

UNIVERSITY OF COPENHAGEN

# Center for Healthy Aging

# End Report CEHA III, 2019–2023

With this report we are finalizing the exciting and groundbreaking journey of Center for Healthy Aging (CEHA) towards becoming a world-leading interdisciplinary research center empowering people to live longer, healthier, and more meaningful lives. The report tells the story of CEHA III while naturally reflecting the previous work of CEHA I and II.

CEHA III facts in brief				
	CEHA III (2019–2023) – 5 yrs.	Entire CEHA I-III period (2009–2023) – 15 yrs.		
Center grant from Nordea-fonden	78 million DKK	378 million DKK		
External grants	>300 million DKK in addition to the Nordea-fonden center grant	>870 million DKK in addition to the Nordea-fonden center grant		
Publications	>750 peer reviewed	>2000 peer reviewed		
Completed PhD projects	60	193		
Postdoctoral projects	>100	>200		
Summer schools	IARU Summer School on Interdisciplinary Aspects of Healthy Aging (Held annually 2011–2021, except for 2020, where it was cancelled due to the COVID-19 pandemic) PhD Summer School on Mitochondrial Physiology (2013, 2015, 2017, 2019, 2023)			
International networks (selected)	International Alliance of Research Universities (IARU) Alliance for Healthy Aging Network on Basic and Translational Aging Research, with University of Groningen Medical Center European Institute of Innovation and Technology (EIT Health)			
Communication and outreach (selected)	2015–2023: Folkemødet (Bornholm) 2017–2023: Culture Night at the University of Copenhagen 2020–2023: Outreach project: From Work Life to Retirement 2023: Bloom Festival and Bloom Summer School International visits from Canada, Hong Kong, Brazil, Korea, the Netherlands			
Awards (selected)	Kirsten and Freddy Johansen Fondens Research Prize Young Investigator Award, British Society of Matrix Biology 1st Prize, Late Night PhD Talk, University of Copenhagen Association of PhDs			

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# **Executive summary**

The Center for Healthy Aging (CEHA) was established in 2009 to tackle challenges and opportunities associated with an aging population nationally and internationally. Because aging is the leading risk factor for nearly all major chronic diseases, living longer poses major economic, cultural, medical, social, and public health challenges for individuals, communities, and governments. CEHA was launched to generate the knowledge needed to better understand the aging process and develop strategies for harnessing biological, psychological, and social mechanisms to maximize not only lifespan but also the duration of healthy, high-quality life.

Aging research is multifaceted, encompassing molecular mechanisms, interactions between aging and the environment, and interactions between genes, lifestyle, and health. CEHA became an interdisciplinary research center that empowered people to live longer, healthier, more active, and more meaningful lives by translating the insights generated from research into clinical practice, policy, and public awareness.

CEHA evolved through three phases:

 CEHA I focused on frailty, with five research programs:
1) molecular aging, 2) neuroscience, 3) muscle and metabolism, 4) body and life, and 5) culture and society.

- CEHA II focused on energy and vitality and was organized around three research themes related to interdisciplinary dimensions of aging at the 1) cellular, 2) individual, and 3) community levels.
- CEHA III focused on stakeholder engagement, and interventions for healthy aging and was organized into three research tracks: 1) modifiable pathways of damage and repair in aging, 2) retirement and transitions, and 3) individualized health.

The key achievements of CEHA III can be categorized into the following themes: a) molecular determinants of healthy lifespan, b) exercise is medicine, c) psychological and societal dimensions of healthy aging, and d) maximizing societal impact.

To ensure that aging research becomes embedded at the University of Copenhagen (UCPH) and that it continues to be strong and relevant, the accumulated knowledge, collaborations, alliances, and experiences of CEHA will be integrated in the new interdisciplinary initiative named 'University of Copenhagen Collaborative Aging Research Initiative (UCPH-CARI)'. In addition, scientists will pursue projects and activities individually or in groups. Thus, aging research continues to be a strong strategic focus at the University of Copenhagen.

Professor Lene Juel Rasmussen Professor Maria Kristiansen Professor Michael Kjær Professor Karsten Vrangbæk Associate Professor Steen Larsen

# CEHA – facilitating longer, healthier, and more meaningful lives

### 1.1 Brief history

Nordea-fonden was both generous and visionary when the foundation recognized the importance of tackling the challenges and opportunities connected with an aging population. Nordea-fonden chose already in 2009 to support and invest in the establishment of Center for Healthy Aging (CEHA) as well as the long-term running of CEHA. The vision of CEHA was to become a world-leading interdisciplinary research center that empowers people to live longer, healthier, and more meaningful lives.

Together, we launched this initiative because longer lifespans in Denmark and other Western countries pose major challenges for healthcare, the economy, culture, and social institutions. CEHA was designed to tackle pressing questions: How can people live not only longer but also healthier, and how can communities, healthcare, and society prepare for these demographic changes? To answer these questions, **CEHA's mission was twofold:** 

- Develop and apply a common conceptual framework to understand the complex interplay of biological, psychological, social, and cultural factors that influence health and well-being at the individual and societal levels.
- 2 Translate the insights generated through this framework into health care and clinical practice, policy, and public awareness to promote healthy living and active aging.

To achieve this mission, CEHA brought together passionate researchers, healthcare and clinical professionals, and other key stakeholders from seven departments, three university hospitals, three faculties at the University of Copenhagen (UCPH), and municipalities and non-governmental organizations (NGOs) from across Denmark and beyond.

During its 15-year journey, CEHA significantly broadened its ambition, scope, impact, and crossdisciplinary synergies. The initial research programs of CEHA I (2009–2013) uncovered vital insights into ageassociated disease and frailty that served as steppingstones to three interdisciplinary themes in CEHA II (2014– 2018). CEHA II also expanded CEHA's focus to include promoting prevention and health in collaboration with Danish municipalities and launching an outreach and communication program.

CEHA III (2019–2023) scaled up CEHA's translational activities and engagement with key stakeholders to roll out medical and societal interventions. Active engagement and concrete partnerships with societal stakeholders—such as municipalities, apartment associations, patient and civil society organizations—was one of CEHA's most important impacts. CEHA researchers worked hand in hand with societal stakeholders to research interventions to improve the well-being of aging Danes. As a result, CEHA emerged early on as a leader of aging research and a key driver of societal change for healthy aging in Denmark and beyond.

### 1.2 Aging: a global societal challenge

Major demographic changes will occur globally as people live longer (Fig. 1). By 2050, 20 percent of the global population will be older than 60, and the number of people over the age of 80 will more than triple<sup>1</sup>. Average life expectancy increased over the 20th century and is expected to gradually approach 100 years during the 21st century. These developments pose major economic, cultural, medical, social, and public health challenges because aging is the leading risk factor for nearly all major chronic diseases<sup>2</sup>. Healthy aging has therefore

<sup>1</sup> Population Division, DESA, United Nations: https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/files/documents/2021/ Nov/undesa\_pd\_2002\_wpa\_1950-2050\_web.pdf

<sup>2</sup> Global status report on non-communicable diseases 2010, WHO: https://www.who.int/nmh/publications/ncd\_report\_full\_en.pdf

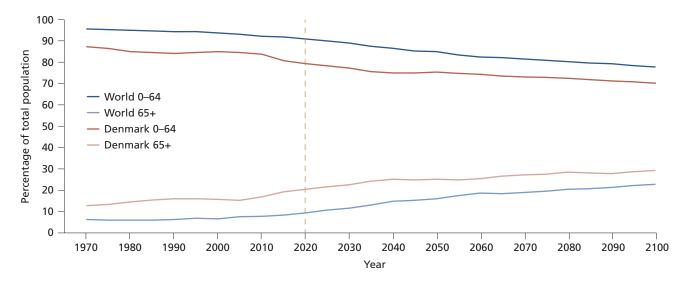


Figure 1: Historical and forecasted demographic changes in Denmark and globally. Source: Statistics Denmark

been designated an urgent priority by the World Health Organization (WHO) in 2020 <sup>3</sup>.

Active, healthy aging has also been proposed as a keystone for a sustainable Europe<sup>4</sup>. Danish policies and priorities reflect this approach to aging. For example, Danish welfare policies outline a range of intersectoral strategies to improve individual and structural factors that affect the ability to maintain health and live actively and independently into old age<sup>5</sup>.

Meeting this challenge requires a better understanding of not only the aging process per se but also ways to use this new knowledge to harness biological, psychological, and social mechanisms to maximize both lifespan and the duration of healthy, high-quality life. Increasing the number of active older individuals who can actively engage in civil society and the workforce would have tremendous positive impacts at the individual and community levels.

### 1.3 Aging: a multi-faceted scientific challenge

Understanding aging is a highly challenging scientific endeavor because the complex interactions between biological, social, psychological, and cultural dimensions (Fig. 2) need to be elucidated and translated into actionable know-how at the individual, clinical, policy, and community levels. The specific facets of this challenge include:

- 1 Establishing the intricate molecular mechanisms underlying the biology of aging to mitigate chronic diseases associated with increased age.
- 2 Uncovering the interactions between aging and the environment to enable a longer 'health span'—the

number of years that people can stay active and live without disability.

- 3 Translating laboratory findings into clinical practice and healthcare.
- 4 Mapping interactions between genes, lifestyle, and health to address the challenges of the aging population on the healthcare system.
- 5 Accounting for local community heterogeneity in aging policy development, as neighborhoods play central roles in individuals' health and the implementation of care.

Addressing this multifaceted challenge requires a concerted, interdisciplinary approach, which has been largely absent not only in Denmark but also globally – in fact, most efforts have been siloed in disciplines and/or tackled only one of the above dimensions.

### 1.4 CEHA's holistic research and translational strategy to address the complexities of aging

CEHA evolved into a leading interdisciplinary aging research initiative. What made CEHA unique was its exploration of the complex interplay between cellular, organismal, and societal factors that influence aging. This holistic perspective was essential for understanding the human aging process in all its facets. CEHA's development rested on six strategic pillars: interdisciplinarity, scientific excellence, a holistic framework, outreach and stakeholder engagement, challenging stereotypes, and capacity building.

At its interdisciplinary inception in 2009, CEHA brought together scientific excellence in biology, health sciences,

<sup>3</sup> 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.

<sup>4</sup> The European Commission, Healthy Ageing: keystone for a sustainable Europe:

https://ec.europa.eu/health/archive/ph\_information/indicators/docs/healthy\_ageing\_en.pdf

Social-, Bolig- og Ældreministeriet, Aftaletekst, Det Gode Ældreliv 2020: https://sm.dk/Media/637717030070118708/Aftaletekst\_Det\_gode\_aeldreliv\_dec2020\_t.pdf

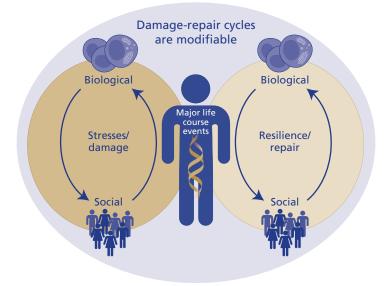


Figure 2: Understanding aging is a complex undertaking because of the intricate interplay between internal (i.e., biological) and external (i.e., social) factors.

medical sciences, social sciences, and humanities from universities around the world (Fig. 3). At the University of Copenhagen alone, researchers hailed from three disparate faculties that rarely interact: Health and Medical Sciences, Humanities, and Social Sciences. By bridging scientific, methodological, and cultural divides, CEHA crossed disciplinary boundaries and embraced an interdisciplinary research approach that has developed through the years. This approach allowed CEHA researchers to employ a

common, holistic framework to understand the complex interplay of biological, psychological, social, and cultural factors that influence health and well-being at the individual and societal levels.

In parallel, CEHA expanded outreach and stakeholder engagement by increasing its range of partners to include healthcare providers, patient organizations, municipalities, organizations for the elderly, and other key societal stakeholders (Fig. 2) while building multi-faceted



Figure 3: CEHA built a holistic, interdisciplinary framework for aging research and engaged with key stakeholders through effective communications, outreach, and interventions to translate our aging research know-how into clinical practice, awareness of key issues, policy-making, and other societal impacts.

communications capabilities. Involving different societal actors shaped CEHA's research and maximized its translation and impact and the generation of medical and societal interventions. A key factor in these efforts was challenging stereotypes related to ageism and offering strategies to mitigate these stereotypes.

Finally, through our capacity-building efforts and highquality educational program(s), CEHA trained the next generation of aging researchers in our holistic research framework and techniques for engaging with the media, citizens, and stakeholders.

### 1.5 CEHA III's strategic goals

CEHA III (2019–2023) harnessed the holistic framework developed in CEHA I & II to pursue a multilevel—individual, community, and society—approach to aging research (Fig. 3). Specifically, CEHA III pursued five strategic research and translational goals:

• Employing a systems approach encompassing the individual and societal levels and biological, cultural, ethical, and

psychological perspectives to understand aging.

- Developing a multifaceted understanding of the aging process through cutting-edge interdisciplinary research.
- Fostering healthy aging and awareness through meaningful stakeholder engagement.
- Challenging the negative public discourse on aging, frailty, and dependency by focusing the public's attention on the damage/repair, energy, resilience, intrinsic, and psychosocial (functional) capacities of healthy older people and those with chronic diseases.
- Providing new knowledge on human aging by intensifying jointly planned and executed research programs.

In this report, we describe some of the key achievements of CEHA III and briefly summarize progress in its preceding installments.

## **2** Research achievements

Below follows an overview of the rationale, developments, and key research achievements during CEHA's three grant periods (Fig. 4); please see Appendix A1 'Publication list' for detailed information.

### 2.1 CEHA I – focus on frailty

From 2009 to 2013, CEHA I's focus was conducting cutting-edge research on human health and aging under the common theme of frailty. The emphasis was on understanding how human behavior and lifestyle choices modulate life trajectories and health outcomes. Integrative biological studies investigated the basic biology of aging and connections between aging and the environment.

Crucially, CEHA I probed the links between genes, lifestyle, and health to identify mechanisms for developing and implementing diagnostic and/or preventive interventions to minimize health burdens associated with normal and accelerated aging and agingrelated chronic disease. CEHA I was therefore organized around five research programs (Fig. 4): 1) molecular aging, 2) neuroscience, 3) muscle and metabolism, 4) body and life, and 5) culture and society.

CEHA's approach to aging research was considered groundbreaking by our international review panel. To enable the development and implementation of interventions based on the generated understanding of the interplay of biology, health, and lifestyle, CEHA I built partnerships to translate laboratory findings into clinical applications. See section 3 for selected crossdisciplinary projects and their key outcomes.

### 2.2 CEHA II - focus on energy and vitality

The developments in CEHA I were a steppingstone to CEHA II (2014–2018), which developed strategies for disease prevention and health promotion while addressing the societal and cultural dimensions of aging via interactive projects involving Danish municipalities.

CEHA II aimed to uncover the mechanisms of aging at the societal and individual levels. A common theme in these research efforts was the importance of energy and the retention of vitality in its broadest sense for healthy aging and for society. We probed the significance of energy in aging processes, not only as it relates to individual bodies and processes at the cellular level but also in relation to psychological and social dimensions, including interest in one's surroundings and engagement with other people.

In doing so, CEHA II evolved from the initially mostly monodisciplinary approaches of CEHA I toward a framework organized around three research themes (Fig. 4) focusing on interdisciplinary dimensions of aging at the 1) cellular, 2) individual, and 3) community levels. CEHA II also established a Communication and Outreach Platform to put generated knowledge about healthy aging on the agendas of politicians and policymakers involved in health decisions and recommendations.

### 2.3 CEHA III – focus on stakeholder engagement, and interventions for healthy aging

The first aim of CEHA III (2019–2023) was to build on CEHA I & II to further evolve our interdisciplinary conceptual framework for understanding the complex interplay of biological, psychological, social, and cultural factors that influence health and well-being at the individual and societal levels (Fig. 4). To that end, CEHA III's research activities were structured along three tracks targeting damage-repair cycles that are modifiable by interventions (Fig. 2):

- Track I: Modifiable pathways of damage and repair in aging focused on the basic biology of aging, especially in skeletal muscle and brain.
- Track II: Retirement and transitions examined how behavior and social contexts interact to shape successful responses to critical transitions in later life.
- Track III: Individualized health pursued individual aspects of health and aging.

The second aim of CEHA III was to use big data to gain new insights into aging and increasing collaborations with key stakeholders and partners. Crucially, the holistic framework developed in CEHA I & II allowed us to actively engage with diverse stakeholders to develop interventions and

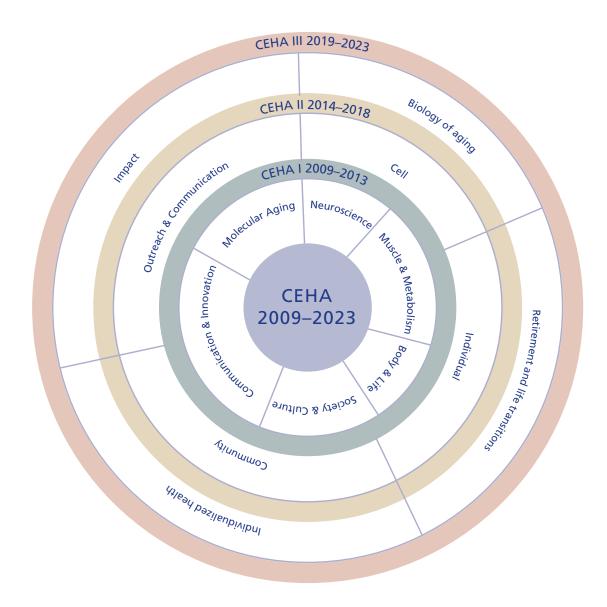


Figure 4: CEHA evolved rapidly, increasingly crossing and merging disciplines from medical and health sciences, social sciences, and humanities and pursuing a holistic framework for aging research capturing complex interactions at and between the cellular, individual, and community levels.

policies to promote healthy living and social participation in old age, thereby increasing CEHA III's communication, outreach, and impact. The next section describes key achievements of these research tracks in more detail, alongside major organizational developments.

### 2.4 CEHA III's research achievements

Molecular determinants of healthy lifespan. CEHA III significantly deepened our understanding of the molecular mechanisms governing the hallmarks of aging, that is, biological aging. Genes and biological pathways that contribute to health and lifespan were identified, and crucial biological elements essential for normal brain function were meticulously explored. In addition, advanced deep learning algorithms were successfully leveraged to predict various health outcomes in humans. These groundbreaking achievements not only paved the way for methods to measure biological age and identify biological clocks but also led to the discovery of novel drugs and interventions that enhance human health and extend lifespan. CEHA further catalyzed such research as a founding member of VitaDAO<sup>6</sup>, a distinguished investment community valued at 170 million USD that actively funds aging research in the academic and industrial sectors.

**Exercise is medicine.** CEHA III's research underscored the pivotal role of basic biological processes and interventions such as physical exercise in mitigating age-related deterioration. Our investigations provided compelling evidence for benefits of alternate-day fasting on glucose and lipid metabolism, especially among obese individuals and patients with type 2 diabetes. We determined how strength training counteracts aging-related declines of skeletal muscle mass, strength, and function and found that inflammation diminishes the positive effects of strength training. Importantly, CEHA III's research established that long-term resistance training can be seamlessly integrated into daily routines to improve

<sup>6</sup> https://www.vitadao.com/

muscle mass, strength, and mental well-being and reduce abdominal fat. Prolonged resistance training counteracts age-related loss in muscle function for years. Additionally, we innovated a simple yet effective method for enhancing muscle mass among the elderly population: walking down stairs. CEHA III's work strengthened the potent concept of 'exercise is medicine' by demonstrating the transformative effects of physical activity on overall health.

Psychological and societal dimensions of healthy

aging. To further unravel the complexities of aging, CEHA III probed its societal dimensions. We identified significant attitude shifts in retirement motivation and the perception of successful retirement in Europe, providing valuable input for policy debates. CEHA III's international collaborations demonstrated that technological solutions are relevant for community interventions among older citizen groups, as long as the social context of technology use is considered. Psychologically, aging is a life transition that influences both mental and physical health. We found that a positive intergenerational workplace climate correlates with higher levels of self-perceived healthy aging across age groups, paving the way for future studies on intergenerational dynamics to combat ageism. Additionally, research exploring responses to critical events (such as the COVID-19 crisis) highlighted the importance of trust, effective health communication, and policy interventions in managing health-related transitions in later life.

Maximizing societal impact. To maximize the societal impact of CEHA III's research, a structured partnership model fostering collaborations across sectors and perspectives was developed. This led to innovations such as play-based conversation games, which were developed with and implemented in community organizations, and tools enhancing person-centered care for use in clinical encounters, which were designed in collaboration with leading clinical scientists, e.g., Mayo Clinic (US). CEHA III also forged strategic partnerships in Danish life science to drive innovation and research in targeting chronic diseases and inequities associated with aging and instituted a joint strategic program with Edinburgh University on models of care for older adults. Collectively, these research initiatives not only deepened scientific understanding but also influenced policy, improved healthcare practices, and enhanced overall quality of life, marking significant strides toward a healthier, more active aging experience for individuals worldwide. The next section provides examples of such efforts.

## **B** Examples of major intervention studies, interdisciplinary research, and collaborative projects

Working across research disciplines and co-creating solutions with clinical and health practitioners was a cornerstone of CEHA from its inception. The following five examples of interdisciplinary research, collaborations and interventions are drawn from CEHA's 15-year history.

### 3.1 Copenhagen Aging and Midlife Biobank (CAMB, 2009–2023)

Project manager: Professor Rikke Lund

**Collaborators:** Steering group of CAMB plus numerous internal and external collaborators among more than 85 research projects

**Rationale and aims.** CAMB was founded with the broad and ambitious aim of enabling assessments of life course determinants of early and later aging. The database encompasses a multitude of biological, psychological, and social measures, and the latest data collection focused strongly on retirement expectations and experiences.

Activities. A comprehensive survey in Spring 2021 collected data from ~10,000 cohort members (response rate 40%). Several research projects addressing questions related to, for example, retirement, low-grade inflammation, and lifecourse social relations were also implemented. These projects combined CAMB data with national registry data to form a rich data source for investigating aging processes over time and across societal groups. CAMB researchers established close collaborations with a network of Nordic researchers with access to similar data sources. These collaborations enabled cross-national and valuable comparisons to countries with relatively similar health and elder care policies.

**Key achievements.** CAMB has given rise to 85+ research projects and 100+ publications, with more on the way. The valuable research infrastructure has provided new

knowledge on determinants of early aging. CAMB is led by a strong steering committee and aspires to secure infrastructure for future use, increase accessibility, and improve the sustainability of research resources.

### 3.2 Copenhagen Longitudinal Study of Male Cognitive Aging (COLOSMA, 2009–2023)

Project manager: Professor Martin Lauritzen Collaborators: Rigshospitalet and Glostrup Hospital

**Rationale and aims.** The clinical project COLOSMA is one of the longest running and most successful multidisciplinary CEHA projects. It investigates how aging influences cognitive functioning in a large cohort of 383 Danish men born in 1953. COLOSMA is one of the first studies to use draft board IQ results as a basis for evaluating midlife cognitive performance. The participants had similar IQ scores when their cognitive function was assessed at draft board examination (baseline) at age 18 but performed differently when data were collected at ages 58, 61–63, and 66–67. COLOSMA probed the biological and brain parameters driving this decline with the aim of developing novel strategies for diagnosing and preventing brain aging, thus promoting healthier late-life years.

Activities. Follow-up of the cohort identified several predictive markers of aging-associated cognitive decline. Rodent studies replicated the findings and provided important information on brain aging. Currently, a follow-up study is investigating the predictive markers by correlating structural findings from magnetic resonance imaging (MRI) with known genetic risk factors for cognitive decline. In addition, a new method combining electroencephalography (EEG) and MRI is being used to explore neurovascular coupling and how it may reflect cognitive differences. **Key achievements.** COLOSMA revealed that cognitive decline can be predicted with high sensitivity by recording changes in cerebral rhythmic activities evoked by complex visual stimuli. Differences in sleep quality, telomere length, and structural and functional MRI were observed between participants with preserved or decreased cognitive performance. Recent findings of decreased mitochondrial complex 1 activity and increased mitochondrial quality control is an initial event in brain aging. This knowledge is important for developing strategies to prevent age-related cognitive decline.

### 3.3 Live Active – Successful Aging (LISA, 2015–2035)

Project manager: Professor Michael Kjær Collaborators: Bispebjerg Hospital

Rationale and aims. Previous CEHA research showed that physical activity counteracts the processes by which reduced stem cell function, increased lowgrade inflammation, and altered cell interplay cause muscle loss with aging. In collaboration with Bispebjerg Hospital, the LISA project investigates how different types of training affect muscle function in a group of senior citizens. The aim of LISA is to provide rehabilitation and prevention practices, training guidelines, health recommendations, and knowledge to promote good exercise habits.

Activities. During the first year of the project, interventions involving healthy individuals and individuals with chronic disease were performed. A blinded assessor allocated each of the 451 participants aged 62–70 years to one of three groups: 1) supervised heavy resistance training, 2) moderate resistance training, or 3) non-exercise cultural activity. During a 20-year period, the effects of the specific intervention on physical ability are surveyed, and detailed physical and cognitive assessments and annual MRI scans of the brain and thighs are performed.

Key achievements. So far, the results have demonstrated that high-intensity resistance training is feasible in elderly individuals and improves muscle mass and strength. Moderate-intensity resistance training also improves muscle mass and strength, albeit to a lesser degree than high-intensity resistance training. Furthermore, one year of strength training reduces body and abdominal fat mass and stimulates the release of anti-inflammatory cytokines, such as interleukin 6. After 4 years, 370 participants remained in the study, and the gain in muscle strength due to the high-intensity resistance training caused a maintenance of strength from 66 to 70 years of age, indicating a long-term effect of the training even if training was not fully continued. The LISA project will continue with measurement of all participants every 3 years.

### 3.4 From work life to retirement (FATS, 2020–2023)

Project manager: Professor Lene Juel Rasmussen/Emilie Johansen

**Collaborators:** Municipalities of Aarhus, Vejle, and Vordingborg and local stakeholders, for example, trade unions, the DanAge Association, and companies with many employees in the target group

Rationale and aims. Every year, approximately 40,000 Danish citizens retire from the active workforce. While some enjoy the freedom and quickly fill their days with various activities, many find the transition difficult. A weakened sense of identity and direction, often combined with reduced physical and social activity, causes their health and well-being to suffer. To address this, CEHA researchers in the humanities and health sciences collaborated with the municipalities of Aarhus, Vejle, and Vordingborg in a comprehensive outreach and intervention project (FATS) to develop scalable formats that support seniors in preparing for and maintaining a healthy, meaningful pensioner life. The outcome was a series of evidence-based recommendations and concepts for inspiration and replication in other Danish municipalities and the national retirement agenda.

Activities. The target group was seniors with little or no education. Over the project's lifespan, approximately 4000 citizens were enrolled (for example, as senior ambassadors, test persons, volunteers, or participants in activities). Through co-creation and involvement, the project defined and tested formats for peer mentoring and local activities involving exercise, social events, volunteer work, and activities at the seniors' (former) workplaces.

**Key achievements.** During its 3-year project period, FATS engaged with more than 5,000 senior citizens, many local stakeholders, and volunteers via the development and testing of initiatives. FATS generated a series of interventions targeting seniors, senior ambassador programs, general meetings, local information campaigns, a knowledge festival, experience conferences, and brochures for inspiration. Many of these programs have been implemented in the municipalities and are inspiring senior policy development by other municipalities.

### 3.5 SlowAge (2021-2024)

Project manager: Associate Professor Morten Scheibye-Knudsen Collaborators: Elysium Biotech

**Rationale and aims.** With a difference between the body's chronological age, i.e. the birth age, and the biological age, i.e. age based on the health condition of the body, the SlowAge aimed at 'hacking' the body's biological age, thereby reducing it and live longer, healthier lives. SlowAge was an open-label randomized clinical trial.

Activities. Eighty healthy elderly individuals over the age of 65 were recruited and assigned to a 12-week intervention protocol to examine the effect of 1) 5 hours of moderate physical exercise per week, 2) 16 hours of fasting per day, 3) supplementation with 2 g of nicotinamide riboside per day, or 4) control. Although the study is complete, we are still analyzing data and performing DNA methylation analysis for age prediction.

**Key achievements.** The main and perhaps most surprising finding is that the fasting group had by far the greatest changes in health markers: 12% loss of fat (without significant muscle or bone loss), reduced resting heart

rate, and a highly significant age-related reduction in biological age. We found little evidence of age-reducing effects of exercise and nicotinamide riboside in healthy elderly, although nicotinamide riboside did reduce levels of interleukin-6, which is an age-associated marker of inflammation. In sum, fasting appears to be beneficial for elderly individuals and represents an easily implementable intervention that could have profound effects on individual and societal health.

SlowAge has received widespread attention in media and in the public. Following a short documentary on a national public service channel, intermediate fasting is getting increasingly popular in the general population.

## **4** Communications, outreach, and engagement

To maximize impact, CEHA has always prioritized research communication, stakeholder relations, and public engagement. Accordingly, CEHA liaised with the health and care sectors, municipalities, patient and interest organizations, and policy makers through collaborations, public debate, research dissemination in the form of press releases and events, networks, councils, think tanks, and strategic meetings. CEHA's excellence in aging research has been translated into social and clinical practice through intervention studies (section 3), outreach and communication (sections 3–5), training (section 5), and collaboration (section 6).

### 4.1 Increasing visibility during CEHA I (2009–2013)

CEHA I focused on providing research insights to a broad audience by building a strong media and online presence and organizing and participating in aging research awareness:

 CEHA websites (in Danish, https://sundaldring.ku.dk, and English, https://healthyaging.ku.dk). The Danish version primarily targeted employees in elder-focused organizations, health professionals, and politicians, while the primary target groups of the English site were researchers, foundations, students, and international partners. provided a forum for advice, awareness, and debate about healthy aging and for CEHA branding.

- EU Year for Active Aging, 2012, which put healthy aging on the public agenda. CEHA participated in aging-dedicated conferences, public meetings, lectures, exhibitions, and a science theater. This kicked off CEHA's continued engagement in a wide range of outreach activities.
- CEHA research was featured on Danish national television. For example, channel DR2 aired the documentary series 'Fauli, Fat and Finished?', which showed physiological and clinical experiments designed and supervised by CEHA researchers.

### 4.2 Strengthening outreach during CEHA II (2014–2018)

CEHA II dedicated more resources to outreach and communication with the aim of placing knowledge of healthy aging on the public agenda and providing research-based recommendations to decisionmakers and citizens. To that end, we initiated our Communication and Outreach platform. Highlights from these efforts include:

- Medical Museion and CEHA researchers created engaging exhibitions with surprising, dialoguestimulating perspectives on aging, e.g., the 'Kintsugi— Golden Body Repair' exhibition (Fig. 5), which later
- CEHA Facebook page. This page targeted the public and



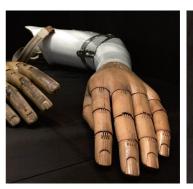




Figure 5. Items displayed at the 'Kintsugi—Golden Body Repair' exhibition at the Medical Museion.

became the basis of an awareness project integrated in the education of future healthcare professionals.

- The 'Life on the Line' game was based on CEHA research outcomes and launched at Medical Museion. It was played at Folkemødet on Bornholm, the science fair 'Science in Forum 2018' for primary and secondary schools, PKA Pension's 'Pension's Day', and the University of Konstanz (Germany), among others.
- CEHA hosted more than 100 research dissemination events at UCPH. Folkemødet on Bornholm, the Danish Science Festival, and various stakeholder venues. Creative dissemination formats—such as cross-disciplinary science slams in which three researchers from different fields presented their most important points in 3 minutes each—were a hit among both guests and researchers.
- Public events on social media, for example, videos on becoming older starring the comedienne and author Hella Joof.
- The separately Nordea-funded project 'Keep Your Brain Healthy' was developed in close collaboration with Danske Gymnastik- og Idrætsforeninger (DGI) and the Agency for Culture and Palaces and aimed at seniors aged 55-75 years. The project combined physical, mental, and cultural activities and lead to coach education in SMART training.
- Together with the DaneAge Association (Ældresagen), CEHA arranged joint events at Folkemødet in 2015–2018 and published a series entitled 'The Good Life' in the Danish newspaper Politiken.

### 4.3 Consolidating pathways to impact during CEHA III (2019-2023)

CEHA III built on the successes, experiences, frameworks, and collaborations from CEHA I & II to consolidate clear pathways for impact (Fig. 6), where were pursued in full in 2019–2023. CEHA III engaged stakeholders in various ways with the aim to disseminate our latest research findings to the public. Highlights of these efforts include:

- Contributing to more balanced rhetoric in the aging debate in Denmark through mass media (for example, Altinget, Dagens Medicin, and Berlingske) and ongoing dialogues with various stakeholders: the National Association of Municipalities, PFA Pension, the DaneAge Association, the Minister for Social Affairs and Senior Citizens, and several foundations and patient organizations.
- Hosting official visits by stakeholders from, e.g., the public sector and universities from Hong Kong, The Netherlands, Canada, and Brazil in 2023.
- Participating in political hearings on topics related to the elderly and helping to shape legislation concerning, e.g., social services, quality of homecare standards, preventive homecare, dignity standards in eldercare, and the use of digital communication tools with the elderly. Because of these engagements, CEHA earned a place in Tænketanken for Fremtidens Velfærd (Thinktank for Future Welfare).
- Contributing to a wide range of councils, international research networks and forums, advisory boards, and think tanks to shape the public discourse on aging and related matters; please see Appendix 2 'Expert Panel Memberships' for detailed information.

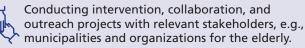
Non-academic activities included talks and presentations at public and private hospitals, societies, associations, and organizations and for the public, such as:

- The annual Copenhagen Culture Night at UCPH, 'Minilab – How old are you?'
- The Faculty of Health and Medical Sciences public lectures, 'Talks of the Top'
- Talk and guided tour for >120 general practitioners, 'What do they do at Panum?'
- Contributions to podcasts
- Talk at The Danish Patient Safety Authority
- Talks at Folkeuniversitetet
- Participation at Folkemødet on Bornholm
- Participation at Bloom Festival and School



Pathways to impact

Producing research results that increase the understanding of aging process at the cellular, organ, individual, and societal levels.





Participating in ongoing dialogue with stakeholders such as politicians, interest organizations, foundain tions, and people in the health and care sectors.

Educating future aging experts to help solve society's aging-related challenges.

Contributing to research-based guidelines and policy documents to improve people's quality of life.



(( $\phi$ )) Communication to the society to qualify public discourse with the newest research-based knowledge.

Figure 6. Pathways to impact during CEHA's history.

## **5** Capacity building during CEHA I-III

Another strategic priority of CEHA was building capacity for research and translation by educating the next generation of aging researchers. This was accomplished by 1) providing high-quality educational resources to students and trainees via lectures, online courses, and mentorships; 2) organizing research training via summer schools, networks, and the PhD Academy; 3) recruiting excellent junior and senior scientists with relevant expertise for CEHA's interdisciplinary ambitions; and 4) securing additional external funding to enable worldclass research and the training of future researchers.

### 5.1 Education

From its inception in 2009, CEHA trained students across all levels—pre-graduate, bachelor, masters, PhD, and research assistants—and postdoctoral researchers in agingrelated disciplines. Table 1 shows the extend of training of students and early-stage researchers during CEHA III.

CEHA's portfolio of educational activities expanded over the years. The initially offered PhD courses were complemented by new summer schools, bachelor's/master's/ PhD courses, and a massive online open course (MOOC) focusing on aspects of healthy aging, interdisciplinarity, and innovation (Table 2 and section 5.2). All educational programs included undergraduate- and graduate-level courses on aging. These courses were conducted by all faculties contributing to CEHA and were embedded in the respective departments' course offerings.

### 5.2 Research training and networking

Research training. CEHA also heavily promoted and invested in developing new talent in aging research. For example, CEHA supported local early-career researchers under the auspices of UCPH and developed specific research application support services for early-career researchers from abroad. These early-career researchers were encouraged to apply for independent research grants or fellowships and to become affiliated with CEHA. Funding was secured from many Danish funders (for example, the Lundbeck and Novo Nordisk Foundations) and international funding programs (for example, the European Research Council's Marie Skłodowska-Curie Actions). Through these activities, CEHA fostered the brightest young minds in aging research and exposed early-career researchers to a variety of outreach tasks, built their capabilities to engage in public dialogue and dissemination, and created opportunities for collaboration with external stakeholders.

Furthermore, we developed several initiatives to scale up our training and network ambitions:

Massive open online courses (MOOC). To rapidly increase the number of future experts in the field of aging research, we created multiple MOOCs targeted at an international audience. One MOOC, 'Alive and KICking', focused on innovative solutions to aging-related challenges and was attended by participants from around the world. Another one, 'Business Models for Innovative Care for Older People', introduces learners to healthcare innovation within the field of healthy living and active aging and has been attended by several thousand internationally.

Table 1: Number of individuals in various categories trained during CEHA III (2019–2023).						
Trainee category	2019	2020	2021	2022	2023	
Pre-graduate, bachelor, masters	53	59	59	30	27	
Research assistants	14	14	10	8	7	
PhD students	49	55	52	36	38	
Postdoctoral researchers	31	31	30	36	31	

### Table 2. Number of pre- and post-graduate educationalactivities in 2021–2023.

Educational activity	2021	2022	2023
PhD courses	3	1	4
Other post-graduate activities	8	8	7
Master-level courses and teaching	18	15	13
Other pre-graduate level activities	34	34	32

Table 3. Additional external funding.			
Year	Mio DKK		
2019	76,5		
2020	74,3		
2021 Jan–Aug	38,8		
2022	39,2		
2023	104,3		

International Alliance of Research Universities (IARU) Summer School: Interdisciplinary Aspects of Healthy Aging. Several summer schools were held to disseminate cuttingedge advances in aging research and bring together researchers and doctors. A prominent example is the IARU Summer School 'Interdisciplinary Aspects of Healthy Aging', which was part of the IARU Courses initiative (previously known as the IARU Global Summer Program). This summer school at UCPH was devised as an intensive series of lectures and seminars by CEHA staff and internationally recognized scientists on all aspects of aging research. The summer school lasted for 3 weeks and was open to students from around the world. The course provided students with opportunities to explore diverse research methods across disciplines, with an emphasis on interdisciplinary approaches spanning from the cellular to the societal level; to get to know CEHA faculty; and to interact with students from all over the world.

At the end of the summer school, the students prepared a sample grant application under the supervision of course faculty. This required the use and/or consideration of interdisciplinary research methods and provided handson experience with the process of developing a research program or agenda addressing critical questions or problems in the study of aging.

Network for Young Scientists (NYS). Young researchers affiliated with CEHA were connected via the NYS, which was initiated in 2010 as a platform for interactions between research assistants, PhD students, and postdoctoral researchers and to promote educational and research activities in the field of aging. In 2020, the NYS began arranging a principal investigator (PI) lunch series in which young researchers met with the center's affiliated Pls to discuss career development in an informal setting. These events attracted many participants from across CEHA. NYS was key to promoting student engagement in CEHA's research fields and building international networks.

**PhD Academy for Interdisciplinary Aging Research (PAIAR).** Through PAIAR, CEHA developed and organized high-level, internationally recognized, interdisciplinary PhD courses in the field of aging research. The courses primarily targeted CEHA's PhD students but they were open to students at UCPH and other universities within and outside Denmark.

### 5.3 Recruitment and career development

To recruit the best talent, CEHA developed a careerflow program to ensure that the center's considerable investment in aging research capacity was put to the best possible use, both within and outside UCPH. Pls at CEHA contributed by 1) identifying promising PhD students and postdoctoral researchers who demonstrated excellence in aging research, 2) mentoring them, and 3) supporting their efforts to secure extended or permanent employment in their home departments. Such interventions included holding meetings with department heads and/or providing teaching opportunities, pedagogical training, and mentorship programs for early-career scientists.

### 5.4 External funding

Nordea-fonden's generous grant and long-term support of CEHA has initiated interdisciplinary aging research at the University of Copenhagen and elevated the quality of aging research in Denmark. This has had a significant impact on the healthy aging agenda nationally and on how to handle the demographic challenges of an increasingly aging population. With CEHA as a frontrunner within interdisciplinary aging research, it also paved the way for obtaining grants for other aging projects and initiatives (Table 3). Examples of grants and projects reaching into the future include:

- Postdoc grant for a project on the correlations of type 2 diabetes mellitus with depression and age-related cognitive impairment (The Lundbeck Foundation, 2023–2026).
- The Challenge programme investigating the use of big data to solve societal challenges of aging (Novo Nordisk Foundation, 2018–2024).
- Grant for research on the aging of the human brain and the correlations of hearing loss and hearing aid use with cognition (Demant Foundation, 2023–2026).
- Grant for a project on the effects of exercise on glucose metabolism and mitochondrial function in patients with type 2 diabetes (Novo Nordisk Foundation, 2021–2024).
- Grant for a study of the effect of strength training on muscle strength and mitochondrial function in the elderly (Asiros Nordic, 2023–2025).
- Several ongoing projects related to chromosomal instability and the development of age-related human diseases, e.g. Werner's syndrome. For example, folate deficiency, which is common in the elderly, leads to destabilization of the human genome (Danish National Research Foundation, 2015–2025).
- 'Making Care Fit', a partnership for person-centered treatment and care in the health services between CEHA, Mayo Clinic (US), and a wide range of patient organizations, hospitals, and healthcare managers across several countries.
- Grant for characterizing the role of the conserved longevity gene OSER1 in aging (Novo Nordisk Foundation 2024–2025).
- Grant for a project on developing innovative strategies for the prevention and management of non-communicable diseases that arise as complications during the post-acute phase of COVID-19 (EU Horizon Health 2023 2024–2027).

# **6** Research collaborations and networks

CEHA actively collaborated with several institutions and networks in Denmark and around the world (Fig. 7). In addition to providing scientific and outreach advantages, these collaborations stimulated the mobility of researchers and students and played a key role in the recruitment of researchers at all levels. Below, we describe some of our major formal collaborations—CEHA researchers also participated in many ongoing, topical, or ad-hoc research networks.

#### 6.1 International collaborations

**International Alliance of Research Universities (IARU).** The University of Copenhagen and CEHA are closely linked with the prestigious IARU<sup>7</sup>, an international

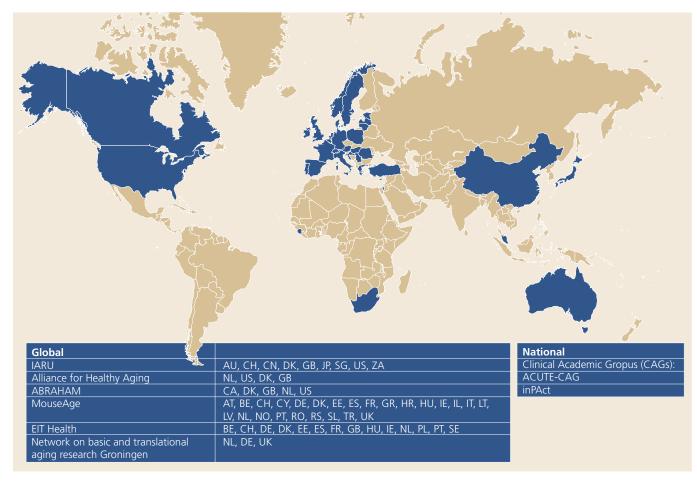


Figure 7: Major national and international collaborations and networks that CEHA participated in.

7 http://www.iaruni.org

alliance of research universities (Fig. 7) that functions as a forum for collaborations and promoting the research activities of member universities. The association of CEHA with IARU was a cornerstone of efforts to internationalize the center and provided valuable networking opportunities for CEHA members.

A crucial component of the CEHA–IARU collaboration was the joint research initiative IARU Aging, Longevity & Health (ALH), which started in 2006 with the aim of increasing engagement across IARU campuses and promoting joint activity and funding opportunities for IARU ALH participants within the international aging research community. In 2012 and 2023, CEHA hosted the IARU ALH Conference in Copenhagen. In 2023, the IARU early-career research (ECR) network was launched.

As part of the IARU collaboration, CEHA established several important research collaborations with researchers at Oxford, Cambridge, and Australian National University and hosted an annual summer course called 'Interdisciplinary Aspects of Healthy Aging' (see section 5.2). Another IARU-instigated collaboration was the IARU online course 'Sustainable Aging', which was initiated in 2020 by CEHA and the University of Tokyo. The course primarily targeted students from IARU universities but was open to students from other universities.

European Institute of Innovation and Technology (EIT) Health (2014–2022). CEHA participated in EIT Health, a consortium of EU partners founded to promote entrepreneurship and develop innovations in healthy living and active aging to provide Europe with new opportunities and resources to improve quality of life and healthcare. EIT Health consists of more than 50 core partners and their 90 associate organizations. These include leading businesses, public partners, research centers, and universities (including UCPH) from nine EU countries.

CEHA was involved in several EIT Health activities:

- 'Innovating Solutions for Aging Populations' was a summer course developed in collaboration with the Copenhagen Business School, Novo Nordisk A/S, and the innovation and entrepreneurship hub SUND Vækst (2016).
- BRIDGE—a network involving UCPH, Copenhagen Business School, Uppsala University, and Erasmus University Rotterdam—was set up to share and implement pedagogic and digital didactic practices in connection with a summer school at each campus (2017).
- 'Healthy Aging in 6 Steps' was a MOOC on healthy environments and citizen involvement that CEHA developed and delivered in collaboration with the Leyden Academy on Vitality and Ageing and Delft University of Technology (2017).
- EIT Health Ageing PhD School sought to promote true integration of the knowledge triangle through advanced teaching of aging-related PhD training and fostering science-based innovation and entrepreneurship skills in Europe.

CEHA researchers further participated in the EIT Health project iPDM-GO (2019–2021) in collaboration with Roche Diabetes Care and academic partners in Denmark and Germany. The project aimed to develop a personalized, digitally supported diabetes management program and to demonstrate its implementation in Danish regions and municipalities with aging populations.

Alliance for Healthy Aging (2019–2024). CEHA joined the Alliance for Healthy Aging in 2019. Founded by the Robert and Arlene Kogod Center on Aging at Mayo Clinic (US), University Medical Center Groningen, University of Groningen, the Noaber Foundation (Lunteren), and Vita Valley (Ede) in the Netherlands, the alliance's aim is to provide a forum for scientists, clinicians, and engineers to exchange ideas through a series of annual meetings dedicated to translational research on aging. The first meeting was held in June 2010. Titled 'The Next Step in Aging Research: From Bench to Bedside: A Forum for Collaboration between Clinicians and Researchers', it focused on the basic biology of aging and its relationship with clinical practice. The meeting was a resounding success and was followed by annual meetings. CEHA hosted the 13th international meeting on August 25–27, 2023, at the University of Copenhagen.

National Institute on Aging at National Institutes of Health (NIA/NIH). CEHA actively collaborated with NIH/NIA, another pioneer in aging research. CEHA was represented by Professor Vilhelm Bohr who was instrumental in CEHA's establishment and has been an active group leader during CEHA I-III. This collaboration enhanced CEHA's ability to recruit accomplished scientists, such as Professors Ian Hickson and Linda Bergersen and Associate Professor Morten Scheibye-Knudsen.

### 6.2 National collaborations

From the outset, CEHA worked diligently to engage with organizations for the elderly, municipal decision-makers, healthcare professionals, and selected patient organizations (see also sections 3–5). CEHA organized events, workshops, seminars, and lectures, e.g., at Folkemødet in 2016–2019 and post-COVID in 2022 and 2023, to promote its aging research know-how. These strong communication efforts and work with stakeholders paved the way for new types of collaborations integrating research, communication, and implementation. CEHA's stakeholder strategy provided a framework for engagement and external collaborations in the last 5 years, such as the following:

**Partnerships.** CEHA established long-term strategic partnerships across a range of public, private, and civil spheres, for example, with University College Copenhagen (KP); Pensionsforsikringsanstalten (PFA); and the Lighthouse Life Science partnerships involving all municipalities in the Capital Region, the Capital Region, Novo Nordisk A/S, Lundbeck A/S, Greater Copenhagen Office, Danish Life Science Cluster, PensionDanmark, Copenhagen Capacity, and Kommune Kontakt Rådet. All these partnerships were aimed at facilitating the implementation and scaling of the science and interventions generated by CEHA. In 2023, CEHA became a member of Denmark's first National Partnership against Loneliness. The Partnership, which was facilitated by the DaneAge Association (Ældresagen), Red Cross Denmark, and the Ministry of Social Affairs and Senior Citizens, presented Denmark's first national strategy and action plan against loneliness, co-signed by CEHA, to Minister of Social Affairs and Housing Pernille Rosenkrantz-Theil.

**Collaborating with municipalities.** Much of CEHA's research was done in dialogue with citizens and with professionals working to create a good framework for citizens' healthy aging. Municipalities were the natural collaborative partners because they have political responsibility for many of the areas that affect healthy aging. The project 'From Work Life to Retirement (FATS)' (see 3.4 above) is an example of these municipal collaborations.

Connecting national researchers to solve complex issues. To bring aging-related university research, clinical research, and clinical practice closer together, CEHA researchers chaired and participated in two clinical academic groups (CAGs) hosted by the Greater Copenhagen Health Science Partners, a partnership between the University of Copenhagen, the Technical University of Copenhagen, Region Zealand, and the Capital Region of Denmark. The CAGs are forums for close collaboration between university and hospital researchers, enabling participants to learn from each other and develop new ideas for rapid scientific progress and improved patient treatment. CEHA contributed to the ACUTE CAG and the CAG on Physical Activity and Sports in Clinical Medicine, which focused on improving acute treatments for people suffering from multimorbidity and on using physical activity to prevent and treat chronic diseases and prolonged injuries, respectively.

# Future perspectives – embedding aging research at the University of Copenhagen

The launch of a new cross-faculty research initiative in 2025 will help to embed and further strengthen aging research at UCPH. This initiative, the University of Copenhagen Collaborative Aging Research Initiative (UCPH-CARI), will build on the successes and experiences of CEHA I-III and expand the critical mass of aging researchers, research results, innovations, and infrastructure and activities established by CEHA over the years. Crucially, UCPH-CARI will develop activities and research projects in a bottom-up, collaborative, and inclusive process that brings together researchers from across UCPH as well as external partners and focus on stakeholder engagement. Several CEHA researchers hold external grants and participate in ongoing international projects that can be incorporated into UCPH-CARI. Furthermore, CEHA researchers contribute to and manage cohorts that can be used for future research projects in the interdisciplinary activities of UCPH-CARI.

A bottom-up approach to identifying cross-disciplinary/ sectoral challenges and mission-driven research. A key aspect of UCPH-CARI will be a continued focus on initiating, facilitating, and supporting innovative, interdisciplinary mission-driven aging research. Missiondriven research that can fully address the multi-faceted complexities and challenges of aging is a natural progression of the interdisciplinary framework developed during CEHA I–III and is in line with the European Union's mission-focused Horizon Europe framework program, where "EU Missions are a new way to bring concrete solutions to some of our greatest challenges."<sup>8</sup> We will develop these missions and embed related activities and projects in a bottom-up process with broad involvement of UCPH's researchers and in close strategic partnerships with a wide range of actors from the public and private sectors and civil society. This approach will further strengthen and facilitate existing and new cross-sectoral collaborations that bring researchers and stakeholders together on specific aging challenges that require interdisciplinary research, positioning UCPH as a leading contributor to groundbreaking research and evidence-based policy and practice in the aging area.

Scaling innovation for impact. Finally, in addition to further developing and expanding our training and education efforts for professionals and students in the fields of health and social care, we will scale up our research solutions and interventions. For example, we will explore digital solutions and new welfare technologies to significantly boost the effectiveness of approaches to prevention, treatment, community empowerment, and intergenerational involvement.

The interdisciplinary mission-driven aging research approach of UCPH-CARI, in collaboration with practitioners, policymakers, and companies, will focus on research, innovation, translation, and implementation of impactful solutions for key aging-related challenges. UCPH's innovation ecosystem will be instrumental for generating state of the art research as well as transformative know-how and interventions that promote meaningful aging that inform policy and practice in aging societies in Denmark and across the globe.

<sup>8</sup> https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/eu-missions-horizon-europe\_en

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