitative data on aging, health promotion initiatives, and practices of everyday life has been gathered and analyzed.

Multidisciplinary projects

In addition to the main focus of each Program described above, several multidisciplinary projects were conducted across the programs (Fig. 7).

Fatigue and everyday life – experiences of fatigue among healthy people and people suffering from apoplexy (Programs 1b and 5).

Coordinator: Lene Otto (Astrid Jespersen)

Combining the expertise of ethnological/qualitative approaches (M Andersen from Program 5) and healthcare professionals from the outpatient clinic and neurological department at Glostrup Hospital (Paul Jennum and Hysse Birgitte Forchammer, Program 1b), we analyzed the experiences of fatigue among healthy people and people with apoplexy. We found among other things that current rehabilitation practices are based on the idea of “a return to the everyday life one had before the incident.” However, this ideal fails to recognize that incidents in late life mark a threshold of a new life phase, often characterized by increased frailty (PhD Thesis A question of location – life with fatigue after stroke; Andersen M, 2013).

Cross-border healthcare – among Turkish immigrants in Denmark with particular focus on the elderly (Programs 4 and 5).

Coordinator: Lene Otto (Astrid Jespersen)

A joint project between ethnology and public health combining a quantitative study on the use of healthcare services among Turkish immigrants with a qualitative study⁴ among 30 Turkish immigrants investigating the concrete health practices such as the practice of utilizing cross-border healthcare services and medication consumption. Among other things the project found that elderly Turkish immigrants engage in highly complex cross-border health practices, which are often unrecognized by the Danish health authorities.

4. Nielsen SS, Yazici S, Petersen SG, Blaakilde AL, Krasnik A Use of cross-border healthcare services among ethnic Danes, Turkish immigrants and Turkish descendants in Denmark: a combined survey and registry study. *BMC Health Services Research* 13 (12, 1): 390, 2012.

KEY OUTCOMES OF CEHA I

- **Science**
791 publications
- **Capacity-building**
81 individual PhD students/employed-enrolled and 54 individual postdocs/employed during the five years of CEHA I
- **Funding from external grants**
more than DKK 223m (approximately EUR 30m) in addition to the Nordea-fonden grant
- **Awareness**
672 media mentions (of which 47 on radio; 41 on TV)

Continuity of care – an international comparative analysis of tools and settings for coordination of preventive drug medication (Programs 3, 4, and 5).

Coordinator: Allan Krasnik

This cross-national study was done in collaboration between public health and medical researchers in Denmark and the US. By conducting qualitative interviews with providers and health managers in the Veterans Health Administration and in the Danish Healthcare System, we identified elements of importance for the provision of care to vulnerable people with type-2 diabetes and ways to improve the quality of care to vulnerable type-2 diabetes patients in Denmark. A manuscript will be submitted to BMC Health Services Research in December 2016.

Fatigue (low subjective vitality) in middle-aged men correlates with levels of reactive oxygen species, dNTPs, DNA damage, body mass index, and physical performance (Programs 1a, 2, and 3).

Coordinators: Kirsten Avlund and Vilhelm Bohr

By combining the experience in DNA metabolism in group 1 with the epidemiological experience of group 3 we detected novel biomarkers in a human cohort with individuals with fatigue⁵. This insight may help us in future to provide earlier indications of signs of fatigue and therefore provide earlier intervention.

Skin and tissue characterization of a patient with apparent dimorphic rates of skin aging (Programs 1a and 2).

Coordinator: Michael Kjær

By combining the molecular expertise within DNA, the imaging experience within electron microscopy, the physiological knowledge within connective tissue, and the clinical approach to dermatology, it was possible across disciplines to carry out this study that supported the idea that lack of elastic fibres in skin allowed for enhanced local skin proliferation⁶.

The interdisciplinary neuroscience project (Programs 1a, 1b, and 3).

Coordinator: Martin Lauritzen

This project was initiated as a collaboration between the Research Centre for Prevention and Health, The Capital Region of Denmark, the Department of Public Health at the University of Copenhagen, and diagnostic departments at Rigshospitalet Glostrup and Panum-based research groups at the Center for Healthy Aging. The overall purpose has been to identify early indicators of cognitive decline in a Danish birth cohort of males born in 1953, as indicated by repeated follow-up examinations of cognitive function since childhood. The study^{7,8} has already now provided important information of potential biomarkers of cognitive decline.

5. Maynard S, Keijzers G, Gram M, Desler C, Bendix L, Budtz-Jørgensen E, Molbo D, Croteau DL, Osler M, Stevnsner T, Rasmussen LJ, Dela F, Avlund K, Bohr VA. *Aging* (Albany NY) 5(11): 850-64, 2013.

6. Nygaard RH, Maynard S, Schjerling P, Kjaer M, Qvortrup K, Bohr VA, Rasmussen LJ, Jemec GB, Heidenheim M. Acquired cutis laxa localized to the upper body in an adult female. *Case Reports in Dermatology* 8: 42-51, 2016.

7. Hansen NL, Lauritzen M, Mortensen EL, Osler M, Avlund K, Fagerlund B, Rostrop E. Subclinical cognitive decline in middle-age is associated with reduced task-induced deactivation of the brain's default mode network. *Human Brain Mapping* 35: 4488-4498, 2014.

8. Desler C, Frederiksen JH, Angleys M, Maynard S, Keijzers G, Fagerlund B, Mortensen EL, Osler M, Lauritzen M, Bohr VA, Rasmussen LJ. Increased deoxythymidine triphosphate levels is a feature of relative cognitive decline. *Mitochondrion* 25: 34-37, 2015.



CEHA II overview

During CEHA I, the Center established a solid research platform that has provided new knowledge and insights into the mechanisms of aging at the societal and individual levels. An important common theme at the time was ‘frailty’ and the retention of vitality in its broadest sense, for healthy aging and for society. In CEHA II we decided to reorganize our research specifically focusing on the significance of ‘energy’ in aging processes, not only as it relates to individual bodies and processes at the cellular level, but also as it relates to psychological and social dimensions, including interest in one’s surroundings and engagement with other people. This reorganization was a natural development from disciplinary and multidisciplinary approaches in CEHA I to a growing tendency toward interdisciplinarity in CEHA II. This is a transition we are expecting to be completed in CEHA III where the focus areas are “FLOW” and “FABRIC” (see Strategy paper).

Building on knowledge gained from CEHA I (See Appendix A.2 for achievement overview), and the large number of successful interdisciplinary collaborations that have been facilitated by the establishment of the Center, we reorganized the Center around three research themes in CEHA II. These themes have been chosen to enhance the multidisciplinary collaborations at CEHA (see Fig. 8).

CEHA II themes

1. Community innovation for healthy aging

CEHA researchers investigate the significance of the local community and opportunities for promoting the health and energy of the elderly in the last stage of life. Much of this work is being done in collaboration with four Danish municipalities. Our researchers are also engaged in studying how historical and social changes have influenced relations between people and between generations.

2. Lifecourse aging processes: lifespan exposures and healthy aging

This is an area in which CEHA’s researchers investigate the different factors that influence aging processes throughout life, how citizens could be motivated into active lifestyles and what happens to cells, muscles, and the brain as we get older. Researchers are also carrying out an intervention project focusing on physical activity to protect against age-related changes in musculature and the brain.

3. Energy balance in humans: what are the mechanisms underlying reduced energy? In this theme researchers focus on the cellular and physiological mechanisms that cause energy levels to dwindle as we age.

See Appendix A.3 for achievement overview.

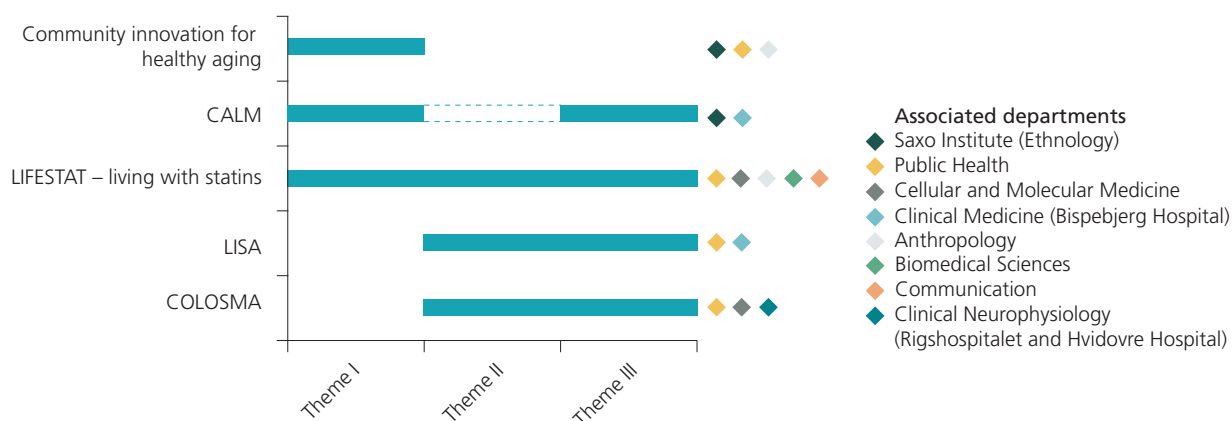


Figure 8. Overview of multidisciplinary projects during CEHA II.



Key multidisciplinary projects

CALM (Themes I and III): the Counteracting Age-Related Loss of Skeletal Muscle Mass project (CALM; 2013-2017, <http://calm.ku.dk>) is an interdisciplinary research collaboration focusing on age-related loss of skeletal muscle mass and the effect of dietary protein and physical activity in achieving a healthier and more active lifestyle among older people. A systems approach that is both qualitative and quantitative is being used, and addresses the roles of biological, sensory, clinical, physiological, and cultural factors. CALM aims to generate scientific evidence, recommendations, and innovative solutions to counteract age-related loss of skeletal muscle mass in elderly Danes. CALM is one of the 18 initiatives established in 2013 with a grant from the University of Copenhagen Excellence Programme for Interdisciplinary Research. CALM was granted a total of DKK 19.6m (EUR 2.6m) and involves three faculties and four research groups.

LIFESTAT – living with statins (Themes I-III): this is an interdisciplinary project that leverages approaches and knowledge from medicine, the humanities, and the social sciences to analyze the impact of statin use on health, lifestyle, and well-being among Danes who are 40-60 years old. LIFESTAT has been granted DKK 20.8m (EUR 2.8m) from the University

of Copenhagen Excellence Programme for Interdisciplinary Research to cover research activities from 2013 to 2018.

LISA (Themes II-III): the Live active – Successful Aging project is investigating the influence of different training types on muscle function over a prolonged period. Interventions are being performed over the course of a year both in healthy people and in those with chronic disease and the participants will be followed for 10 years after the intervention to assess the ability to adhere to training long term and to potentially change behavior and attitude to exercise. The study was initiated during CEHA II and ongoing recruitment for the first three years of CEHA II; thereafter the included subjects are studied at years two, three, five, seven and ten after inclusion.

COLOSMA (Themes II-III): this ongoing clinical neuroproject (since 2009), the Copenhagen Longitudinal Study of Male Cognitive Aging, has provided important information on associations between cognitive functioning and biological and brain parameters. The COLOSMA study indicates that cognitive decline can be predicted with high sensitivity by recording changes in cerebral rhythmic activities evoked by complex visual stimuli.



CEHA II – Theme I

Community innovation for healthy aging

Group leaders

Astrid Jespersen, Ethnology, Saxo Institute, Faculty of Humanities

Discipline: Cultural analysis, health in everyday life, qualitative methods, innovation studies

Karsten Vrangbæk, Health Economics and Policy, Department of Public Health, Faculty of Health and Medical Sciences

Discipline: Health policy and economics, comparative health policy, health services research

Bjarke Oxlund, Anthropology, Department of Anthropology, Faculty of Social Sciences

Discipline: Anthropology of life and health, aging, gender, technologies, community studies

Maria Kristiansen, Public Health Sciences, Department of Public Health, Faculty of Health and Medical Sciences

Discipline: Health services research, mixed-methods, intervention studies, inequality in healthy aging

Rationale, focus, and aims

Perceptions of a meaningful and fulfilling life, and the ability to achieve this, are shaped by individual experiences and values across the lifespan. Local communities are important settings to study, as they incorporate the many facets of everyday life that shape health behaviors and quality of life for diverse groups of elderly people. Such community factors include the availability and relevance of health promotion initiatives, spaces for interaction with others, leisure activities for diverse groups of elderly people, the built environment and social capital/networks within elderly populations and across generations. There are also important social and structural differences within communities that affect people's ability and interest in health interventions, including differences in services (level and types), health status, functional capacity, gender, education, (former) occupation, ethnicity, and familial situation.

The rationale of Theme I is rooted in this recognition of the importance of focusing not only on individual knowledge and skills in health promotion initiatives, but rather contextualizing health in the lifecourse (time) and context (space) of people. An important contextual change is the 2007 Danish municipal reform, which enhanced the responsibility of municipalities for health promotion and challenged them to focus on citizen-oriented health promotion aiming at creating, shaping, and facilitating ways of aging healthily. We made use of this development to examine the impact of new policies and health technologies as applied in a given municipality in promoting health and well-being.

Health-promoting interventions to address healthy aging among heterogeneous populations need to engage local communities directly, and hence require cross-disciplinary research and close collaboration between a variety of stakeholders such as civic organizations, municipalities, general practitioners, hospitals, and aging citizens themselves.

Our studies have focused on achieving an understanding of the actual *doing* of health – that is, the ongoing everyday practices, meanings and negotiations of health – rather than a normative assessment of health knowledge and behavior, as the foundation for promoting health successfully among aging citizens, which is a central theme in CEHA II.

The general aim of Theme I is to build sustainable academic networks across different disciplines, including health services research, anthropology, and ethnology, and with clinical researchers in other parts of CEHA, and to extend these to collaboration with societal partners primarily at the local community (municipal) level including NGOs and informal citizen groups.

Specific aims of the theme are:

- to develop sustainable interdisciplinary academic networks to explore how new understanding of aging and the heterogeneity of local communities influences the ways in which health and energy are promoted in aging citizens;
- to explore the various opportunities and barriers to healthy aging and lifelong energy at the community level, and apply this knowledge in collaboration with societal partners;
- to identify innovative approaches to private-public

Theme in numbers

Number of publications: 66 + book chapters 4

2014: 15 + book chapter 1

2015: 13 + book chapters 3

2016 (until Sept): 38

Multidisciplinary publications: 7

2014: 3

2015: 1

2016 (until Sept): 3

PhD students (completed): 8

2014: 7

2015: 0

Sept 2016: 1

Media mentions: 129 (national) + 13 (international)

2014: 70 (national) + 13 (international)

2015: 38 (national) + 0 (international)

Sept 2016: 21 (national) + 0 (international)

**External funding (excluding the Nordea-fonden grant)
(total amount DKK):** 18,822,550 DKK

2014: 17,600,000

2015: 1,032,550

Sept 2016: 190,000

collaboration in health and aging and devise new modalities for the active participation of aging individuals in shaping policies and services.

We expect that the following perspectives and results will help promote healthy and active aging in the communities under study:

- analysis of the concepts of healthy aging and lifelong energy;
- mapping core 'health and aging' stakeholders in the four selected municipalities;
- analysis of the various opportunities for and barriers to healthy aging and lifelong energy of individuals, population sub-groups and at the community level in each municipality;
- a comparison of the four municipalities to identify enabling and limiting contextual factors with regard to healthy aging and the maintenance of lifelong energy;
- analysis and development of methods and tools for health promotion that are participatory and based on the involvement of various local stakeholders.

As this theme builds on a framework that emphasizes the importance of social and cultural factors as humans interact in extended personal and professional networks over time, we pursue the CEHA II mission by exploring how this affects the opportunities for health-related behavior, health and well-being in the aging population, and creating a close connection between research and practical dissemination.

Organizational developments

In 2015, Prof. Allan Krasnik left the management group of Theme I due to other research obligations and was replaced by Professor Karsten Vrangbæk (theme leader together with Associate Professor Astrid Jespersen) and Associate Professor Maria Kristiansen. Together with Associate Professor Bjarke Oxlund, these are the four group leaders of Theme I.

Key achievements

Establishing close relationships with selected municipalities and engaging in interaction research projects are key achievements of Theme I. This has led to insights into the complexities, challenges, and opportunities of developing in-depth collaborative health and social care within municipal settings. This is manifest in the sub-projects studying policies to address loneliness among the elderly; in the efforts to establish municipal health houses; and

in the ambitions to engage the voluntary sector in developing health and elderly care. Theme I has also developed a deeper insight into the challenges of providing healthcare to aging immigrants and ethnic minorities in Denmark.

Active aging promotes a specific version of the good old age based on a strong body and an active lifestyle, which contrasts with an image of old age with frailty and decline. The ongoing dynamic relation between frailty and strength, and between activity and passivity, is being investigated in the Counteracting Age-Related Loss of Skeletal Muscle Mass (CALM) randomized clinical trial. An important 'collateral benefit' from the RCT is that an awareness of physical decline has been raised among the participants and combined with the newly gained knowledge on the importance and effect of muscle training; this awareness is enhancing the propensity to be more physically active.

There are diverging attitudes in the older population about healthy diet e.g. the relevance of protein intake. Cultural and historical conditions shape the perceptions of food, and protein is typically seen in relation to a desire to develop and sustain muscular strength. However, through analysis of the CALM data (using data from the RCT as well as insights from stakeholder workshops in the partner municipalities), we have found that for the older generation other aspects are equally important, such as tradition, ambience, memories, and the ever-shifting health recommendations (Jensen et al., 2016).

There is a layering of dietary experiences and habits over the lifecourse, which affects the diet among elderly people. An important insight is that life-changing moments (divorce, death of spouse, and retirement) influence and often change meal preferences, which often lead to malnutrition or at-risk malnutrition among the frail elderly. In order to understand the meal habits among elderly people, we need to understand much more about the eating strategies that older people in different situations develop (Jensen et al., forthcoming).

With increasing longevity and the medicalization of the lifecourse, measurements have become more important for managing aging bodies. Our ethnographic studies of practices of measurements, welfare technologies, and aging show that the overall trend towards increasing quantification of health takes different forms for different people and purposes. Numbers can facilitate reflection and communication although they may be interpreted differently by different actors.



CEHA II – Theme II

Lifecourse aging processes

Group leaders

Erik Lykke-Mortensen, Department of Public Health, Faculty of Health and Medical Sciences

Discipline: Psychology, behavioral science, public health and lifecourse

Martin Lauritzen, Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences and Department of Clinical Neurophysiology, Rigshospitalet, Glostrup, Denmark

Discipline: Aging, human brain function and neurodegenerative disorders

Rikke Lund, Department of Public Health, Faculty of Health and Medical Sciences

Discipline: Social epidemiology, public health and lifecourse

Flemming Dela, Department of Biomedical Sciences, Faculty of Health and Medical Sciences

Discipline: Diabetes, metabolism, physical activity, exercise, cardio-vascular diseases, mitochondrial physiology

Rudi Westendorp, Department of Public Health, Faculty of Health and Medical Sciences

Discipline: Geriatric medicine and all disciplines related to aging research

be possible to stimulate an energetic and active lifestyle in aging individuals by implementing physical training and other interventions to promote higher energy levels and a physically active and energetic lifestyle throughout old age.

The theme's principal aims are:

- to analyze the influence of lifecourse exposures on aging trajectories and individual differences in aging;
- to characterize early cognitive decline and identify early predictors of age-related cognitive decline;
- to evaluate the effects of physical activity interventions and to evaluate adherence to high and low intensity interventions;
- to establish a cohort of statin users and to conduct interdisciplinary research to describe the complexity of a medical issue from biological, humanistic, and anthropological points of view.

Since aging processes are ongoing over most of the lifespan, lifecourse studies are essential to understand individual differences in aging and to design interventions which optimally stimulate an active lifestyle and promote healthy aging. Thus, lifecourse studies are essential for working toward the vision and mission of CEHA to identify and create innovations that enable individuals and the population to age more successfully. Because many lifecourse issues relate to biological, behavioral, and social sciences, lifecourse research is inherently interdisciplinary. Within CEHA, lifecourse researchers have initiated and contributed to several interdisciplinary projects, thus furthering CEHA's aspiration to work across disciplines.

Organizational developments

This theme has been substantially strengthened by the recruitment of Professor Rudi Westendorp in 2015 from Leiden University Medical Centre, Netherlands, and recruitment of an Associate Professor in Gerontology, Charlotte Juul Nilsson. In 2014-16 the close collaboration between CEHA lifecourse researchers and the Danish Aging Research Center (Kaare Christensen) has been further developed with collaborative PhD and postdoc projects and the initiation of a large Nordic

Rationale, focus, and aims

The lifecourse perspective on aging assumes that aging processes are ongoing over most of the lifespan and that behavior, exposures, and morbidity during any life period will affect functioning, health, and morbidity during later life. It is further assumed that there are cumulative and combined effects on individual aging trajectories of exposure to different adversities and exposure to risk factors throughout the lifespan. Thus, our rationale is that it should be possible to characterize individuals by their lifetime exposures and their associated risk for early aging and dysfunction. In addition, we suggest that it should

Theme in numbers**Number of publications:** 223

2014: 51

2015: 90

2016 (until Sept): 82

Multidisciplinary publications: 57

2014: 18

2015: 24

Sept 2016: 15

PhD students (completed): 28 + 1 dissertation

2014: 7

2015: 10

Sept 2016: 11 + 1 dissertation

Media mentions: 355 (national) + 256 (international)

2014: 117 (national) + 0 (international)

2015: 149 (national) + 251 (international)

Sept 2016: 89 (national) + 5 (international)

External funding (excluding the Nordea-fonden grant)
(total amount DKK): 21,904,116 DKK

2014: 5,282,547

2015: 5,685,500

Sept 2016: 10,936,069

collaboration (NordForsk Social Inequalities in Aging project). The collaboration between lifecourse researchers and Michael Kjaer's physical intervention group at Bispebjerg Hospital (Theme III) has also been strengthened and close project collaboration has been initiated with the Danish Research Centre for Magnetic Resonance at Hvidovre Hospital: as a result Ellen Garde is now a 50 percent CEHA funded Associate Professor in the Department of Public Health at the University of Copenhagen.

Key achievements

During CEHA II, data collection has been an important effort for Theme II researchers: several databases have been completed, including the CAMB database, the Danish Conscript Database, and the registry based Folkesundhedsdatabasen. There are now more than 50 individual projects based on the CAMB database and several projects based on the conscript database or on Folkesundhedsdatabasen. The CAMB database has been described by R Lund et al. in *International Journal of Epidemiology*, 2015.

Several projects with data collection are ongoing, two of which combine cognitive assessment and MRI scanning (Copenhagen Longitudinal Study of Male Cognitive Aging (COLOSMA) and Life-Mabs) and also the first ever cognitive follow-up study based on the Danish Draft Board Intelligence (Liko-15; currently >1500 participants). In addition, the physical intervention project Live active – Successful Aging (LISA) has been very successful in recruiting participants (350 of 450 are recruited) and the

LIFESTAT project on the use of statins as cholesterol-lowering therapy in primary prevention of cardiovascular diseases has completed data collection on patients with and without statin-induced myalgia. Additional data collection in LIFESTAT on the effect of Q10 supplementation in statin users will finish by the end of 2016, along with the start of a longitudinal physical training in statin users.

Theme II lifecourse researchers have demonstrated how early life exposures, including stress and individual characteristics in young adulthood (e. g. intelligence), predict physical functioning, morbidity, and mortality across the lifespan (M Osler et al. in *World Psychiatry*, 2015 and RH Meincke et al. in *Journal of Aging and Health*, 2016). These studies demonstrate substantial continuity across the lifespan, and individual differences in aging must be identified and interpreted with this perspective.

The clinical neuroproject COLOSMA, a joint project with researchers in Theme III, has provided important information on associations between cognitive functioning and biological and brain parameters while a recent epidemiological study suggests an association between social resources and cognitive decline (A Gow et al. *Age and Ageing*, 2016). COLOSMA is one of the first studies to use draft board IQ results as a basis for evaluating midlife cognitive performance. The results suggest a neurobiological basis for subclinical cognitive decline in late midlife, which includes task-induced deactivation alterations similar to the pattern seen in patients with AD and mild cognitive impairment (NL Hansen et al. in *Human Brain Mapping*, 2014).



CEHA II – Theme III

Community innovation for healthy aging

Group leaders

Lene Juel Rasmussen, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: Aging, human molecular biology, mitochondrial biology, DNA repair and genomic stability, nucleotide metabolism

Ian Hickson, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: Aging, chromosome stability, DNA repair, age-associated disease

Michael Kjær, Department of Clinical Medicine, Faculty of Health and Medical Sciences

Discipline: Skeletal muscle and tendon tissue, aging, physical activity, injury

Jørn Helge, Department of Biomedical Sciences, Faculty of Health and Medical Sciences

Discipline: Aging, training, insulin resistance, metabolism, inactivity

Linda Bergersen, Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences

Discipline: Aging, mitochondrial DNA repair, brain energy failure, exercise

Vilhelm Bohr, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: Aging, DNA repair, neuroscience, metabolism, neurodegeneration

Tom Kirkwood, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: Aging, evolution and genetics, mitochondrial mutation, systems biology

Hocine Mankouri, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: Genome stability, aging, DNA repair

Andres Lopez-Contreras, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: DNA damage, replication stress, mouse models, cancer

Simon Holst Bekker-Jensen, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: Cell stress responses, signal transduction, MAP kinases, DNA damage response, aging

Morten Scheibye-Knudsen, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: Aging, accelerated aging, aging interventions

Javier Pena-Diaz, Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences

Discipline: Molecular aging, DNA repair, neurodegenerative disorders

Rationale, focus, and aims

Aging is associated with a general decline in energy levels or 'vitality'. At the cellular and tissue levels, this reduction in vitality correlates with an inability to adequately replace or repair 'worn-out' or damaged components. Theme III aims to better understand the molecular and physiological mechanisms that cause age-associated impairment in physical function. This knowledge will ultimately lead to the development of novel strategies to diagnose and counteract age-associated functional

decline, and hence allow individuals to attain a better quality of life as they age.

The theme's principal aims are:

- to better understand how nuclear and mitochondrial dysfunction affects specific tissues and organs and leads to loss of vitality during aging;
- to investigate the molecular and cellular basis for age-related pathologies such as cognitive decline and muscle dysfunction;

Theme in numbers

Number of publications: 199 + book chapters: 12

2014: 101 + book chapters 7

2015: 44 + book chapters 5

2016 (until Sept): 54

Multidisciplinary publications: 51

2014: 15

2015: 23

Sept 2016: 13

PhD students (completed): 14 + 1 dissertation

2014: 7 + 1 doctoral dissertation

2015: 4

Sept 2016: 3

Media mentions: 76 (national) + 77 (international)

2014: 29 (national) + 65 (international)

2015: 27 (national) + 12 (international)

Sept 2016: 20 (national) + 0 (international)

External funding (excluding the Nordea-fonden grant)

(total amount DKK): 134,762,846 DKK

2014: 80,458,744

2015: 31,407,091

Sept 2016: 22,897,011

- to study human premature aging disorders, as a model for rapid/extreme aging;
- to better understand how inherently unstable regions of the genome are maintained during our lifespans, and how they contribute to age-related diseases;
- to identify novel 'early warning' biomarkers and prognostic markers for age-related pathologies;
- to establish mouse models for studying organ- and tissue-specific functions during aging;
- to examine how physical training induces physiological changes in muscle tissue, and how this knowledge could be exploited to improve vitality during aging;
- to determine molecular causes of, and novel strategies for, effective interventions that can promote healthy aging.

By studying the molecular and cellular mechanisms of aging, Theme III researchers aim to better understand the principal causes of various age-related pathologies. Further characterization, as well as an improved understanding, of reliable 'early warning' biomarkers associated with various pathologies will allow individuals to make informed lifestyle changes to counteract age-related diseases. Theme III therefore integrates biomedical research with human physiology and psychology, and utilizes CEHA's unique links with local municipalities to engage the general public with aging research.

Organizational developments

In CEHA II, Theme III has expanded to recruit a number of internationally renowned young scientists. These include Javier Pena-Diaz (2014), Andrés López-Contreras (2014), Morten Scheibye-Knudsen (2015), Chloé Yeung (2016) and Simon Holst Bekker-Jensen (2016). Each of these brings key expertise, and their established international network, to CEHA II.

More recently, Professor Tom Kirkwood, a prominent scientist in the field of aging research with a strong international profile, has also joined CEHA II on a part-time basis. Professor Kirkwood has been a leading scientist in the field of aging research for

many years, and also has extensive experience in managing a competitive multidisciplinary aging research institute.

In 2015, a Danish National Research Foundation (DNRF) Center of Excellence, the Center for Chromosome Stability, was established (funded for up to 10 years). This Center is directed by Professor Ian Hickson, and also involves Hocine Mankouri and Andrés López-Contreras as principal investigators and steering committee members.

Key achievements

Certain regions of the human genome are inherently unstable, and difficult to maintain throughout our lifespans. We characterized a new DNA repair process that is required to maintain chromosomal 'fragile sites'. This landmark study, from Professor Ian Hickson's group, was published in *Nature* in 2015, and gained widespread international media attention.

Mitochondrial dysfunction can lead to altered bioenergetics, as well as a number of secondary cellular changes, that contribute to age-related pathologies. These include increased DNA damage and altered nucleotide metabolism, which we have demonstrated to be associated with cognitive decline and reduced subjective vitality. These studies, involving many researchers across CEHA II, were published in *Aging* (2013 & 2015), *Cell* (2014), *Cell Metabolism* (2014), *Mitochondrion* (2015), and *Acta Physiologica* (2015).

More recently, we have expanded our research portfolio to include the study of mouse models of human pathologies or premature aging. Importantly, these mouse models will provide a unique insight into physiological mechanisms of aging, and permit experimental determination of how age-associated impairment can be counteracted.

In addition, we have demonstrated in human volunteers that muscle mass and function deterioration (e.g. during periods of inactivity) can be counteracted by exogenous growth hormone and/or anti-inflammatory medication. This discovery will be useful for the counteraction of permanent muscle loss in both surgical patients as well as in acutely ill patients that undergo bedridden inactivity for short periods.

RESEARCH OUTPUT, MULTIDISCIPLINARITY, AND DISSEMINATION

Research output

CEHA researchers have published almost 1300 scientific publications in the period 2009-2016 (see Appendix A.4 for a list of selected publications). These include a publication arising from the Communication and Outreach Platform in 2014. A significant number of these were published in high-ranking international journals within the humanities, social sciences, and biomedicine. These publications have contributed to the understanding that with increasing longevity and the medicalization of the lifecourse, measurements have become more important for managing aging bodies.

Several databases have been fully or partly completed, including the CAMB database, the Danish Conscript Database, COLOSMA, and the registry-based Folkesundhedsdatabasen (Public Health Database), and results from these cohort studies have been reported in several scientific publications during the period 2009-2016.

In addition, the first publications from the LISA and COLOSMA studies are beginning to get published. These studies have demonstrated how early life exposures, including stress, and individual characteristics in young adulthood (e. g. intelligence), predict physical functioning, morbidity, and mortality across the lifespan. They have provided important information on associations between cognitive functioning and biological and brain parameters while a recent epidemiological study suggests an association between social resources and cognitive decline.

CEHA researchers have published ground-breaking new knowledge on how basic biological mechanisms determine human physiology. These include how DNA repair and mitochondrial function are hallmarks of human aging. Also, the inclusion of mouse models of human pathologies or premature aging have provided a unique insight into physiological mechanisms of aging, and permit experimental determination of how age-associated impairment can be counteracted.

Multidisciplinarity

The output of CEHA researchers in CEHA I and II represents a multidisciplinary endeavor to understand the highly complex process of aging using sophisticated and powerful techniques and approaches. CEHA projects appreciate that aging reflects the influences of biological, socio-cultural, and socio-economic factors, as well as individual lifestyle choices, all of which

modulate the quantity (lifespan) and quality (healthspan) of an individual's life. Our published work shows that endogenous (cellular/biological) and exogenous (social, interpersonal) stress can adversely influence both lifespan and healthspan.

CEHA has contributed to defining how genetic factors, social class, lifestyle, and education influence aging, not only as individual factors but also in combination with each other. Our growing number of publications authored by CEHA researchers from different scientific fields, as well as between CEHA scientists and their national and international colleagues, show that collaboration stimulates creativity and growth, leading to synergy between the participating groups. This trend will continue in CEHA III, and hopefully further develop, to allow each researcher to accomplish more than he or she could accomplish working independently.

Dissemination of research results

CEHA focuses strongly on the dissemination of research results to the scientific community around the world. Each researcher has a busy program participating in conferences, seminars, workshops, etc. worldwide (Table 1). For example, during the last year CEHA group leaders were actively involved 142 times as speakers, panel members, chairs, etc. in academic events nationally and internationally. During the last two years for example: Rudi Westendorp was keynote speaker at the 23NKG Nordic Congress of Gerontology, Tampere, Finland, 2016; Lene Juel Rasmussen was invited speaker at the Aravind Eye Hospital conference, Madurai, India, 2015; Jørn W Helge was invited speaker at the conference on *Exercise, Muscle & Metabolism*, Melbourne University, Australia, 2015; and Astrid Jespersen presented a paper at the 4S/EASST Conference, Barcelona, 2016.

Seminars and academic events

CEHA hosts or co-hosts academic events to facilitate dissemination of data and promote discussion. Since 2014, CEHA and the Biotech Research & Innovation Centre (BRIC), University of Copenhagen, have organized six annual research seminars on important topics in biological sciences. This seminar series features international speakers, who are at the forefront of their respective fields, and who present seminars on research and/or technologies that are having a major impact on biological and biomedical sciences. Examples are Manuel Serrano from the Spanish National Cancer Research Center and Stephen West

Table 1. Participation by CEHA group leaders in national and international academic events (Sept 2015-Sept 2016)

	Meeting	Seminar	Workshop	Conference	Symposium	TOTAL
Keynote speaker	0	0	1	17	2	20
Invited speaker	19	13	3	43	4	82
Regular talk	3	2	0	9	4	18
Poster	1	0	0	2	0	3
Organizer	0	0	0	2	1	3
Chair	0	2	3	5	0	10
Paper	0	0	0	3	0	3
Panel	0	1	1	1	0	3
TOTAL	23	18	8	82	11	142

from the Francis Crick Institute, London.

These seminars are usually attended by 50-100 participants and, in connection with the seminars, discussions are arranged between the international guest speakers and CEHA PhD students and postdocs.

IARU conferences

Further, the IARU network is an important dissemination platform and CEHA has hosted scientific international IARU conferences on multiple topics related to the Aging, Longevity and Health project in 2010, as well as two international conferences *Cultures of Health* and *Biology of Aging* and an IARU Graduate Student Conference – *Aging Research and Scientific Careers* – in 2014.

At the 2010 conference, 123 participants attended and a report was published in the *American journal Mechanisms of Ageing and Development* (132 (10): 522-32. Epub 2011).

The *Biology of Aging* conference was organized by Theme III researchers Lene Juel Rasmussen and Vilhelm Bohr together with external partners Profs Yosef Shiloh, Tel Aviv University, and Tone Tønjum, Oslo University. It included 32 scientific presentations and 10 posters by young researchers. The conference *Cultures of Health* covered 29 scientific presentations. It was organized by CEHA researchers from Themes I and II (Allan Krasnik, Astrid Jespersen, Bjarke Oxlund, and Erik Lykke Mortensen) and had 60 participants. An outcome of the latter is the article "The challenges of human population ageing" (*Age and Ageing* 44: 185–187, 2015; doi: 10.1093/ageing/afu189).

At the IARU Graduate Student Conference (*Aging Research and Scientific Careers*) organized by the Network for Young Scholars (NYS), 20 graduate students shared their research through scientific presentations and explored the possibility of collaborative partnerships within the IARU network.

Network of Young Scholars

As the example above indicates, the NYS is an active dissemination player, focusing on the PhD student level. In 2011 and 2012, NYS conducted two interdisciplinary conferences, *Forever Young?* (100 participants) and *Active Aging* (100 participants), the latter arranged within the framework of the EU Year for Active Aging. The first conference proved that not only is there a need for cross-disciplinary discussions on aging and health inside CEHA, there is also an actual desire for these discussions from the outside. The latter was a distinct example of how far CEHA's young researchers have come in thinking and communicating in interdisciplinary terms. Again

in 2015, NYS led a mini-conference on interdisciplinary research projects – management and communication aiming at grasping the challenges that potentially hinder interdisciplinary projects and collaborations to succeed (25 participants).

Workshops

In 2014, an international workshop on interdisciplinarity was organized by CEHA Theme I researcher Astrid Jespersen in collaboration with Dr Laura Meagher and Dr Catherine Lyall, University of Edinburgh. Participants included 45 researchers from CEHA and many individuals from other interdisciplinary research initiatives at the University of Copenhagen.

Theme I also conduct two annual workshops, focused on research results, practice-based knowledge, and future collaboration, for their collaborators from the municipalities of Ishøj, Copenhagen, Vordingborg, and Gentofte, as part of the ongoing collaboration with societal partners, NGOs, and informal citizen groups. These workshops, which are well attended with about 50-60 participants each, address jointly selected topics, such as inequality, loneliness, and interaction with civil-society organizations. They are organized by a group of Theme I senior and junior researchers and are led by the senior researchers. The seminars are evaluated in situ (dialog based) and Theme I also receives written feedback based on a template.

Symposium on Genome Instability and Neurodegeneration

In 2016, CEHA Profs Lene Juel Rasmussen and Ian Hickson (Theme III) organized and hosted an international *Benzon Symposium on Genome Instability and Neurodegeneration* (70 participants from more than 10 countries). The format was a combination of state-of-the art lectures by leading experts, and selected oral poster presentations by young scientists. From CEHA, results on, for example, how defects in mitochondrial respiration influence aging phenotypes, and how problems arising during the replication of cellular DNA underlie premature aging syndromes in humans, were presented. CEHA researchers Lene Juel Rasmussen, Ian Hickson, Vilhelm Bohr, Tom Kirkwood, Rudi Westendorp, Claus Desler, and Morten Scheibye-Knudsen gave presentations, whereas Linda Bergersen, Javier Peña Diaz, Thomas Lau Hansen, and Nima Fakouri presented posters.

Engagement and dissemination activities for stakeholders outside academic settings are discussed in "Societal impact: engagement, outreach, and communication".

RESEARCH TRAINING

An important goal for CEHA is to educate the next generation of aging researchers. To this end, CEHA scientists make a concerted effort to provide high-quality educational resources to CEHA students/trainees, and to recruit junior and senior scientists with appropriate research interests and/or expertise to the CEHA faculty (Table 2). CEHA's educational programs include undergraduate- and graduate-level courses on aging-related topics and specialties as well as opportunities for postdoctoral studies under the mentorship of the CEHA faculty. Educational activities increase year on year and we offer – and are developing – interdisciplinary courses and degree programs in health innovation that will help strengthen the innovation capabilities and stimulate the entrepreneurial mindset among students, teachers, and health professionals. (See annual reports for details at <http://www.healthysaging.ku.dk/communicationandoutreach/annualreports/>) A selection of major educational activities developed by CEHA is described below.

EIT Health summer course

As part of EIT Health, CEHA coordinated the development of a new international summer course on health innovation for the elderly population. The course *Alive and KICKing* – innovative solutions to aging-related challenges aims to contribute to the education of professional health innovators and entrepreneurs on an international level. It includes online lectures, on campus teaching, and flipped classroom techniques. The course ran for the first time in 2016 with 24 participants from all over the world, including from the EIT Health and IARU partner universities, which form part of the recruitment base for the course. The aim of the course is to contribute to the education of professional health innovators and entrepreneurs on an international level.

The course includes online lectures on the Coursera platform (1400 learners from June to September 2016) as well as an on-campus part at the University of Copenhagen in August 2016. Rudi Westendorp coordinated the course and he also taught and supervised both online and on campus. Among the involved researchers were Flemming Dela and Andreas Vigelsø from CEHA and academics from Erasmus University Rotterdam, Copenhagen Business School, Novo Nordisk, Steno Diabetes Center and the Danish company DigiRehab, as well as from the Department of Public Health and the Faculty of Science at the University of Copenhagen.

MARRIAGE training network

Since 2012, CEHA has been a member of the EU-funded Initial Training Network MARRIAGE. The overall objective is to provide state-of-the-art training in the study of the biology of aging. The network includes European Aging Centers, and the Training Network will create a pan-European Network focused on aging research. CEHA Profs Lene Juel Rasmussen, Vilhelm Bohr, and Ian Hickson are involved, and CEHA has two PhD projects connected to the program (Nima Fakouri and Ösgün Ozer). Multiple complementary training schemes have been implemented in the Network (research projects, courses organized by the Network academic partners, and training organized by the industrial partners). The ABRAHAM groups are part of this Network.

PhD courses

Since 2015, the NYS has focused on developing PhD courses on Aging and/or Interdisciplinarity at the University of Copenhagen, primarily for PhD students within CEHA. In 2015, their first PhD course was launched at CEHA, called *Interdisciplinary Research*:

Table 2. Number of individuals from various categories that were trained by CEHA since its launch

	2009	2010	2011	2012	2013	2014	2015	2016
Postdocs	15	24	29	27	31	25	38	38
PhD Students	9	32	43	43	57	51	59	64
MA/BA Students	2	4	0	15	13	14	20	14
Pregraduate Research Students	0	0	13	17	13	18	17	8



Students at the EIT Health Summer School in 2016.

Aging as a field of study targeted at PhD students working in the field of aging, but also relevant for students who wanted to learn about interdisciplinary research per se (reached full capacity with 12 participants). Among CEHA teachers were for example: Professor Linda Bergersen; Assistant Professor Claus Desler (Theme III); Professor Rudi Westendorp and Associate Professor Ellen Garde (Theme II); Professor Susan Reynolds and Postdoc Henrik Hvenegaard (Theme I); as well as Postdoc Morten Bülow Hilgaard (Communication and Outreach Platform). The course

was successful and is expected to run again in 2017. Over the next years, NYS will launch new courses.

CEHA is also engaged in dissemination activities outside the university giving lectures and presentations at public and private hospitals, societies, associations, and organizations, as well as for the general public via, for example, the Danish Open Universities. See the section “Societal impact: engagement, outreach, and communication” for details on outreach to stakeholders and the general public.

SOCIETAL IMPACT: ENGAGEMENT, OUTREACH, AND COMMUNICATION

The basic and applied research carried out at CEHA is directed toward moving into a world where people live longer, healthier, and more meaningful lives. The Center thus engages with a wide range of stakeholders and the wider public to ensure that its research helps inform actions aimed at fostering healthy aging. This work is coordinated by the Communication and Outreach Platform. Through the work of Medical Museion at the University of Copenhagen, our engagement efforts also seek to encourage a critical awareness of issues related to healthy aging and ongoing research that addresses these issues. CEHA also uses its insight into factors that can predict healthy aging to perform intervention studies; this aspect of engagement is covered in “Research themes and programs”.

Activity during CEHA I

During CEHA I we focused on using different communication channels to convey aging and health-related information to a broad audience. General information on the Center was provided on the CEHA website in both Danish and English. During the EU Year for Active Aging in 2012, healthy aging was part of the public agenda both in Denmark and internationally. This provided an excellent outreach platform for CEHA, which played an active role in conferences, public meetings, lectures, exhibitions, and Science Theater during the year. Moreover, CEHA featured several times on the Danish National Television channel, DR2. For example, the production company DocEye and CEHA developed a TV documentary series, *Fauli, Fat and Finished?*, where the audience followed a Danish actor (Fauli) and his health in the context of aging. The CEHA researchers designed and supervised the physiological and clinical experiments and were interviewed during the six episodes. The series had approximately 825,000 viewers (about 15 percent of the Danish population).

In 2013, CEHA launched a Facebook page in Danish, as a forum for advice, awareness, and debate about healthy aging and for branding of CEHA, targeting those citizens aged 25–60 years old with an interest in healthy living. It reached 10,000 followers within nine months.

Research undertaken within the Communication and Outreach Platform resulted in two PhDs during CEHA I – Adrian Bertoli’s work on social-media-based disease management and Morten Bülow’s work on the history of the ‘successful aging’ concept. In

addition, artist Lucy Lyons’ postdoctoral project *Drawing Aging* culminated in an exhibition called *Experiences of Aging* in 2012.

CEHA II engagement strategy

As part of CEHA II, we acknowledged that engaging and innovative science communication is a prerequisite for research to be useful to society and thereby invested more resources into outreach and communication. The Communication and Outreach Platform works strategically to put knowledge about healthy aging on the agenda and ensure that our research forms the basis for recommendations to both decision-makers and citizens.

The activities undertaken in Medical Museion also exploit more dialog-based methodologies, adding a slower but deeper way for audiences to think through some of the complex aging-associated issues. The Platform, which is headed by Professor Ken Arnold, assisted by Senior Curator Bente Vinge Pedersen, includes four employees: an Event Coordinator who works with events and exhibitions at the Medical Museion; a Social Media Curator who primarily works with dialog-based communications via SoMe (Medical Museion and CEHA Secretariat); a Senior Communication Consultant (CEHA Secretariat and Communication Department at the Faculty of Health and Medical Sciences) who focuses on press, Facebook, mass communication, and stakeholder relations; as well as an Event Coordinator in the CEHA Secretariat who focuses on stakeholder relations and events in public spaces.

We work across multiple media and seek to be engaging, innovative, and collaborative. Our methods are adjusted to specific settings, target groups, media platforms, and messages. We develop our formats continuously to adapt to the changing media landscape. Our work operates on three levels: (1) assistance with, and innovation around, direct communications; (2) provision of a platform (e.g. the Medical Museion’s auditorium and other public spaces) for interdisciplinary stakeholder dialog and engagement; and (3) experimental public programming including exhibitions, live events, games, and other activities.

The communication platform collaborates closely with the researchers, with a special focus on supporting young researchers to become skilled communicators with outreach as an integral part of their work.

Table 3. Social media activities

FACEBOOK	Followers (growth)	Posts Year/month	Reach Year/month/post	Engagement rate	
May 2013-Jan 2014	10,119	62/-	-	-	
Sept 2014-Sept 2015	10,405	129/11	517,179/43,098/4,009	9%	
Oct 2015-Oct 2016	12,155	126/11	1,691,415/140,951/13,423	7%	
TWITTER	Followers (growth)	Tweets Year/month	Reach Year/month/tweet	Engagement	Interaction Year/month/tweet
Jul 2014-Sept 2014	44	53/-	8,100/2,700/153	1.1%	64/21/1
Oct 2014-Sept 2015	173	308/26	64,200/4,586/208	0.8%	405/29/1
Oct 2015-Sept 2016	214	101/8	18,492/1,541/183	0.6%	91/8/1
INSTAGRAM	Followers	Post	Likes		
Aug 2015-Sept 2016	321	99	917		
Video campaigns on FB	Number	Views	Average % of video viewed		
May 2016-Aug 2016	24	594,684	27%		

Communicating research to the wider public using mass media

The Danish version of the CEHA website is primarily targeted at stakeholders like employees in elderly organizations, health professionals, and politicians, while the primary target groups on the English site are researchers, students, and international partners. The web traffic has increased from 2520 in 2012 to 11,438 in 2015, an increase of 350 percent.

The communication team are facilitators and build bridges between researchers and journalists. The team help researchers find the right angle and the right media for the story, then help sell the story to journalists and assist the journalists with pinpointing the relevant experts. One specific example is the collaboration with Andreas Vigelsø Hansen to successfully communicate his PhD thesis to the media on inactivity followed by training in young and older men. Andreas was coached in media appearance before the press release. The story was picked up by a number of media outlets, with live interviews on the national television and radio, and more than 190 articles in Danish and international media, including CBS News in the USA and *Die Welt* in Germany.

A large project to increase awareness of how we age is one example of creating content that sets an agenda. This was undertaken in association with the popular Danish People's Political Festival in 2016. This festival is held annually on the island of Bornholm and is a platform for open debate and informal dialog between politicians, citizens, business people, and organizations (100,000 visitors in 2016). We interviewed Danish celebrities and researchers via two video campaigns that we produced in collaboration with the communication department at the Faculty of Health and Medical Sciences. One of the video campaigns was used after the festival by a Danish national newspaper on their website and Facebook page, together with interviews with CEHA researchers.

The press coverage of CEHA research and activities has expanded from 87 articles in 2009 to 498 in 2015. During the past few years, journalists frequently turn to our researchers as experts in healthy aging, and our research results have been covered from local Danish newspapers to international newspapers, such as *The Times* in the UK.

Using social media for communicating research

Social media are important channels for engagement and dialog and we have experimented with various social media in CEHA II (Table 3). These experiments have led us to focus on Facebook, Twitter and Instagram, which are used by 73 percent, 12 percent and 16 percent of the Danish population, respectively.

In August 2016 we had 12,150 followers on our Facebook page, with a high degree of interaction. The editorial team consists of a representative from the Communication and Outreach Platform as well as young researchers from the three research themes that have received coaching in effective communication on social media. The video campaigns launched in association with the Danish People's Political Festival in 2016 were publicized via the Facebook page and had more than 450,000 views. The campaigns increased the numbers of followers and attracted an average of 521 likes, 214 shares and 54 comments per post.

The CEHA Twitter account @sundaldring (which translates as healthy aging) was launched in 2014. In August 2016, we had 221 followers. The account is used to live-tweet from events, to promote researchers and events. During the People's Political Festival, 21 events were covered and in that month @sundaldring had 7900 exposures, 209 visitors, and gained 19 new followers.

In August 2015, the Instagram account @sundaldring (healthy aging) was launched. It is used to communicate the research process rather than results. Leading up to the event, researchers participating in the Political Festival were portrayed here, and afterwards the number of followers more than doubled. The account has 338 followers at present (October 2016).

Events and exhibitions

CEHA is working on innovative dissemination and richer engagement about research findings to the general public through lively dialog-based events and exhibitions, where researchers and the Communication and Outreach Platform work together. We investigate the framework for good communication and meaningful, lasting engagement. We learn from our experiments and strive to come up with fresh

approaches that enable us to try new ideas as well as stand out in an ever-more-crowded and busy public arena.

In 2014, CEHA organized or co-organized 24 events, in 2015, 35, and in 2016, 55 events are planned. We have developed several new formats for events and exhibitions that are described below:

Science slams

In a science slam, three researchers from different parts of the CEHA present their research in a five-minute format followed by a moderated discussion with the audience. This illustrates the multidisciplinary nature of CEHA and the dialogue between researchers and audience is engaging. The audience respond positively and the researchers value the coaching from the Communication and Outreach Platform. The researchers also gain experience of how their research can inform and enrich the research of each other.

Tales from retirement

Anthropologist Kamilla Nørtoft's project Tales from Retirement investigates identity and attainment associated with retirement and life's transitions, and is also a participatory outreach process for retirees and those approaching retirement that challenges perceptions of life after retirement. Participants take photographs of important situations for them as retirees. The project paves the way to considerable contribution from the public. It has resulted in a tour in Copenhagen, exhibitions, talks, and a podcast, and has been posted on Facebook and Instagram.

Room for aging

Part of Medical Museion's contribution to the societal impact of CEHA has been to devote a specific room to showcasing age-related displays and other initiatives. One of the projects hosted here entitled The Brain as We Age showed the historical development of the understanding of the brain, focusing in particular on imaging, and included a Lego brain model to conceptualize how such images are built up of small building blocks.

Life on the Line game

We have also produced an innovative group game called "Life on the Line" based on research outcomes from the Center. It looks at the entire process of aging – how the body and life conditions change over a lifetime – in a powerfully informative and fun manner. It has become the centerpiece in the Room for Aging and was used to great effect during the People's Political Festival in 2016. We are currently exploring the possibility of producing a touring version of the game that would be used in community centers and other public spaces, as well as a board game that might be sold commercially.

Guided brain-focused tours for children and their grandparents

A highly successful set of events sought to engage grandparents with healthy aging topics by attracting their grandchildren. This intergenerational project focused on the young and aging brain, including the idea of brain plasticity and how brains can be 'trained'.

Engaging stakeholders

In 2014, CEHA agreed a stakeholder strategy, with the aim of highlighting and discussing healthy aging with stakeholders in an

engaging and entertaining way; profiling research results focused on achieving longer and healthier lifespans; and giving examples of the relevance for stakeholders. The primary target groups are elderly organizations, municipal decision-makers, pension companies, government agencies, healthcare professionals, and selected patient organizations. An example of a close relationship with a primary stakeholder is the collaboration with the most influential organization for the elderly in Denmark, Dane Age (750,000 members), with whom we also arranged joint events during the People's Political Festival in 2015 and have published a series of four supplements ("The Good Life") in the Danish newspaper *Politiken*.

People's Political Festival

Our work at the People's Political Festival in 2016 serves as a good example of our diverse, successful approaches to strengthen stakeholder relations, set agendas, and showcase our research to attract future funding. At the festival, CEHA led a communication project encompassing 10 other projects funded by Nordea-fonden under the headline Sund4life (Healthy4life) and hosted 17 events and 4 exhibitions. Ten researchers, the Communication and Outreach Platform team, the CEHA secretariat, and the communication department at the Faculty of Health and Medical Sciences participated in the development and the execution of these activities. One novel aspect was that we involved invited stakeholders in planning workshops, to engage them in the creative process of developing new ideas and pinpointing new ways of solving issues related to healthy aging, and to build strong relations with the stakeholders. As mentioned previously, the project included two video campaigns, and one of these ("Life in 10 Ages"), which focused on when you are old, was shared on Facebook by the largest organization for the elderly in Denmark, Dane Age, which has 750,000 members and 100,000 followers on Facebook.

One of the exhibitions was a controversial exhibition of erotic photos of elderly people called *Timeless Love* by the Dutch artist Marrie Bot. The exhibition created a forum for interesting conversations about old age and quality of life, challenged visitor stereotypes of older people, and created publicity and visibility. The exhibition was mentioned in two television spots. In addition, the "Life on the Line" game and elements of The Brain as We Age display were incorporated into the CEHA festival venue, providing additional points of visual interest as well as unusual activities that proved to be popular and triggered topical conversations, even among strangers.

The CEHA events were visited by approximately 1000 people on each day of the four-day festival. The research dissemination was strengthened and the agenda of the CEHA and the individual researchers was boosted. The researchers got new ideas for research projects and it opened doors to relevant stakeholders. Internally, the participation strengthened the relations between researchers, as well as between researchers and the Communication and Outreach Platform.

Political hearings

Finally, CEHA participates frequently in political hearings on topics related to the elderly. It happens on average two to three times yearly and these have addressed legislation concerning, for example, social services, quality of homecare standards, preventive homecare, dignity standards in the eldercare, and use of digital communication tools with the elderly.



Science slam event at the Cultural Night in Copenhagen, 2015.

FINANCIAL OVERVIEW (2009-2016)

Funding from Nordea-fonden

CEHA was established in 2009 by a visionary and generous donation of DKK 150m (EUR 20m) by the Danish foundation Nordea-fonden. In 2012, the Center was successfully evaluated and in 2013, CEHA was awarded another grant of DKK 150m for the period 2014-2018 (CEHA II) by Nordea-fonden.

By the end of 2015, CEHA's total cumulative expenditure relating to the use of the Nordea-fonden grant came to DKK 202.3m (EUR 27m), distributed per year as follows:

- CEHA I (2009-2013): DKK 149.4m (EUR 20.1m)*
 - 2009: DKK 20.0m (EUR 2.7m)
 - 2010: DKK 30.4m (EUR 4m)
 - 2011: DKK 34.5m (EUR 4.8m)
 - 2012: DKK 32.2m (EUR 4.3m)
 - 2013: DKK 32.3m (EUR 4.3m)
- CEHA II (2014-2015): DKK 52.9m (EUR 7.1m)**
 - 2014: DKK 25.2m (EUR 3.4m)
 - 2015: DKK 27.7m (EUR 3.7m)

*Of this, DKK 13.8m (EUR 1.9m; 9.2%) used for Center Administration, including full salary for the Managing Director.

**Of this, DKK 5.9m (EUR 0.8m; 11.1%) used for Center Administration, including full salary for the Managing Director and DKK 3.8m (EUR 0.5m; 7.1%) used for the Communication and Outreach Platform.

For a further breakdown of costs for CEHA II, see Appendix A.5.

During CEHA I, annual research work-years paid by the Nordea-fonden grant more than tripled from 11.7 annual work-years in 2009 to 35.6 work-years in 2011. This high level was maintained during 2012 (37.3), 2013 (36.7), 2014 (31.3) and 2015 (38.5). The number of research employees paid by other funding sources (head count; part or full time) were: 50 in 2009, 61 in 2010, 88 in 2011, 94 in 2012, 117 in 2013, 144 in 2014, and 163 in 2015.

Details on exact expenditures on research, administration, equipment and operational costs from the Nordea-fonden grant are provided in Appendix A.5.

External funding

2010 was a breakthrough year for CEHA in establishing our credibility, as we secured a sizeable amount of funding (DKK 30m; EUR 4m) over and above the grant from Nordea-fonden; this should be viewed as a 'spin-off effect' of the Nordea-fonden grant. This achievement was well beyond our expectations, especially considering the amount raised by CEHA's fundraising efforts in 2009, amounting to DKK 6m (EUR 0.8m). Since then, we have succeeded in securing more than DKK 38m (EUR 5.1m) each year, with some years raising DKK 100m (EUR 13.5m).

At CEHA we have thus attracted about DKK 421m (EUR 56.6m) from external national and international sources in addition to the grant from Nordea-fonden (Table 4). DKK 96m (EUR 12.9m) came from the University of Copenhagen as direct funding, of which DKK 73.8m (EUR 9.9m) was granted through the University of Copenhagen Excellence Program for Interdisciplinary Research Funds, and DKK 22m (EUR 3m) was donated as 38 stipends that funded a third of PhDs (DKK 0.5m each; EUR 0.07m) and two stipends that funded PhDs fully (DKK 1.5m each; EUR 0.2m). In addition, the University of Copenhagen supports CEHA substantially with salaries of senior faculty (more than 10 senior researchers) and providing infrastructure and location in the Panum Institute as well as in the new Mærsk Building from 2017.

In conclusion, the external and internal funding secured by CEHA reflects the fact that the Center has become established as a highly reputable research center.

Table 4. External funding in addition to the Nordea-fonden grant		
Year	External funding [†]	DKK (EUR)
2009		5.7m (0.8m)
2010		30.1m (4.1m)
2011		32m (4.3m)
2012		55.3m (7.4m)
2013		26.4m (3.5m)
2014		103.3m (13.8m)
2015		38.4m (5.2m)
2016*		34m (4.6m)
2013	University of Copenhagen Excellence Program for Interdisciplinary Research Funds	73.8m (9.9m)
2009-2016	PhD stipends from the University of Copenhagen (2009-2016)	22m (3m)
Total		421m (56.6m)
*Until October 2016		

National funding sources

Examples of national funders that have supported CEHA:

- University of Copenhagen
- University of Copenhagen Excellence Program for Interdisciplinary Research Funds
- Municipality of Copenhagen
- Ishøj Municipality
- Nordfyn Municipality
- Region South Denmark
- Hospital Region Centre of Excellence
- Denmark's Innovation Foundation
- Danish Council for Independent Research
- Ministry of Culture
- Novo Nordisk Foundation
- Lundbeck Foundation
- VELUX Foundation
- Villum Kann Rasmussen Block Scholarship
- Tryg Foundation
- Carlsberg Foundation

- A.P. Møller and Chastine Mc-Kinney Møller Foundation
- Danish Cancer Society
- Danish Association for Rheumatic Diseases
- Danish Diabetes Academy
- Parkinson Foundation
- Danish Heart Foundation

International funding sources[†]

Examples of international funders that have supported CEHA:

- DNRF-funded Center of Excellence
- EU FP7, Horizon 2020 (2009-2016)
- ERC
- EU research and Innovation Staff Exchange Network (RUBICON)
- JNPD European Grant
- Olav Thon Foundation
- Association for International Cancer Research
- Manpei-Suzuki Diabetes Foundation
- Foundation Leducq Transatlantic NoE Grant
- National Institutes of Health

SWOT ANALYSIS

SWOT analysis

The Management has conducted a SWOT analysis based on input from a bottom-up self-evaluation process. This analysis is a simple way to guide new efforts by capitalizing on strengths and minimizing weaknesses. It will also help identify possible obstacles and challenges. We employ this analysis as a basis for adjusting and refining plans in order to focus on the continuation of CEHA III after 2018. The accompanying Strategy document builds directly on the results of the SWOT analysis.

STRENGTHS

- **A vibrant research environment.** CEHA is embedded in the University of Copenhagen, one of the best universities of continental Europe, which together with three university hospitals in the Copenhagen area make substantial investments in CEHA. When the core laboratory groups move to the new Mærsk building in the beginning of 2017, CEHA will have access to a whole new suite of state-of-the-art biomedical laboratories, clinical research facilities, and lecture rooms that will create even more coherence between the various disciplines. This will assemble a large part of the leadership team as well as strengthen the established international collaborations.
- **A common conceptual framework rooted in interdisciplinary research.** The integration of different biological, psycho-social, cultural, public health policy, and clinical expertise at CEHA leads to a rapid understanding of the mechanisms that underlie human aging. Citizen engagement and intervention studies will ensure that we create practical and effective interventions to extend our healthy lifespan. The strong commitment of CEHA to continue our international collaborations with IARU, ABRAHAM, EIT Health and more will further contribute to the impact of our research.
- **A citizen-centric approach.** While health and disease are the result of a complex interplay of biological and environmental factors, optimizing these interactions will provide citizens with unprecedented capabilities for repair. CEHA has developed a positive perspective that focuses on resilience, intrinsic capacity, and functional ability. CEHA cultivates strong relations with citizens and stakeholders such as decision-makers in business, aging interest groups, academia, and

politicians from parliament, EU, municipalities, and regions. An important example of engagement with citizens and relevant stakeholders is the successful activities created by CEHA at the annual People's Political Festival.

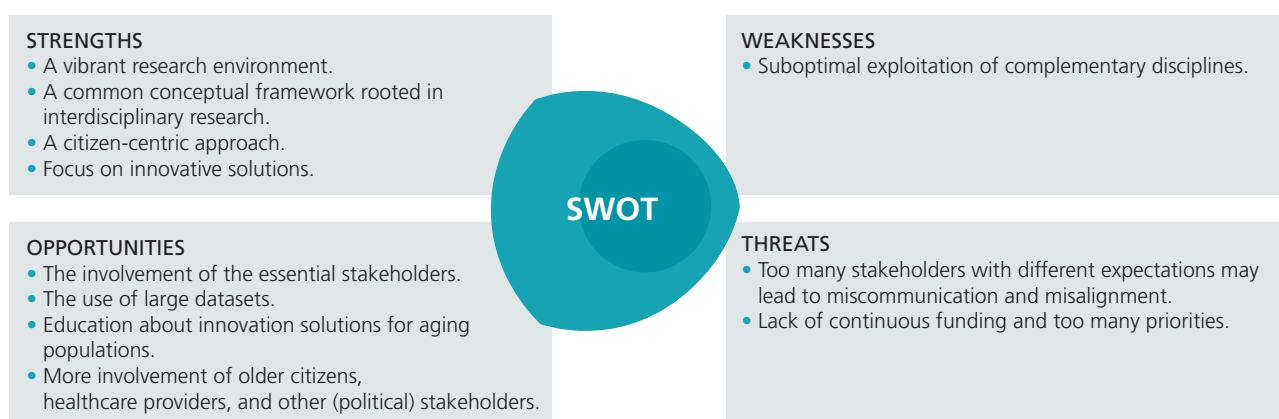
- **Focus on innovative solutions.** There is a widespread misconception that the aging process is not amenable to intervention, which has arrested innovation. By contrast, CEHA strives to translate research into preventive action. CEHA has been instrumental in setting up the EIT Health consortium, which aims to promote entrepreneurship and innovations in healthy living and active aging, to improve quality of life and healthcare across Europe.

WEAKNESSES

- **Suboptimal exploitation of complementary disciplines.** In order to understand and address the complexity of human aging it is important to align scholars, ideas, means, and activities. We have therefore developed new vision and mission statements to highlight this. For example, we will launch a systems-biology initiative to study complex molecular mechanisms in age-related decline, and correlate the factors that influence personal trajectories of health at the level of cohorts/communities. Strategic appointments will foster interactions with the Center of Protein Research, at the Faculty of Health and Medical Sciences, which has expertise in developing integrated technology platforms and large heterogeneous data-management systems to solve a range of fundamental problems in biomedicine.

OPPORTUNITIES

- **The involvement of the essential stakeholders.** As a key partner in the IARU and EIT Health networks we work with the best-in-class organizations in education, research, technology, business creation, and corporate and social innovation. These partnerships will foster cooperation, unlock innovation, and develop the potential for growth. It will give the opportunity to recruit and retain the best talents, creating high-quality jobs and boosting the global competitiveness of a suite of European stakeholders.
- **The use of large datasets.** Collaboration with Statistics Denmark and other Danish registries provides CEHA with



unprecedented access to electronic health transaction data that can be quantitatively analyzed. Relationships between diseases will provide knowledge that can inform the underlying network biology of disease and aid development of targeted therapeutic strategies. Big data offers an as-yet-untapped opportunity for new health insights and for understanding human health behavior at the systemic level to develop personalized medicine, prevent diseases, and support healthy life.

- **Education about innovation solutions for aging populations.** There is a need to invest in education and apprenticeship training programs to strengthen innovation capabilities and stimulate the entrepreneurial mindset among students, teachers, and health professionals. In addition, enhanced engagement with citizens will empower older people to take control and responsibility for their own health.
- **More involvement of older citizens, healthcare providers, and other (political) stakeholders.** In order to provide innovative solutions to deal with the increasing number of elderly people it is important to focus on engaging key stakeholders. Therefore, we need to strengthen these relations and so have developed a proactive strategy for outreach to the essential stakeholders. For instance, by aligning our

activities with the Danish Society for Patient Safety, a non-profit organization working to ensure that quality of service provisions, particularly patient safety and healthcare quality, is an aspect of all decisions made in Danish healthcare.

THREATS

- **Too many stakeholders with different expectations may lead to miscommunication and misalignment.** To address the demographic challenge, CEHA must undertake a variety of aligned and interacting projects. To ensure that CEHA's vision and strategy are fulfilled, we will develop benchmarks to ensure the quality of the people, their concepts, and the accrued means; the scientific, translational, and educational activities; the academic output, the stakeholder involvement, and innovations; the accrued knowledge, experts, and consciousness of demographic challenge; and the quality of care and cure provisions, the personal- and population-health status.
- **Lack of continuous funding and too many priorities.** CEHA has the potential to become an internationally leading interdisciplinary aging research center and the main aging research center in Denmark, but this requires continuous funding and focus.



APPENDICES

A.1 CEHA II management structure

Grant holder (Nordea-fonden Grant)

- Dean Ulla Wewer, Faculty of Health and Medical Sciences

CEHA Steering Group members:

- Managing Director – Professor Lene Juel Rasmussen (Chair)
- Associate Professor Astrid Pernille Jespersen (Theme I)
- Professor Karsten Vrangbæk (Theme I)
- Professor Erik Lykke Mortensen (Theme II)
- Professor Martin Lauritzen (Theme II)
- Co-Director – Professor Rudi Westendorp (Theme II)
- Professor Michael Kjær (Theme III)
- Professor Ian Hickson/Associate Professor Hocine Mankouri (Theme III)
- Professor Ken Arnold (Communication and outreach)

The SAB members are:

- Professor Boo Johansson, Göteborg University, Sweden (Chair)
- Professor Sarah Lamb, Brandeis University, US
- Professor Dr Ulrika Winblad, Uppsala University, Sweden
- Professor Erik Boddeke, University of Groningen, Netherlands
- Professor George Brooks, University of California, Berkeley, US
- Professor Tone Tønjum, Oslo University, Norway
- Professor Jan Vijg, Albert Einstein College of Medicine, US
- Dr Erinma Ochu, University of Manchester, UK.

Deans from:

- Faculty of Humanities, Professor Ulf Hedetoft
- Faculty of Social Sciences, Associate Professor Troels Østergaard Sørensen.

A.2: CEHA I (2009-2013): Overview and achievements of the research programs

1a. Molecular Aging – Program leader: Ian Hickson

The Molecular Aging Program is studying the role of DNA repair in conserving genome stability and counteracting aging. DNA repair protects the nuclear and mitochondrial genomes from intrinsic and external DNA-damaging agents. We have characterized mitochondrial and nuclear DNA repair pathways, and demonstrated how defects in DNA repair can cause premature aging. A major focus of our research is human RecQ helicases, which are mutated in a number of distinct premature aging disorders. We have shown that RecQ helicases perform an evolutionarily conserved role in 'dissolving' problematic DNA structures that naturally arise during DNA replication and chromosome segregation. Surprisingly, aberrant DNA replication intermediates are remarkably prevalent, and cells frequently attempt to segregate incompletely replicated, or inadequately processed chromosomes after DNA replication. This is a major potential source of genome instability. We also demonstrated that mitochondrial dysfunction can lead to an array of physiological changes in cells and tissues that manifest as progressive age-related pathologies. Furthermore, we have investigated how extrinsic sources of cellular stress contribute to cellular and tissue aging. For example, we characterized cellular responses to inflammatory cytokines and pathogenic infections, and demonstrated that they can exacerbate cellular aging. Ultimately, we envision that these analyses will lead to novel strategies or tools for diagnosing, preventing, and treating age-related diseases, thus promoting healthy aging.

1b. Neuroscience – Program leader: Martin Lauritzen

Program 1b is exploring how aging influences brain function in the context of animal model systems and a cohort of Danish men born in 1953. One research goal is to identify factors that influence or predict changes in cognitive function, especially cognitive decline in middle or late life leading to dementia. For this purpose we examined cognitive performance of 207 men, without evidence of differences in IQ when cognitive function was assessed at draft-board examination (baseline), but with important differences when they were 58 years old. We demonstrated significant differences in sleep quality, structural and functional MRI and autonomic function between test-persons with preserved and with decreased cognitive performance. Surprisingly the perturbation of the so-called resting state network activity by functional MRI was disrupted in test-persons with cognitive decline and reminiscent of the patterns observed in patients with Alzheimer's disease. This could suggest that disrupted resting state patterns in functional MRI may accompany cognitive decline. In our current research project we explore this possibility by follow-up examinations of IQ and cognitive tests and fMRI in the same test-persons with five-year intervals. In animal model systems, we have identified unique features of brain repair mechanisms in astrocytes linked to aging. In addition, we have demonstrated that activity of the interneuronal network which underlies cognitive processes and brain information processing are dysregulated during normal aging. The defects in network activity are energy demanding and accompanied by a doubling of the consumption of oxygen, while the supply is reduced. This may explain some of the deficits in cognitive function

that accompanies even healthy aging and may pave the way for an understanding of brain frailty underlying the increased susceptibility of old brains to contract neurodegenerative diseases. Ultimately, we envision that these novel findings will lead to novel strategies or tools for diagnosing and preventing brain frailty, thus promoting healthy aging.

2. Muscle and matrix – Program leaders: Michael Kjær and Flemming Dela

Aging of the musculo-skeletal system is associated with gradual loss of muscle mass and function, impaired recovery of function after disease or inactivity, and degenerative changes in connective tissue. Aging is also associated with lifestyle related diseases, particularly due to decreased daily physical activity. In CEHA I, Program 2 researchers have been studying the mechanisms that underlie these and other age-associated changes in metabolism and the musculo-skeletal system. Regular physical activity improves your inflammatory status, and maintains muscle mass and function. In old age, muscle loss with inactivity occurs extremely fast, and the regain of muscle is impaired. Connective tissue can retain its elasticity and can be stabilized by regular physical activity throughout life; local growth factors (i.e., estrogen and growth hormone) also improve matrix function in the elderly. In some types of connective tissue (tendon and cartilage) the growth is only present in childhood and adolescence whereas adult cartilage does not display turnover of the collagen tissue, and the breakdown associated with development of osteoarthritis is not associated with any compensatory tissue replacement (2).

Aging skeletal muscles contain myonuclei that cover a certain area of cytoplasm (myonuclear domain) and in fibers of similar size neither training nor age had any influence on myonuclear domain, but the fact that older muscle had lower myonuclear domain was simply explained by the presence of a greater proportion of small fibers than in younger counterparts (1). Regular life-long training is associated with a reduction of the circulating inflammation levels and this is likely to be coupled to maintenance of skeletal muscle mass either directly or via adipose tissue (3).

Cholesterol-lowering drugs (statins) interfere with skeletal muscle performance and mitochondrial respiration, a fact to be considered when statins are prescribed to prevent cardiovascular disease.

3. Body and life – Program leaders: Kirsten Avlund and Erik Lykke Mortensen

Program 3 addresses the influence of lifecourse processes on frailty and specific signs of early aging. Our focus is on the biological, psychological, and social factors that influence aging processes over the entire lifecourse, and we analyze 1) whether it is possible to explore strain factors over the lifespan, i.e., when and how long they typically influence the individual; 2) whether there are certain vulnerable periods in life, and 3) if the duration of strain is of special importance. We also aim to understand the variety of health outcomes that are potentially influenced by negative aspects of social relations, low socioeconomic position, and stress. This has not previously been investigated in detail in longitudinal designs.

The focus of CEHA Program 3 was to identify biomarkers of early aging and lifecourse influences on aging. Program 3 scientists used epidemiologic methods to analyze large data sets on midlife and old-age cohorts as well as data from national registries.

Key findings:

- The total number of leukocytes, lymphocytes, and neutrophils is associated with fatigue in young and old individuals, and length of telomeres in leukocytes from fatigued older individuals appears to be shorter than telomeres from non-fatigued older individuals (1).
- Increased leisure activity from age 50 to 80 is consistently associated with the level of cognitive ability, but not with age-related cognitive decline (2).
- Mobility-related fatigue is associated with slower walking speed in older adults which suggests that muscle strength is one of the underlying factors explaining the association between mobility-related fatigue and walking speed (3).
- Men who live alone may alleviate their risk of disability onset by being socially active and by having access to satisfactory social relations. Women do not seem to benefit as much from cohabitation as men, although women who live alone and who are not satisfied with their social relations also constitute a significant risk category (4).

Findings from these studies may contribute to developing and refining interventions, which can delay aging-related disability and loss of independence.

4. Society, culture, and healthcare policy – Program leader: Allan Krasnik

The research in Program 4 is based on a cross-disciplinary approach to the role of preventive medication as a major intervention with strong implications for society, health services, and the health of an aging population. The studies combine public health and social sciences taking advantage of the unique opportunities in Denmark for research on issues of healthy aging related to society, policy, and health services. These include the vast amount of Danish registry data on health and social determinants of healthy aging, as well as the easy access to informants from different social and ethnic population groups, community organizations, and from the national health-care system. A series of qualitative and quantitative studies are grouped by three sub-themes. The three sub-themes represent key issues related to actors, processes, and effects of policies and health services relevant to preventive medication, as follows: a) decision-making by diverse health professionals and consumers regarding use of preventive medication; b) social and ethnic inequalities in prescription and use of preventive medication; and c) development, use, and effects of coordinating tools relevant to preventive medication.

Key findings:

- General practitioners in Denmark seldom take an initiative to discontinue preventive medication once an aging individual has been prescribed anti-hypertensives, cholesterol-lowering drugs or pre-diabetes medication. This leads to a condition of poly-pharmacy, where a considerable number of individuals end up being hospitalized due to dangerous drug interactions.
- Low-cost measurement technologies such as pedometers, blood pressure meters, and smartphone health apps have become so prevalent that many aging Danes monitor their own health and well-being. While this is in many ways a

positive development trend in terms of the overall population health, it simultaneously creates new uncertainties and anxieties as well as a narrow focus on bodily data rather than overall quality of life. Numerical health standards thus have a tendency to become moral standards.

- New treatment guidelines, lower drug prices, and more generous public reimbursement patterns have seriously influenced the uptake of anti-hypertensives and cholesterol-lowering drugs over the past 15 years. The scientific evidence behind the medical standardization has become stabilized thereby making the encounter between patients and general practitioners in relation to cardiovascular health one in which medicines are prescribed without much further ado. Preventive medication has moved from being controversial to being mundane.
- Home nurses play an important role in the management of the medication of the oldest citizens who receive home nursing assistance. As a kind of state-sponsored, extended family members the home nurses take on the responsibility of providing advice and ensuring compliance in relation to cardiovascular health and other conditions.
- Denmark's health information systems are widely admired, yet barriers to integration of care include organizational fragmentation, unjustified financial incentives, and the absence of a single electronic medical record, which makes rational decision-making difficult to bring about.

Health in everyday life – Program leaders: Lene Otto, Thomas Söderqvist, and Astrid Jespersen

Researchers in Program 5 perform extensive ethnographic fieldwork, such as observations, interviews, visual ethnography, archive studies and auto-ethnography. The focus has been on different aspects and different understandings of aging and processes of aging in everyday life. Fieldwork is conducted in activity centers, out-patient clinics, lifestyle and fitness centers, and in the home environment. Although fieldwork is time-consuming, it produces a unique collection of qualitative data that are being analyzed. Program 5 has made significant progress towards establishing humanistic aging research and cultural gerontology as an important and central field of study in Denmark.

Key findings:

- The concept of active aging is a tool often used to set the agenda for policies that target the elderly in Europe. In a Danish context, 'active aging' is primarily promoted as physical activity, an approach that risks overlooking other health-promoting activities, such as participating in sustainable social networks.
- Many research-based health-promotion initiatives fail to include insights about elderly people's everyday lives and thus end up producing non-relevant and non-appropriate evidence for the target population.
- Implementing 'successful' and relevant initiatives for elderly people requires a multi-faceted, integral approach that is adaptable to the everyday lives of the target group.
- The widespread use of small, easily accessible health technologies in relation to exercise practices is likely to motivate and to help lifestyle changes.

A.3: CEHA II (2014-2016): Overview of the key research achievements

Theme I:

- We have established close relationships with four selected municipalities and have collaborated with them to implement a number of interaction research projects. This has provided insights into the complexities of, and challenges and opportunities for, developing in-depth collaborative health and social care within municipal settings.
- Our participation in the Counteracting Age-Related Loss of Skeletal Muscle Mass project (CALM) has created an awareness of physical decline among the participants. Combined with the newly gained knowledge on the importance and effect of muscle training, this awareness is enhancing the propensity to be more physically active.
- Our ethnographic studies of measurements and aging show that the overall trend toward increasing quantification takes different forms for different people and purposes. Numbers can facilitate reflection and communication although they may be interpreted differently by different actors.

Theme II:

- We have characterized the resting connectivity network in subclinical cognitive decline by functional magnetic resonance imaging.
- We have demonstrated how early-life exposures, including stress, and individual characteristics in young adulthood (e.g. intelligence) predict physical functioning, morbidity, and mortality across the lifespan.
- We have shown that statin treatment for elevated cholesterol displays a negative effect on skeletal mitochondrial respiratory capacity, which may be explained by the simultaneous finding of decreased Q10 content in the muscle. This is likely to be the mechanism for statin-induced myalgia, a well-known side-effect in statin treatment.

Theme III:

- We characterized a new DNA repair process that is required to maintain chromosomal 'fragile sites'.
- We have demonstrated mitochondrial dysfunction to be associated with cognitive decline and reduced subjective vitality.
- We have demonstrated that muscle mass and function deterioration (e.g. during periods of inactivity) can be counteracted by exogenous growth hormone and/or anti-inflammatory medication.

A.4: Selected publications: 2009-Sept 2016

Theme I

Jensen T, Bechschøft RL, Giacalone D, Otto MH, Bin Ahmad HF, Reitelseder S, and **Jespersen AP**. Whey protein stories. An experiment in writing a multidisciplinary biography. *Appetite* 285-294, 2016. Impact factor: 3.7

Summary: An interdisciplinary paper investigating one of the key entities in the CALM project, whey protein. The article reveals how whey scientifically is enacted as more than one single, coherent object, and the paper suggests that this amalgamate quality of whey (and thus studies of protein) not only opens up new interdisciplinary research questions, but also points to key issues in how to relate scientific knowledge and everyday life practices.

Dept./Faculties: Saxo Institute, Faculty of Humanities, Department of Biomedical Sciences, Faculty of Health and Medical Sciences, Department of Food Science, Faculty of Science.

Jespersen AP, Bønnelycke J, and **Eriksen HH**. Careful science? Bodywork and care practices in randomised clinical trials. *Sociology of Health and Illness* 35: 8, 2013. <http://dx.doi.org/10.1111/1467-9566.12094>. Impact factor: 2.0

Summary: Care practices are an inherent part of producing scientific facts but they are removed from the recognized results of scientific practice and thus from common public health recommendations. Knowledge about the strategic use of care practices in lifestyle interventions is important for public health initiatives and future efforts should incorporate this aspect, and suggest that broadening the focus to reflect everyday practices would foster better targeted public health campaigns.

Dept./Faculties: Saxo Institute, Faculty of Humanities.

Lassen AJ. Billiards, rhythms, collectives – billiards at a Danish activity centre as a culturally specific form of active ageing. *Ethnologia Europaea* 44: 57-74, 2014. BFI-credited: 2

Summary: Activities are culturally significant forms of practice, but this is often overlooked on active aging policies, which install a hierarchy between activities based on health factors. However, billiards occupy the men in the study for many hours a day due to its mild level of physical activity, thereby enabling a large dose of social activity and introducing physical activity under the radar.

Implications: The rhythm of billiards consists of both activity and passivity. This entanglement of activity and passivity could be used to develop other types of active aging policies that accept passivity as part of an active life in old age. The article has spurred a lot of media interest, nationally as well as internationally.

See for instance: Medicalxpress.com: <http://medicalxpress.com/news/2014-10-aging.html> and *Berlingske* (b.dk): <http://www.b.dk/sundhed/billard-og-en-bajer-er-ogsaa-sundhed>
Dept./Faculties: Saxo Institute, Faculty of Humanities.

Lassen AJ and **Jespersen AP**. Getting old and keeping going: the motivation techniques of active ageing in Denmark. In Lamb, S (ed.): *Successful Aging? Global perspectives on a contemporary obsession*. Rutgers University Press. May 2017, in print. Impact factor: N/A

Summary: In the realm of the Danish welfare state, active aging policies target every aspect of the lifestyle of old people and are not just about physical activity or diet, but also about social activity and mental health.

Implication: While active aging provides the answer that independence and activity are good for all, it does not answer what happens to those who cannot live up to the expectations of an active and healthy old age, and who might envision other ways of aging well. Thus, old age policies need to focus on more than barely activity regimes.

Dept./Faculties: Saxo Institute, Faculty of Humanities.

Lassen AJ and Moreira T. Unmaking old age – political and cognitive formats of active ageing. *Journal of Aging Studies* 30: 33-46, 2014. Impact factor 1.4

Summary: The policy concept of active aging is an attempt at unmaking old age by the EU and the WHO, by engaging in the plasticity of ageing in distinct ways based on different knowledge apparatus.

Implications: The diversity and comprehensiveness of active aging makes it adaptable to everyday life practices and thereby extensively changes the lives of older people.

Dept./Faculties: Saxo Institute, Faculty of Humanities, in collaboration with Durham University.

Mikkelsen HM. Unthinkable solitude: successful aging in Denmark through the Lacanian Real. *ETHOS*, 2016. *ETHOS*'s impact factor: 1.0

Summary: Based on fieldwork among healthcare workers and solitary elderly men in the rural area of southern Sealand, Denmark, this article lays out the Danish configuration of what has been called the paradigm of 'successful aging' and uncovers how the current discourse on successful aging frames solitude as 'loneliness'. By shedding light on one of the most taken-for-granted ideas within the field of gerontology and health care in general – that is, the value of social relations – the article seeks to reframe the debates on social inclusion and loneliness.

Dept./Faculties: Department of Anthropology, Faculty of Social Sciences.

Norredam M, Sheikh A, Dynnes Svendsen K, Holm Petersen J, Garvey LH, and **Kristiansen M**. Differences in hospital attendance for anaphylaxis between immigrants and non-immigrants: a cohort study. *Clinical & Experimental Allergy* 46: 973-80, 2016. Impact factor: 5.6

Summary: This Danish register-based study using nationwide data revealed fewer hospital attendances for anaphylaxis among non-Western immigrants compared to Danish-born.

However, this protection was lost with aging pointing to a need for adapting to ethnic diversity in anaphylaxis prevention and care.

Dept./Faculties: Department of Public Health, Faculty of Health and Medical Sciences.

Oxlund B. Living by numbers. The dynamic interplay of measurement technologies, asymptomatic conditions and preventive medication among older adults in Denmark. *Suomen Antropologi: Journal of the Finnish Anthropological Society* 37 (3), 2012. Impact: BFI-level of 1 and a ScoPus SJR value of 0.2

Summary: The article traces how numerical expressions of the body have become pivotal for the everyday practices of older adults and the work they perform on themselves. The findings have been widely disseminated in the Danish media and widely quoted in academic circles (14 quotes in Google Scholar/6 in Scopus/4 in SciVal).

Dept./Faculties: Department of Anthropology, Faculty of Social Sciences.

Rudkjøbing A, Olejaz M, Birk HO, Juul A, Hernández-Quevedo C, and **Krasnik A**. Integrated care: a Danish perspective. *British Medical Journal* (international ed.) 345: 445, 2012. Impact factor of 20.0 and ranked fourth among general medical journals.

Summary: The analysis describes the Danish health-care system's challenges in terms of integrating care.

Dept./Faculties: Department of Public Health, Faculty of Health Sciences.

Rudkjøbing A, Vrangbaek K, Birk HO, Andersen JS, and **Krasnik A**. Evaluation of a policy to strengthen case management and quality of diabetes care in general practice in Denmark. *Health Policy* 119 (8): 1023-30, doi: 10.1016/j.healthpol.2015.04.004. Impact factor: 2.2. Average health policy ranking.

Summary: The policy analysis showed the policy in question was unable to transform provision and financing of diabetes care in general practice. Policies needs to be carefully designed to avoid

unintended implications. Impact: The policy was subsequently abolished.

Dept./Faculties: Department of Public Health, Faculty of Health and Medical Sciences.

Theme II

Gow AJ, and **Mortensen EL**. Social resources and cognitive ageing across 30 years: the Glostrup 1914 Cohort. *Age and Ageing* 45: 480-486, 2016. Impact factor: 4.2

Summary: It has proven difficult to identify predictors of individual differences in cognitive decline. This study presents evidence that living without a partner and social isolation influence cognitive decline over a 30-year period.

Dept./Faculties: Department of Public Health and Department of Psychology, Faculties of Health and Social Sciences. Heriot-Watt University, Edinburgh, UK.

Hansen M, **Palsøe MK**, **Helge JW**, and **Dela F**. The effect of metformin on glucose homeostasis during moderate exercise. *Diabetes Care* 38: 293-301, 2015. Impact factor: 8.9

Summary: The study investigated the role of metformin on glucose kinetics during moderate exercise and found that metformin has a positive effect on glucose homeostasis during exercise.

Dept./Faculties: Department of Biomedical Sciences, Faculty of Health and Medical Sciences.

Hansen NL, **Lauritzen M**, **Mortensen EL**, **Osler M**, **Avlund K**, **Fagerlund B**, and **Rostrup E**. Subclinical cognitive decline in middle-age is associated with reduced task-induced deactivation of the brain's default mode network. *Human Brain Mapping* 35: 4488-4498, 2014. Impact factor 4.9

Summary: This study is one of the first to use draft-board IQ results as a basis for evaluating midlife cognitive performance. The results suggest a neurobiological basis for subclinical cognitive decline in late midlife, which includes task-induced deactivation alterations similar to the pattern seen in patients with AD and mild cognitive impairment. Hence, task-induced deactivation reduction might be suggested as an early marker for subtle cognitive decline in aging.

Dept./Faculties: Functional Imaging Unit, Diagnostic Department, Glostrup Hospital, Department of Public Health, Faculty of Health and Medical Sciences, and Research Center for Prevention and Health, Glostrup.

Larsen S, **Stride N**, **Hey-Mogensen M**, **Hansen CN**, **Bang LE**, **Bundgaard H**, **Nielsen LB**, **Helge JW**, and **Dela F**. Simvastatin effects on skeletal muscle: relation to decreased mitochondrial function and glucose intolerance. *Journal of American College of*

Cardiology 61: 44-53, 2013. Impact factor: 17.8

Summary: Statin treatment for elevated cholesterol displays a negative effect on skeletal mitochondrial respiratory capacity which may be explained by the simultaneous finding of decreased Q10 content in the muscle. This is likely to be the mechanism for statin-induced myalgia, a well-known side-effect in statin treatment. In addition, patients in statin treatment were shown to be glucose intolerant, increasing the risk of type-2 diabetes.

Dept./Faculties: Department of Biomedical Sciences, Faculty of Health and Medical Sciences.

Lund R, Mortensen EL, Christensen U, Bruunsgaard H, Holm-Pedersen P, Fiehn N, Molbo D, Jepsen E, Hansen ÅM, and Osler M. Cohort Profile: The Copenhagen Aging and Midlife Biobank. *International Journal of Epidemiology* 2015, doi: 10.1093/ije/dyv149. Impact factor: 7.5

Summary: Describes Copenhagen Aging and Midlife Biobank as a research infrastructure and presents selected findings. From earlier published papers based on CAMB. Implications: CAMB is known to the wider research community as an important research infrastructure.

Dept./Faculties: Department of Public Health, Faculty of Health and Medical Sciences and Department of Clinical Immunology and Center for Inflammation and Metabolism, National University Hospital, Copenhagen, Denmark.

Lund R, Nilsson CJ, and Avlund K. Can the higher risk of disability onset among older people who live alone be alleviated by strong social relations? A longitudinal study of non-disabled men and women. *Age and Ageing* 39 (3): 319-26, 2010. Impact factor: 4.2

Summary: Finds that older men living alone are at increased risk of functional decline, but that higher levels of social participation and satisfaction with social relations may alleviate this effect. The implications are that we have identified a vulnerable group in which preventive initiatives focused on social relations may be effective in preserving functional ability.

Dept./Faculties: Department of Public Health, Faculty of Health and Medical Sciences.

Mänty M, Mendes de Leon C, Rantanen T, Era P, Pedersen AN, Ekmann A, Schroll M, and Avlund K. Mobility-related fatigue, walking speed and muscle strength in older people. *Journal of Gerontology: Medical Sciences* 67A: 523-529, 2012. Impact factor: 5.5

Summary: Fatigue is an important early marker of functional decline among older people, but the mechanisms underlying this

association are not fully understood. This study demonstrates that mobility-related fatigue is associated with slower walking speed in older adults and the results suggest that muscle strength is one of the underlying factors explaining this association.

Dept./Faculties: Department of Public Health, Faculty of Health and Medical Sciences.

Osler M, Rostrup E, Nordentoft M, Mortensen EL, Bruunsgaard H, and Fagerlund B. Influence of early life characteristics on psychiatric admissions and impact of psychiatric disease on inflammatory biomarkers and survival: a Danish cohort study. *World Psychiatry* 14: 364-365, 2015. Impact factor 20.2

Summary: This is a lifecourse study of predictors of mental disease based on the Metropolit cohort. The findings suggest that low birth weight, low socioeconomic position and low intelligence early in life increase the risk of psychiatric disease, in particular alcohol and drug abuse which are strongly associated with inflammatory biomarkers and poor survival.

Dept./Faculties: Research Center for Prevention and Health, Functional Imaging Unit, Diagnostic Department, Glostrup Hospital, Glostrup, Department of Public Health, Faculty of Health and Medical Sciences and Department of Clinical Immunology and Center for Inflammation and Metabolism, National University Hospital, Copenhagen.

Rosenkilde M, Morville T, Riis AP, Kjaer K, Rasmussen H, Holst JJ, Dela F, Westerterp K, Sjodin A, and Helge JW. Inability to match energy intake with energy expenditure at sustained near-maximal rates of energy expenditure in older men during a 14-d cycling expedition. *American Journal of Clinical Nutrition* 102: 1398-1405, 2015. Impact factor: 6.7

Summary: The upper rates of energy expenditure (EE) and the corresponding regulation of energy intake (EI), as described in younger trained subjects, are not well elucidated in older subjects. This study of older men during prolonged cycling showed that the older male cyclists sustained near-maximal rates of EE during prolonged cycling but were unable to upregulate EI to maintain energy balance. Despite the presence of increased motivation to eat, a more profound counteracting physiological stimulus inhibiting increases in EI was present.

Dept./Faculties: Department of Biomedical Sciences, Faculty of Health and Medical Sciences.

van de Vijver PL, van Bodegom D, and Westendorp RG. Early and extraordinary peaks in physical performance come with a longevity cost. *Aging (Albany NY)* 8 (8): 1822-1829, 2016. Impact factor: 6.4

Summary: This is the first time a life history trade-off between physical performance and longevity has been found in humans. It deepens our understanding of how early development influences the variation of longevity. Featured in *The Sunday Times*, 31 August.

Dept./Faculties: Department of Public Health, Faculty of Health and Medical Sciences.

Theme III

Scheibye-Knudsen M, Mitchell SJ, Fang EF, Iyama T, Ward T, Wang J, Dunn CA, Singh N, Veith S, Hasan-Olive M, Mangerich A, Wilson MA, Mattson MP, **Bergersen LH**, Cogger VC, Warren A, Le Couteur DG, Moaddel R, Wilson III DM, Croteau DL, de Cabo R, and **Bohr VA**. A high-fat diet and NAD⁺ activate Sirt1 to rescue premature aging in Cockayne syndrome. *Cell Metabolism*. 20: 840–855, 2014. Impact factor: 17.6

Summary: This study shows how dietary modulation could be a useful intervention for certain premature aging disorders.

Dept./Faculties: Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences.

Minocherhomji S, Ying S, **Bjerregaard VA**, **Bursomanno S**, **Aleliunaite A**, **Wu W**, **Mankouri HW**, Shen H, **Liu Y**, and **Hickson ID**. Replication stress activates DNA repair synthesis in mitosis. *Nature* 528: 286–290, 2015. Impact factor: 38.1

Summary: This landmark study redefines current dogma in the aging/genome stability field, and reveals a new DNA repair process operating in mitosis.

Dept./Faculties: Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences.

Desler C, **Frederiksen JH**, **Angleys M**, **Maynard S**, **Keijzers G**, **Fagerlund B**, **Mortensen EL**, **Osler M**, **Lauritzen M**, **Bohr VA**, and **Rasmussen LJ**. Increased deoxythymidine triphosphate levels is a feature of relative cognitive decline. *Mitochondrion* 25: 34–37, 2015. Impact factor: 3.6

Summary: This study involves multiple researchers from across CEHA, and reveals a novel potential ‘early warning’ biomarker that is associated with cognitive decline.

Dept./Faculties: Department of Cellular and Molecular Medicine, Department of Public Health, Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences.

Maynard S, **Keijzers G**, Gram M, **Desler C**, **Bendix L**, **Budtz-Jørgensen E**, **Molbo D**, **Croteau DL**, **Osler M**, **Stevnsner T**, **Rasmussen LJ**, **Dela F**, **Avlund K**, and **Bohr VA**. Relationships between human vitality and mitochondrial respiratory

parameters, reactive oxygen species and dNTP levels in peripheral blood mononuclear cells. *Aging* 5: 850–864, 2014. Impact factor: 6.4

Summary: This study involves multiple researchers from across CEHA, and reveals that dNTP imbalance and altered ROS production may contribute to loss of vitality during aging.

Dept./Faculties: Department of Cellular and Molecular Medicine, Department of Public Health and Department of Biomedical Sciences, Faculty of Health and Medical Sciences.

Maynard S, **Keijzers G**, **Hansen ÅM**, **Osler M**, **Molbo D**, **Bendix L**, **Møller P**, **Loft S**, **Moreno-Villanueva M**, **Bürkle A**, **Poulsen Hvitby C**, **Schurman SH**, **Stevnsner T**, **Rasmussen LJ**, **Avlund K**, and **Bohr VA**. Associations of subjective vitality with DNA damage, cardiovascular risk factors and physical performance. *Acta Physiologica* 5 (213): 156–170, 2015. Impact factor: 4.4

Summary: This study involves multiple researchers from across CEHA, and reveals that vitality correlates with lower abundance of spontaneous DNA breaks, and several parameters of physical performance.

Dept./Faculties: Department of Cellular and Molecular Medicine and Department of Public Health, Faculty of Health and Medical Sciences.

Maynard S, **Hejl AM**, **Dinh TST**, **Keijzers G**, **Hansen ÅM**, **Desler C**, **Moreno-Villanueva M**, **Bürkle A**, **Rasmussen LJ**, **Waldemar G**, and **Bohr VA**. Defective mitochondrial respiration, altered dNTP pools and reduced AP endonuclease 1 activity in peripheral blood mononuclear cells of Alzheimer’s disease patients. *Aging* 7: 793–815, 2015. Impact factor: 6.4

Summary: This study involves multiple researchers from across CEHA, and reveals novel potential ‘early warning’ biomarkers that are associated with Alzheimer’s disease.

Dept./Faculties: Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences.

Karlsen A, **Couppé C**, **Andersen JL**, **Mikkelsen UR**, **Nielsen RH**, **Magnusson P**, **Kjaer M** and **Mackey AL**. Matters of fiber size and myonuclear domain; does size matter more than age? *Muscle Nerve* 52: 1040–1046, 2015. Impact factor: 4.3

Summary: The paper deals with understanding the area of muscle cytoplasm that each myonucleus in a muscle cell can cover (myonuclear domain) with respect to aging and physical training. In fibers of similar size neither training nor age had any influence on myonuclear domain, but the fact that older muscle

had lower myonuclear domain was simply explained by the presence of a greater proportion of small fibers than in younger counterparts.

Dept./Faculties: Department of Clinical Medicine, Faculty of Health and Medical Sciences.

Heinemeier KM, Schjerling P, Heinemeier J, Møller MB, Krosgaard MR, Grum-Schwensen T, Petersen MM, and Kjaer M. Radiocarbon dating of adult human articular cartilage shows minimal collagen turnover in both healthy and osteoarthritic tissue. *Science Translational Medicine* 8: 346-56, 2016. Impact factor: 16.2

Summary: The paper demonstrates that turnover of collagen tissue in cartilage is only taking place in the younger years (<17yrs) and that the primary structure of cartilage is maintained until old age. Furthermore, the development of osteoarthritis does not accelerate turnover and is more a sign of tissue breakdown. Glucosaminoglycans are dynamic in nature and are ones that can modify water content of cartilage and thus explain the beneficial effects of e.g. moderate exercise.

Dept./Faculties: Department of Clinical Medicine, Faculty of Health and Medical Sciences.

Mackey AL, Rasmussen LK, Kadi F, Schjerling P, Helmark IC, Ponsot E, Aagaard P, Durigan JLQ, and Kjaer M. Activation of satellite cells and the regeneration of human skeletal muscle

are expedited by ingestion of non-steroidal anti-inflammatory medication. *The FASEB Journal* 30: 2266-2281. Impact factor: 5.5

Summary: This paper demonstrates that in muscle recovery and regeneration after damaging exercise the inhibition of inflammatory pathways can prove beneficial, and that this effect is coupled with the activation of muscle stem cells. Whether this accelerated recovery leads to optimal healing or rather fibrosis is not known, but it illustrates that inflammation plays a role in muscle regeneration.

Dept./Faculties: Department of Clinical Medicine, Faculty of Health and Medical Sciences.

Bieler T, Siersma V, Magnusson SP, Kjaer M, Christensen HR, and Beyer N. In hip osteoarthritis, Nordic walking is superior to strength training and home-based exercise for improving function. *Scandinavian Journal of Medicine & Science in Sports* In press 2016. Impact factor: 3.4

Summary: This paper demonstrates the beneficial effect of both strength training and Nordic walking upon clinical symptoms of hip osteoarthritis. Furthermore, Nordic walking was in the long run superior to other training types with regards to functional improvement in elderly patients with osteoarthritis.

Dept./Faculties: Department of Clinical Medicine, Faculty of Health and Medical Sciences.

A.5: Financial breakdown (2014-2015)

2014 Principal Expenditure Items, DKK					
	Research staff	Administrative staff	Equipment	Operational costs*	
Theme I	2,701,956	293,110	24,060	662,191	3,681,317
Theme II	3,675,964	1,050,007	49,862	3,211,926	7,987,758
Theme III	3,581,046	847,583	250,000	2,652,044	7,330,673
Communication/outreach	75,334	1,142,196	3925	464,338	1,685,793
Recruitment	963,572	258,915	0	400,069	1,622,556
Center Management & Administration	958,676	1,236,163	7601	698,097	2,900,537
Total	11,956,548	4,827,974	335,449	8,088,665	25,208,635
2015 Principal Expenditure Items, DKK					
	Research staff	Administrative staff	Equipment	Operational costs*	
Theme I	4,337,178	230,124	7060	1,235,538	5,809,899
Theme II	4,497,129	936.385	123,080	2,445,042	8,001,636
Theme III	3,863,066	938.209	0	1,370,650	6,171,924
Communication/outreach	24,094	1,764,528	716	378,708	2,168,046
Recruitment	1,659,096	33,365	0	790,507	2,482,968
Center Management & Administration	937,142	1,486,706	0	642,866	3,066,713
Total	15,317,704	5,389,317	130,856	6,863,311	27,701,187
External funding	Public	Private	Total		
2014	92,737,947	10,603,344	103,341,291		
2015	28,655,091	9,770,050	38,425,141		
2016 (Sept)	21,463,069	12,560,011	34,023,080		
Total	142,856,107	32,933,405	175,789,512		
* Includes 3.6% overhead					



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