Activity report 2017–2019









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Aging Research Center

A multidisciplinary center devoted to the study of aging and health



Our mission...

...is to improve the health and well-being of older individuals by contributing to the understanding of the aging process from a biomedical, psychological and sociological perspective in relation to life-long social and physical contexts.

ARC conducts research and education and spreads research findings within and outside the scientific community.





Photos: Victor Celis Schüberg, Ian Gadelius and Erik Somnäs

Research questions

- Why do we age?
- Why do we age so differently?
- How can we decrease disease and disability?
- How can we provide better treatment and care?

Research areas

- Morbidity and function
- Health trends and inequalities
- Treatment and care of older people
- Brain aging
- Body-mind connection

ki-su-arc.se Located at KI campus Solna Tomtebodavägen 18A, floor 9-10 171 65 Solna





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Message from the Director

It is with great pride that I write this short note with some reflections on our achievements. The past three years have brought about a great deal of changes for ARC. ARC's long period of being the largest Forte Centre came to an end at the beginning of 2017, and we started working hard to try to secure basic funding. We also realized that we had to move from our earlier office space. By the end of 2017 we were happy to have a new long-term contract with our two founding universities, Karolinska Institutet and Stockholm University, and everything was settled for our physical move in spring 2018 to the Karolinska Institutet Campus and our pleasant new offices at Widerströmska huset.

Throughout this turbulent period, we still managed to continue to be the cutting-edge center for multidisciplinary aging research. Over the years, several evaluations of ARC have been carried out and in the latest one from fall 2018 we were described as "an exemplar of a successful research center with vision, mission, strategy and inbuilt sustainability". We have been extremely successful in receiving external grants over the three-year period that this activity report covers, including the funding and birth of a national infrastructure on aging research (NEAR) supported by the Swedish Research Council (VR). For us at ARC this was a double-win. Firstly, because VR decided that an infrastructure on aging research was of key interest in competition with all sciences, and secondly, of course, because ARC became the head office for this endeavor.

A three-year period naturally includes several staff changes. Some researchers have attained positions elsewhere, and some excellent researchers from abroad have joined us, in both cases good proof of our standing in the academic world. My teammate in ARC leadership Kristina Johnell became Head of Department at MEB, KI in January 2019. While such losses inevitably create some problems, we continue to have fruitful collaborations with most of those who have continued their careers at other places. Another remarkable achievement is that 20 new high-quality doctoral theses have been defended during this three-year period. It is my firm belief that having a critical mass of talented doctoral students is a key ingredient of a successful research environment.

We have also had our share or losses and sad events. One of the people so central to the startup of ARC and who continued to play a leading role was Marti Parker. Marti's scientific rigor and her personal creativity were indeed extraordinary. Following a long period of illness Marti passed away right before Christmas 2017. Marti will always have a central place in ARC's history.

On the international scene it becomes more and more evident that the challenges and opportunities created by aging populations will continue to be a fundamental societal change in the new decade. Accordingly, WHO has now established the 2020s as "The decade of healthy ageing". Hence, aging research is needed now more than ever, and ARC is in an excellent position to continue carrying out cutting-edge research on socially relevant topics related to aging. To do this you need excellent researchers and excellent data, but equally important is a friendly and open working environment. All the staff at ARC contribute greatly to creating this!



Jol Rill

Johan Fritzell Director of ARC, Head of division

Photo: Stefan Zimmerman

Introduction

The Aging Research Center (ARC) was established in 2000 by Karolinska Institutet (KI) and Stockholm University (SU). ARC is internationally renowned for its research on the health status of older adults, trends and inequality among older people, brain aging, and prevention of dementia.





Photos: Maria Leck, Cecilia Öhlund

Our research activities are characterized by:

- A focus on health in aging with the goal of preventing, delaying, or decreasing morbidity and disability in old age.
- An acknowledgement of the importance of life course processes on health and functioning in old age.
- A focus on both individual and social group differences in late life health and disability.
- A multidisciplinary approach that includes medicine, social gerontology, psychology, and epidemiology.
- Creation of large databases from population-based studies on aging and health.
- Access to other large databases on aging via national and international collaboration.
- Integration of epidemiological and social science studies with clinical and molecular research.
- Contributions to improve treatment and care of elderly people.
- Special attention on neuroscience with focus on neural correlates of cognitive functions and prevention of brain aging.
- Implementation of intervention studies to prevent cognitive decline, dementia, and multimorbidity.



Organization

Organization and leadership

ARC is a division at the Department of Neurobiology, Care Sciences and Society (NVS) at Karolinska Institutet and is organized in three sectors: medicine, psychology and social gerontology.

Since January 2019 ARC has been led by an executive group, consisting of ARC's Director and Head of Division, Johan Fritzell; the Deputy Heads of Division, Erika Jonsson Laukka and Carin Lennartsson; and the Vice Head of Division, Chengxuan Qiu. During 2017 and 2018 the members of the executive group were: Johan Fritzell (Director), Kristina Johnell (Head of Division) and Jonas Persson (Deputy Head of Division). The executive group implements decisions taken by the internal ARC board, which is led by ARC's Director and Head of Division and consists of senior representatives from each sector and three junior research representatives. The members of the internal ARC board share responsibility for scientific, organizational, and financial issues, including those related to staff, external contractors, and changes in administrative staff. In addition, each sector has research group leaders that are responsible for the members in their research groups.

Until 2018 ARC had an external board. A new contract between Karolinska Institutet and Stockholm University was signed in December 2017 and will extend from January 1, 2018 until December 31, 2023. In this agreement it is stated that ARC should have an external steering group with members selected by the two universities. This group meets at least twice a year. The ARC external steering group supports and fosters the activity at ARC. It has an advisory role in budget issues and the overall planning of major ARC activities. A list of current members of the external steering group and members of the former external board can be found in the appendix.



ARC executive group: Carin Lennartsson, Erika Jonsson Laukka, Johan Fritzell and Chengxuan Qiu.

ARC STAFF

Sector Medicine (n = 34

2 Professors

- 2 Senior Lecturers
- 1 Senior Researcher
- 4 Assistant Professors
- 5 Post docs
- 14 PhD students
- 1 Scientific coordinator
- 3 Database managers
- 1 Statistician
- 1 Database administrator

Sector Psychology (n = 21)

- 2 Professors
- 5 Senior Researchers
- 2 Assistant Professors
- 5 Post docs
- 3 PhD students
- 1 Senior lab manager
- 1 Database manager
- 2 Research assistants

Sector Social Gerontology (n = 19)

- 1 Professor
- 1 Senior Lecturer
- 5 Senior Researchers
- 1 Assistant Professor
- 6 Post docs
- 2 PhD students
- 1 Research coordinator
- 2 Research assistants

Administrative staff (all sectors)

1 Coordinator 3 Administrators



Photo: Stefan Zimmerman

NEW LOCATION; THE WIDERSTRÖM BUILDING, KI CAMPUS SOLNA



Photo: Åke Eson Lindeman

ARC moved to new premises on the KI campus in Solna in May 2018. We are now located on two floors in the Widerström building (Widerströmska huset).

Visiting address:

The Widerström Building, floors 9-10 Tomtebodavägen 18A KI campus Solna 171 65 Solna

Postal address:

Aging Research Center Department of Neurobiology, Care Sciences and Society (NVS) Karolinska Institutet Tomtebodavägen 18A, floors 9-10 171 65 Solna

Organization

MAP OF CAMPUS SOLNA, KAROLINSKA INSTITUTET



Collaborations around the world

ARC has collaborators in Sweden, Europe, Asia, Australia, North America, and South America.



European Union (EU) consortia involving ARC researchers:

- Common mechanisms and pathways in stroke and Alzheimer's disease (CoSTREAM)
- A European DNA bank for deciphering the missing heritability of Alzheimer's disease (EADB)
- The European Prevention of Alzheimer's Dementia (EPAD) Consortium
- The European Study of Cohorts for Air Pollution Effects (ESCAPE)
- European Social Policy Network (ESPN)
- 21st Century EURODEM: A working group on neurodegenerative disorders
- Evolving gender differences in health & care across cohorts (FUTUREGEN)

- Healthy Ageing Through Internet Counselling in the Elderly (HATICE)
- Integrative Analysis of Longitudinal Studies of Aging
 and Dementia (IALSA)
- Multidimensional Prognostic Indices to improve health in frail older persons (MPI-AGE)
- MULTI-MODE: Multimodal strategies to promote a healthy brain in aging, supported by EIT-Health
- New dietary strategies addressing the specific needs of the elderly population (Nu-AGE)
- Reducing Old-Age Social Exclusion: Collaborations in Research and Policy (ROSEnet)
- Social Health And Reserve in the Dementia patient journey (SHARED)

Organization



Guest researchers

Guest researchers from all over the world visit ARC every year. From 2017 to 2019 we had 28 guest researchers and visiting students at ARC (full list in the appendix). Here we present some of the guest researchers' experiences.

"I got the chance to learn about some of the ongoing projects, interact with post docs and faculty, and share my own work. Those discussions gave me new perspectives of how to think about my work, and I went back to California with lots of ideas and energy to move forward!"

SUSANNE JAEGGI, Professor, University of California, Irvine, USA. At ARC: April-May 2019.

"During my residency in geriatrics in Italy, I spent six months at ARC. Few experiences in my life have been so inspiring. The group is friendly, supportive, and knowledgeable: it is a perfect environment for professional and personal growth!"

ALBERTO ZUCCHELLI, MD, PhD student, Brescia, Italy. At ARC: Nov 2017-May 2018.

"As a researcher focusing on social care and social policy, I especially appreciated the broader perspective on older adults and their needs I found at ARC, also including social gerontology, health care and health policy."

PETRA ULMANEN, researcher, Socialhögskolan, Stockholm University, Sweden. At ARC: spring 2017.

"From team lunches to a departmental banquet to the uniquely Swedish fika, I came home with a renewed appreciation for how taking the time to socialize with colleagues improves well-being, creativity, and even productivity. I even instituted a weekly fika in my lab as a result, and I very much hope I will have the opportunity to visit ARC again!"

AMÉLIE QUESNEL-VALLÉE, Professor, McGill University, Canada. At ARC: Weekly visits in 2017 and 2018. "The close teamwork in the research group and the dedicated way of commenting on and discussing the manuscripts and research in seminars was impressive."

LINDA ENROTH, Post doctoral fellow, Tampere University, Finland. At ARC: Sept 2018-Feb 2019.

"The experience of working at ARC is unique and linked to a high educational and personal enrichment. I am very glad for this opportunity that, day by day, provides me with new competencies and ideas"

CATERINA TREVISAN, MD, PhD student, Geriatric Unit, Department of Medicine, Università di Padova , Italy. At ARC: Feb-Nov 2017 and Aug 2019-Jan 2020.

"During this period l enjoyed the scientific research atmosphere, academic research training and cutting-edge research. This experience gave me energy and creativity and will benefit me in the future."

WEI WU, Post doctoral fellow, Hubei University of Chinese Medicine, China. At ARC: March 2019-March 2020.

"I am really grateful for this opportunity to get an insight into all the different perspectives on aging. I have been particularly enjoying weekly seminars and I am looking forward to all the future work and collaboration."

ANDREJA SPEH, MSc, doing a one-year research stay, University of Ljubljana, Slovenia. At ARC: August 2019 to August 2020.

Research

Research infrastructure

The research conducted at ARC is based on data from several large-scale ongoing and completed longitudinal studies (local, national and international), national registers, and from experimental and intervention studies conducted on a smaller scale. In this section, we introduce the research conducted at ARC by first presenting the databases and collaborative projects which form the basis of our most important research findings. In the following, we briefly present a selection of research findings published during the last three years. A full list of all ongoing projects at ARC is found in the Appendix.

Large ongoing studies ARC is responsible for:

- Swedish National Study on Aging and Care in Kungsholmen (SNAC-K) – Population study. PI: Laura Fratiglioni
- The Swedish Panel Study of Living Conditions of the Oldest Old (SWEOLD). PI: Carin Lennartsson
- The Cognition, Brain, and Aging (COBRA) project. PI: Lars Bäckman
- IronAge. PI: Grégoria Kalpouzos

Data sets located at ARC from completed longitudinal studies:

- The Kungsholmen Project
- Dementia in Swedish Twins (HARMONY)
- The Five Countries Oldest Old Project (5-COOP)

We collaborate closely with researchers responsible for other large ongoing studies:

- The Betula Project. PI: Lars Nyberg, Umeå University
- Cardiovascular Risk Factors, Aging and Dementia (CAIDE). PI: Miia Kivipelto, KI
- DopamiNe Age connectoMe Cognition (DyNAMiC). PI: Alireza Salami, Umeå University
- Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). PI: Miia Kivipelto, KI
- Healthy Aging Through Internet Counselling in the Elderly (HATICE). PI: Miia Kivipelto, KI
- The Luxembourg Income Study (LIS). PIs: Daniele Checchi, University of Milan; Janet Gornick, City University of New York
- The Swedish Level of Living Survey (LNU). PIs: Michael Tåhlin, Carina Mood, SU
- Multimodal preventive trials for Alzheimer's disease (MIND-AD). PI: Miia Kivipelto, KI
- The Social Policy Indicators Database (SPIN), PI: Kenneth Nelson, SU

National registers

- The Swedish Prescribed Drug Register
- The National Patient Register
- The Cause of Death Register
- The Social Services Register

We believe that collaboration and a multidisciplinary perspective is necessary to achieve outstanding research goals. Many ARC researchers are therefore part of, and founders of, several national and international research programs and research networks.

- European Institute of Innovation & Technology (EIT) Health
- Evolving gender differences in health & care across cohorts (FUTUREGEN)
- Inequality Dynamics Over The Life-course (IDOL)
- EU Joint Programming Initiative More Years Better Lives (JPImybl)
- EU Joint Programming Initiative Neurodegenerative Disease Research (JPND)
- Reducing Old-Age Social Exclusion: Collaborations in Research and Policy (ROSEnet)
- Social Inequalities in Ageing (SIA)

We are especially proud of The National E-infrastructure for Aging Research (NEAR), a collaborative project that coordinates the existing databases from major population-based longitudinal studies on aging and health in Sweden, founded in 2017 by Laura Fratiglioni, professor and former director of ARC. NEAR is presented on the next page.







Photos: Josefin Lindström, Linn Fryk and Rebecca Lindblad

The National E-infrastructure for Aging Research (NEAR)



The ultimate goal is to identify sustainable intervention strategies for better health and to develop more effective care of the older population.

The National E-infrastructure for Aging Research (NEAR) is a unique and innovative infrastructure that coordinates 15 major population-based longitudinal studies on aging and health in Sweden. It is a multidisciplinary resource including 180 000 individuals, aged 50 years or over, who have been followed between 7 and 40 years.

NEAR was funded by the Swedish Research Council (Vetenskapsrådet). It is a collaboration between seven universities including Karolinska Institutet, University of Gothenburg, Lund University, Umeå University, Jönköping University, Blekinge Institute of Technology and Uppsala University.

The Director of NEAR is Professor Laura Fratiglioni. NEAR is led by a Steering Board that includes one representative from each of the NEAR databases (list of members in the appendix).



The aims of NEAR are:

- To create a National E-infrastructure for aging research
- To promote and facilitate aging research in Sweden
- To increase national as well as international exchange and collaboration
- To enhance research quality and generalizability of research findings

Progression 2018-2019

Objective	Action
Build	Established Steering BoardEstablished the Operational Group*
Collaborate	• Formalized the collaboration with Maelstrom
Enrich	• New data collection for the cohorts SNAC national
Promote	 Participation at: IAGG-ER 2019 conference, Gothenburg, Sweden Optimising Multistudy Integrative Research, Cambridge, UK SWEAH conference, Lund, Sweden Organizing Internal Scientific Workshop
Use	Six projects

*The operational group is comprised of the Project Coordinator, Database Manager, Data Scientists, Statistician, and Scientific Communicator

Scientific production in numbers

Researchers from ARC continue to produce a large number of publications in scientific journals, many with a high impact in the field of aging research. The number of original articles, review articles, book chapters, reports, PhD theses, and other publications published during the last three years is presented below. The number of publications has increased each year. This is shown in a table in the Appendix.



Research - major findings in brief

ARC conducts research within five major research areas with collaborations across sectors. In the following section findings within each of these research areas from the last three years are presented in brief.

1. Morbidity and Function

Challenging questions in aging research include the definition of healthy aging and the interplay between the multiple factors that contribute to health in older populations. Using large population-based studies, ARC researchers attempt to understand the complexity of health in older adults by investigating and monitoring health status during aging and by exploring various determinants of health.

Multimorbidity and frailty

Multimorbidity, defined as the co-occurrence of multiple diseases in one individual, is extremely common in the older population and represents an important source of clinical complexity. Identifying the risk factors for multimorbidity and their impact on health are important goals for researchers. In the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K), we found that higher levels of glutathione in the blood, an important antioxidant molecule, are associated with a slower accumulation of chronic diseases over six years (Perez, et al., 2019). At the same time, a number of sociodemographic (Figure 1) and psychosocial factors have been related to the speed of multimorbidity development in SNAC-K, such as parental and midlife occupation, education, social network and psychological traits such as life satisfaction and health outlook (Dekthyar, et al., 2019; Calderón-Larrañaga, et al., 2019). All together, these findings point toward the existence of risk and protective factors for multimorbidity that are at play during the entire life course and that encompass both personal and contextual characteristics.

It is known that multimorbidity leads to disability, but several factors may influence the progression. A more rapid accumulation of diseases is associated with a faster development of disabilities, but a strong social network seemed to boost older adults' reserves of functional ability, helping them to live independently despite multimorbidity (Calderón-Larrañaga, et al., 2018). The impact of multimorbidity also depends on the combinations (patterns) of diseases people are affected by. Older individuals displaying different combinations of cardiovascular and neuropsychiatric diseases presented a faster functional decline over time, in terms of both mobility function and disability. However, among subjects affected by cardiovascular and neuropsychiatric multimorbidity, those presenting a reduced walking speed, a measure of frailty, showed the highest mortality from both cardiovascular and non-cardiovascular deaths (Vetrano, et al., 2018; Vetrano, et al., 2019). Therefore, integrated clinical and functional assessment tools, such as the Health Assessment Tool (HAT), developed by our group, seem essential in monitoring health changes and predicting care needs in older adults. HAT scores are highly correlated to other physical performance measures and self-rated health, and are highly predictive of medical and social care service use (Calderón-Larrañaga, et al., 2019).



Figure 1. Predicted number of chronic diseases over 9 years of follow-up in relation to the 4 examined life experiences, Swedish National Study on Aging and Care in Kungsholmen, Stockholm, Sweden, 2001–2013. A)

Father's occupation during childhood; B) early-adulthood education; C) job strain in midlife; D) social network in late life.

Physical function and falls

Beyond diseases, functional decline and disability are perceived by older adults as major determinants of their health. Fortunately, the prevalence of mobility limitations and strength deficits decreased in Sweden over the period 2001-2016. This is in line with findings from other countries such as China, where a decline in the prevalence of impairment in basic and instrumental activities of daily living has been detected since the 1990s (Santoni, et al., 2018; Liang, et al., 2017). Falls, and especially injurious falls, represent common causes of functional decline. From the SNAC-K project, we showed that women and men share similar risk factors for injurious falls, but the single factors may have different impact in the two genders. Further, poor social connections increase the risk not only of experiencing an injurious fall, but also of a faster functional decline after this event (Ek, et al., 2019; Trevisan, et al., 2019).

Based on these results, we developed a screening tool for first-time injurious falls, which is able to classify correctly 70% and 72% of all women and men who will fall within 5 years. This tool opens up for primary prevention for first time fallers along with secondary prevention for recurrent fallers (Ek, et al., 2019).

2. Health trends and inequalities

Monitoring population health is like shooting at a moving target. There is constant change, and the patterns vary across groups, areas, time periods, and depend on the type of health indicators used.

Demographic perspectives

Comparing the trends in old age mortality in the Nordic countries during the period 1990-2014, we found both



similarities and differences. All countries experienced an ageing of the population during the period in terms of increasing proportions of adults aged 75+ and 90+. Similarly, remaining life expectancy at age 75 increased for both sexes in all countries, and remaining life expectancy at age 90 increased for all groups except Icelandic men. In terms of the proportion of each birth cohort that reached old age (ages 75 and 90), Finnish women and men lagged behind the other countries in the beginning of the period. Over time, the Finnish women caught up with their counterparts from the other countries, while Finnish men continued to lag behind. These findings emphasize the need to identify those factors that may lie behind this lag (e.g., policies on alcohol consumption and healthcare services) (Jørgensen, et al., 2018).

One of the most robust findings in medical and demographic research is the finding that women live longer than men. While the pattern is robustly observed across societies and across time, the magnitude of the difference is quite variable. In Sweden, as in many other countries, the gender gap in life expectancy has been decreasing lately, as male mortality has decreased at a faster pace than female mortality. In Sweden over the period 1997-2014, decreasing mortality from cardiovascular diseases in general and ischemic heart disease in particular explain most of the decrease in the gender gap (Figure 2). Moreover, changes in the mortality patterns at old ages contributed to the decreasing gender gap more than changes in mortality patterns of younger ages. (Sundberg, et al., 2018).

There is a well-established social gradient in health. Those with higher socioeconomic positions (measured in terms of education, social class, income or wealth) tend to have better health and live longer than those with lower socioeconomic positions. Yet, less is known about how these inequalities evolve throughout the life course. The Swedish registry data covering a 19-year period show that the inequalities increase throughout adulthood but that the peak age differs for men and women, and depends on whether the inequalities were assessed on an absolute or a relative scale (Figure 3). However, only small or no inequalities remained after age 95, regardless of sex or scale used (Rehnberg, et al., 2019).



Figure 3. The probability of having died at a given age, by income and sex.

Similarly, also inequalities in dental health, musculoskeletal pain, and psychological distress are present across the life course. People who had, at least once, been poor are at an increased risk of all types of health problems across the entire adult life course, in comparison to people who had never reported being poor. The inequalities converged, in relative terms, at the latter part of the life course but never fully converged (Celeste & Fritzell, 2018).



Life-course determinants of health and well-being

The impact of traditional risk factors on the health of older adults is not well understood. For example, the longitudinal trajectories of blood pressure in individuals aged 60-104 are influenced by several factors, including survival time, cardiovascular disease, and antihypertensive therapy (Figure 4; Wang, et al., 2019). Further, the association of cardiovascular risk factor burden with the



Figure 4. Longitudinal blood pressure trajectories with age by sex and survival status. Note. Dash lines are for participants who died within 2 years after the last visit; solid lines are for participants who survived ≥2 years after the last visit. risk of physical impairment and functional dependence was evident mainly among young-older adults (age 60-72 years) and absent within the oldest group (Heiland, et al., 2017; Heiland, et al., 2019).

Today, older people drink more alcohol than earlier cohorts of the same age. Social integration has been identified as an important factor for drinking habits, but the association is complex. Based on nationally representative samples of older adults in Sweden, we found that people with low levels of social contacts or social activities were less likely to have a stable daily or weekly drinking frequency, and more likely to be in the low and stable drinking frequency group. Thus, our results suggest that alcohol consumption is embedded in a social context, where older people drink in social situations and integration predicts continued drinking patterns (Agahi, et al., 2019). Moreover, using data from Finland and Sweden, we found that individuals who died from alcohol-related causes tended to have lower incomes and more decreasing income trajectories, compared to survivors and individuals who died from other causes (Figure 5). Yet, these differences were smaller among the highly educated, suggesting that highly educated individuals may be better able to cope with the negative consequences of excessive alcohol consumption. The patterns were largely similar in Finland and Sweden, despite substantial differences in levels of alcohol-related mortality (Tarkiainen, et al., 2019).

As a consequence of population aging and rising life expectancies, the notion of postponing retirement ages has become a fixed feature on the political landscape. Yet, the knowledge of the health impact of working longer is limited. We analyzed the health effects of working beyond 65, both in the general population and for different social classes. We did not find any statistically significant effects of working beyond age 65 in the general population, and the results from the analyses by social class were inconclusive. Thus, we conclude that there are no detectable detrimental health effects of increasing the higher boundaries of the ages at retirement, but more research is needed to assess any impact on later health (Eyjólfsdóttir, et al., 2019).

Another hot topic in the political debate is the potential impact of cognitive abilities on later health and well-being. Following a cohort of individuals born in 1953 in Stockholm, we mapped out the prevalence of different combinations of unemployment, social assistance recipiency, and mental health problems in adulthood and the likelihood of experiencing these different combinations based on social background, IQ measured in childhood, and educational achievements. The results showed that those who performed poorly on a cognitive test in childhood were substantially more likely to experience coexisting disadvantages as adults. However, these associations were entirely contingent on educational achievements. When differences in school



Figure 5. Income trajectories by cause of death or survival for women and men aged 45-64, in 2006-2007 (Finland) and 2007-2008 (Sweden). Income adjusted to 2015 price levels, Sweden: SEK, Finland: Euro.

marks and highest attained education was accounted for, no association remained between childhood IQ and coexisting disadvantages in adulthood. Thus, our results suggest that education is a more powerful predictor of coexisting disadvantages later in life than childhood IQ (Fors, et al., 2018).

Finally, personality and depression may also strongly influence survival and well-being. Extroverted people, who are characterized by higher optimism and high self-efficacy, are prone to healthier behaviors and better health, which may result in up to 65% lower mortality rate among people aged 60+ (Rizzuto, et al., 2017). Depression is a very common disorder among older adults, especially in people without a partner, or physically dependent or affected by dementia. Depressive symptoms seem to be more frequent also in individuals that reported childhood deprivation. Yet, an active social life was shown to buffer such detrimental effect (Sjöberg, et al., 2017; Triolo, et al., 2019). Similarly, people with low mood are at higher risk of dementia but the increased risk was detected only in those who did not have a partner or lived alone (Sjöberg, et al., 2019).

3. Treatment and Care of Older People

With our research in geriatric pharmaco-epidemiology at ARC, we aim to understand and improve drug treatment in older people. This work focuses on the quality of older people's drug therapy, drug treatment in people with dementia, drug utilization at the end of life, and monitoring drug use over time.

Drug utilization

Polypharmacy is the concomitant use of several drugs by a single person. Because polypharmacy is often the consequence of the coexistence of many chronic diseases, it is more frequent among older people than among middle-aged adults. By using large databases covering the entire Swedish older population, we found that the prevalence of polypharmacy (5+ drugs) was 44%, and the prevalence of excessive polypharmacy (10+ drugs) was 12%. The prevalence of polypharmacy increased with age, a handful of drugs make a large contribution to polypharmacy, and the majority of drugs are used in combination with other drugs. This highlights the need to consider other concurrent drug treatments when prescribing for older adults (Morin, et al., 2018; Wastesson, et al., 2018). Compared with younger older adults, in the oldest old (≥ 80 years) statin users were fewer and more often had an established indication. However, there were also signs of some over as well as under-treatment with statins in the elderly (Sundvall, et al., 2019).

In older adults with serious illness and poor prognosis, drugs that are usually appropriate may do more harm than good and may have little chance of achieving their benefit during the patients' short remaining life expectancy. We found that, throughout their last year of life, older people used an increasing number of prescription drugs. Polypharmacy was fueled not only by the initiation of symptomatic drugs but also by the frequent continuation of preventive treatments. In fact, we found that one third of older people who died from serious, progressive diseases continued and 14% initiated at least one medication deemed "often inadequate" at the end of life (Morin, at al., 2017; Morin, et al., 2019).

Health and social care

Measuring health using an integrated clinical and functional assessment tool (i.e. HAT), we observed a clear gradient in the use of social and medical care services by health status. People at the negative vs positive end of the health continuum used more social formal and informal care and primary care, but also hospital and specialist care (i.e. 11 vs 2 hospital admissions per 10 persons/year and 78 vs 37 specialist visits per 10 persons/ year) (Santoni, at al., 2019). The interaction between episodes of care and drug utilization are also of special interest. For example, we found that, a higher number of prescription changes during geriatric care were associated with longer episodes of care and improved quality of drug use. However, the number of prescription changes decreased, suggesting a lower quality of care, along with the shorter care episodes between 2005 and 2015 (Reimers, et al., 2018).

Sweden has often been seen as a typical example of the social democratic welfare regime, with universal and generous welfare policies. Yet, there have been substantial reductions in the provision of social care for older adults over the past decades. Overall, we observed a decline in the receipt of formal care in terms of house cleaning and food shopping across time. The reductions were greater among women than men. The results suggest that public responsibility for care has become more narrowly defined over time in Sweden, and that more responsibility for care is placed on people in need of care and their families (Dahlberg, et al., 2018).

Most older adults report that they would prefer to live at home until the end of life. Yet, transitions between different care settings are common during the end of life. We showed that older adults with high education were less likely to be admitted to nursing homes during the end of life. On the other hand, they were more likely to be hospitalized and die in hospitals during the last months of life. Thus, depending on their education, older adults in Sweden tend to end up on the opposite sides of a "trade-off" at the end of life: being able to realize one commonly stated preference, living at home during the end of life, comes at the price of a lower likelihood of realizing another common preference, dying at home rather than in hospital (Kelfve, et al., 2018).

Treatment and cognition

Cognitive impairment and dementia pose a number of concerns when it comes to pharmacological and non-pharmacological treatments, raising doubts on the appropriateness and quality of drug prescription in such individuals. Anticholinergic drugs may have a detrimental impact on long-term memory in cognitively intact older adults (Papenberg, et al., 2017). Using data from the Swedish Dementia Registry (SveDem), we found that the use of anticholinergic drugs may be associated with an increased risk of stroke and death in people with dementia. A dose-response relationship was observed (Tan, et al., 2018). In another study, we found that in patients with dementia experiencing myocardial infarction, 21% received an invasive treatment (coronary stenting) which led to longer survival. However, such treatments were more common in younger individuals with better cognitive status (Cermanova, et al., 2017).

In another study, antidepressants were most strongly related to injurious falls and death in a dose-response manner and antipsychotics to hospitalizations and death. Our findings support a cautious prescribing of multiple psychotropic drugs to older patients, especially when cognitive problems are at play and may interact with drugs' adverse effects (Johnell, et al., 2017).

4. Brain Aging

People's individual cognitive capabilities differ, and differences widen as people age. At ARC, we focus on understanding the reasons for these differences. Why do some 80-year-olds have better memory than 35-yearolds? Why do some people maintain a youthful brain but others develop dementia? How does behavior over the life course affect brain changes? Is it possible to slow, stop, or reverse cognitive decline by mental and physical training? Several factors typically interact to cause faster cognitive decline and dementia, and some factors can protect against cognitive deterioration.

Aging-related Decline in Dopamine

Brain cells communicate via neurotransmitters, such as dopamine, which support many molecular mechanisms important for cognition. However, the degree of average age-related change in dopamine receptor availability remains unclear, due to the paucity of longitudinal data. This means that current foundations for research on aging, brain, and cognition are imperfect and possibly erroneous. Consequently, the shared and unique contributions of changes in dopamine, grey matter, and white matter to changes in cognitive performance in old age are unknown. Addressing this issue, the Cognition, Brain, and Aging (COBRA) project is a longitudinal study that follows around 180 people who are between 63 and 67 years at baseline across nine years, with three measurement occasions. Multiple brain measures are assessed at each interval using molecular and structural brain imaging.

The first follow-up data collection of COBRA was completed in 2019. However, ten publications were published between 2017-2019 based on the baseline data from COBRA. For instance, our analyses revealed three subgroups of COBRA subjects, characterized by high dopamine receptor availability and good cognition (Figure 6, Group 1), low dopamine receptor availability and poor cognition (Group 2), or very high dopamine receptor availability and very poor cognition (Group 3) (Lövdén et al., 2018). This pattern corroborates the well-established curvilinear relationship between dopamine and cognitive functioning, with insufficient or excessive dopamine resulting in impaired cognition. The group with low cognition but high dopamine receptors was made up of people with low education, high body-mass index, and poor cross-talk between brain regions relevant for memory. In terms of links to lifestyle, we demonstrated that intensity of physical activity was positively linked both to dopamine receptor availability and different types of memory (Köhncke et al., 2017).

<u>Brain Iron in Aging</u>

Recent advances in Magnet Resonance Imaging (MRI) have made it possible to noninvasively quantify iron that accumulates in the brain. Iron is found in two forms in the brain: heme iron, found in the blood, and intracellular nonheme iron. Nonheme iron is a fundamental element that contributes to cellular metabolism. However, an overload of free nonheme iron in the brain is highly toxic, inducing oxidative stress, inflammation, cellular



Figure 6. Mean cognitive performance (EM = episodic memory, WM = working memory, Speed = processing speed) and dopamine receptor availability in cortex, striatum, and hippocampus (HC) for the different groups. Error bars indicate one standard error around the means.

degradation, and cell death. Excessive concentrations of brain iron have been found in virtually all neurodegenerative disorders (e.g., Parkinson's disease, Alzheimer's disease) and also in non-pathological aging (Figure 7). With the exception of a handful of studies that showed a deleterious effect of increased brain iron load on structural brain integrity and cognition in normal aging, very little is known on brain iron metabolism in aging.

In the Iron study that included approximately 40 healthy younger and older adults, we showed that more brain iron deposition was related to lower brain activity, lower cross-talk across brain regions, and poorer memory and motor performance in old age (Kalpouzos et al., 2017; Salami et al., 2018). The longitudinal IronAge study has two major aims: (1) To investigate the effects of age-related brain iron accumulation on structural, molecular and functional neural changes and cognitive decline; (2) To determine the genetic, biological and lifestyle factors associated with brain iron accumulation. Revealing modifiable factors of brain iron accumulation allows lifestyle-based recommendations promoting mental health in older age to be proposed. The baseline data were collected in 208 healthy individuals aged 20-79 years in 2016-2017. Follow-up data collection is taking place in 2019-2020.



Figure 7. MRI images from the IronAge study showing iron load in the basal ganglia in (A) a healthy young woman aged 23 years old, and (B) a healthy older woman aged 79 years old. The arrows point to higher iron load in the pallidum in the young adult, and to higher iron load in the pallidum, putamen and caudate nucleus in the older adult. The colored images zooming in the basal ganglia allow to further appreciate the concentration in iron, going from negligible (green), to red (significant), to black (massive). Figure modified from (Kalpouzos, 2018).

Intervention Studies

The plasticity of the brain, that is, its capacity for change as a response to experiences, is limited after childhood and decreases further during aging. To postpone and prevent cognitive decline, we want to discover and study factors that can increase brain plasticity during adulthood and aging. We study the potential of electrical brain stimulation, physical activity, and pharmacological agents to improve older adults' cognitive ability. We also use MRI to understand which structural and functional brain changes may explain improvements in cognitive performance.

In our study on electrical brain stimulation, we used transcranial direct-current stimulation (tDCS) as a modulator of cognition. Previous research has suggested that tDCS may increase effects of cognitive training. In our study, 123 older adults underwent working memory training across twenty sessions over four weeks (Nilsson et al., 2017). Working memory enables us to maintain and manipulate information in short-term memory. At the same time, we stimulated their left prefrontal cortex, a brain region critical for working memory. As compared to a control group (trained on different domain), stimulation did not further improved gains from cognitive training (Figure 8). In addition, we conducted a meta-analysis based on seven studies, including our data as well as data involving younger individuals. The result suggested that combining cognitive training with tDCS was not much more effective than sham tDCS at changing working memory performance or global cognition assessed in the absence of stimulation. This training study and meta-analysis question the usefulness of tDCS brain stimulation for improving the effects of cognitive training.



Figure 8. Performance on the trained task. White bars indicate pre-test and dark bars indicate post-test. Error bars represent one standard deviation.

<u>Predictors of Cognitive Decline and</u> <u>Early Markers of Dementia</u>

Higher educational attainment is associated with better cognitive ability and a lower risk of developing dementia during aging. However, the association between education and rate of cognitive decline remains unresolved. Using longitudinal data from the BETULA study, we show that educational attainment is associated with level of cognitive function, but we do not find evidence that it alters the rate of decline in old age (Berggren et al., 2018). We conclude that education is only a relevant variable for understanding cognitive performance in older age because of the association between performance and education that is formed in early development.

Instead of focusing on single characteristics, identification of people with high likelihood to develop dementia may be improved by combining different cognitive and biological markers. Most other studies in this area have used clinical samples, thus highly restricting the generalizability of the findings. We investigated this question in the population-based SNAC-K study. Data from the SNAC-K MRI study were used to predict dementia within the next six years (Payton et al., 2018). Variables from cognitive, genetic, and neuroimaging modalities were systematically combined to identify the best predictor models using 1, 2, and up to 5 predictor variables. The most predictive individual markers were perceptual speed (cognitive) and APOE $\varepsilon 4$ (genetic). The most predictive model was obtained by combining markers from all three modalities (category fluency, general knowledge, APOE $\varepsilon 4$, hippocampal volume and white matter hyperintensity volume). The results suggest that prediction of future dementia may be improved by combining markers within and between different modalities.

5. Body-mind connection

In this line of research, we aim to investigate how decline in physical health, reflected in cardiovascular disease, diabetes, and malnutrition, impact older individuals' cognitive trajectories and risk of dementia. Furthermore, certain factors may increase resilience to physiological insults or decline, which may prevent or delay cognitive impairment.

Cardiovascular burden

Among other factors, cardiovascular burden may accelerate cognitive aging across the entire life course. In SNAC-K, we found that cardiovascular risk factors and cardiovascular disease - with specific focus on atrial fibrillation - were associated with an accelerated cognitive decline and dementia (Wang, et al., 2017; Ding, et al., 2018). Interestingly, this association was largely attributable to the mixed cerebral microvascular and neurodegenerative pathologies as shown by the MRI (Wang, et al., 2018). In addition, medical treatments of vascular risk factors and cardiovascular disorders (e.g., antihypertensive and anticoagulant therapy) reduces the risk of dementia (Tan, et al., 2018; Ding, et al., 2018). Taken together, these findings support the pivotal role of small vessel diseases in linking cardiovascular burden with cognitive aging phenotypes, which has implication for

dementia interventions by targeting vascular pathways. Indeed, improvements in cardiovascular patterns could explain, although only partially, the declining incidence of dementia by ~3% per year since the 1980s in central Stockholm. Of note, the changes in the lifetime risk and protective factors for dementia observed over time, contributed to only a small proportion of the decline in dementia incidence (Ding M. PhD Thesis 2019).

Nutrition and metabolism

Diet represents another important health determinant in aging, with important effects on several aspects, including survival, cardiovascular health and cognition. Using SNAC-K data, we were able to identify a specific Nordic prudent dietary pattern that may reduce the risk of cognitive decline. Such beneficial effects were magnified by additionally having an active lifestyle (Shakersain, et al., 2018; Shakersain, et al., 2018). Specific nutrients of the prudent diet are related to maintenance of cognitive function as well as brain integrity (Prinelli, et al., 2018; Prinelli, et al., 2019).

Diabetes and prediabetes are strongly related to nutrition. Fortunately, only 13% of older adults with prediabetes develop diabetes and 64% remain in the prediabetes stage or reverted back to normoglycemia. Lifestyle changes such as weight management and blood pressure control may prevent prediabetes from progressing to diabetes (Shang, et al., 2019). Moreover, having either prediabetes or diabetes may accelerate the decline in fluid abilities and global cognitive function (Marseglia, et al., 2018) and is associated with accumulation of cerebral microvascular lesions and increased dementia risk (Marseglia, et al., 2019). On a positive note, an active and socially integrated lifestyle seems to counteract the deleterious effect of diabetes on brain aging (Marseglia, et al., 2019).

Reserve and resilience

A number of protective and resilience enhancing factors for cognitive decline have been studied at ARC. For example, we found that engagement during late life appeared especially protective, although cumulative experiences of stimulation from early, mid, and late life provided the largest benefit (60% reduced risk) (Wang, et al., 2017). Mental, social, and physical lifelong engagement were also found to be protective against dementia irrespective of genetic predisposition, suggesting that promoting active lives can be a viable prevention strategy even in subpopulations genetically predisposed to dementia (Dekhtyar, et al., 2019). Further, we investigated whether occupational stress (categorized according to job demands and job control) was associated with cognitive decline in older adults. Cognitive decline was accelerated in the presence of a mismatch between job demands and job control and active occupations appear to protect against accelerated cognitive decline (Pan, et al., 2019). These findings highlight the importance of psychosocial working environments in shaping cognitive health in older adults (Pan, et al., 2019).

<u>Mild cognitive impairment</u>

Cognitive impairment non-dementia (CIND), or mild cognitive impairment (MCI), may be considered an intermediate state between normal cognition and dementia. We investigated the impact of physical frailty and motor dysfunctions on the relationship between physical and cognitive health in older individuals with cognitive impairment. Using data spanning 12 years, we found that adding a simple, inexpensive and easy-to-perform motor test, like walking speed, to the neuropsychological battery improves the clinical ability to detect dementia in very early stages (Figure 9; Grande, et al., 2019). Furthermore, the simultaneous presence of cognitive problems and physical impairment is associated with a fast accumulation of disability over time and accounts for 30% of short-term deaths (Grande, et al., 2019). In a meta-analysis including more than 14,000 individuals, having both cognitive impairment and physical frailty

was associated with a 5-fold higher risk of developing dementia compared to having none of these conditions (Grande, et al., 2019). Taken together, these findings point to a strong relation between physical and cognitive abilities in old age, suggesting that markers of both may aid in dementia risk assessment.



Figure 9. Area under the curve (AUC) for dementia prediction according to the presence of cognitive impairment no dementia (CIND) and slow walking speed (WS), in the SNAC-K population.

Photo: Sandra Humer

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Education

Courses

ARC researchers are responsible for and involved in several courses at KI and SU.

Undergraduate (first cycle) courses

<u>Aging</u>

3.0 credits, section 2 of Developmental psychology, within the psychology program at KI. Led by Erika Jonsson Laukka.

Society and health

4.5 credits, within the psychology program at KI. Led by Neda Agahi.

Working life, aging and health

7.5 credits, within the bachelor's program of education and public sciences at SU. Led by Charlotta Nilsen and Harpa Sif Eyjólfsdóttir.

Master's (second cycle) courses

Geriatric epidemiology

Geriatric epidemiology within the master's program in public health epidemiology at KI. Led by Chengxuan Qiu, Anna-Karin Welmer and Rui Wang.

Public health science - concepts and theories

7.5 credits, within the master's program in public health sciences, KI. Led by Janne Agerholm.

Society, ageing and health

3.0 credits, within the master's program in public health sciences, at SU. Led by Stefan Fors and Jonas Wastesson.

Doctoral (third cycle) courses

Aging Societies: Challenges and Opportunities

3.0 credits, within the public health program at KI. Led by Charlotta Nilsen and Neda Agahi.

Application of epidemiological methods in aging research

1.5 credits, within the neuroscience program at KI. Led by Laura Fratiglioni, Debora Rizzuto and Amaia Calderon Larrañaga.

Cognitive Aging

7.5 credits, at the Department of Psychology, Stockholm University. Led by Erika Jonsson Laukka.

<u>Computational modelling for cognitive neuroscience and</u> <u>psychiatry research</u>

1.5 credits, within the neuroscience program at KI. Led by Benjamín Garzón and Marc Guitart-Masip.

Integration of neuroimaging and cognition in normal aging and dementia

2.0 credits, within the neuroscience program at KI. Led by Grégoria Kalpouzos.

Public Health Research - concepts and theories

3.0 credits, within the public health program at KI. Led by Janne Agerholm.

Theoretical perspectives on methodological choices in research on ageing and health

3.0 credits, within the Swedish National Graduate School for Competitive Science on Ageing and Health (SWEAH). Led by Charlotte Löfqvist and Charlotta Nilsen.
Doctoral students' education and activities

ARC had around 35 doctoral students between 2017 and 2019 registered at Karolinska Institutet or Stockholm University. A total of 20 doctoral students defended their theses between January 2017 and December 2019.

International forum and seminars

A part of the doctoral education at ARC consists of attending seminars. ARC hosted several internationally recognized senior researchers in their field. Researchers presented their major findings, opinions, and future perspectives in a 2-hour seminar (international forum) open to all students and researchers at KI. Twenty international forums were held at ARC from 2017 to 2019. A list of all international forums is presented in the appendix. ARC also organizes more regular seminars with junior and senior researchers. A total of 59 seminars were held at ARC between 2017 and 2019.

ARC Juniors

At ARC, doctoral students and post docs have formed the "ARC Juniors," a network that organizes a variety of educational and social activities, for example journal clubs and lunches.

Swedish National Graduate School for Competitive Science on Ageing and Health (SWEAH)

Many of our doctoral students are part of The Swedish National Graduate School for Comparative Science on Ageing and Health (SWEAH). SWEAH was founded in 2014 as a consortium of sixteen partners coordinated by Lund University. The overarching long-term goal of SWEAH is to develop and strengthen the recruitment base of future leaders in research on aging and health. SWEAH will achieve this aim by creating a sustainable multi- and cross-disciplinary national graduate school for competitive science that will ultimately lead to improved quality of life, health, medical treatment, and care for our aging population. KI has been one of the partners from the start, with doctoral students from ARC and section for geriatric epidemiology. Between 2017 and 2019, eighteen of our doctoral students were affiliated with SWEAH.



ARC Juniors Christmas study circle in 2017.

Photo: Anna Marseglia

PhD theses 2017-2019

Between 2017 and 2019 ARC had 20 doctoral students defending their theses. In this section, each thesis is presented in brief.



GIOLA SANTONI 2017

Photo: Maria Yohuang

How well are we aging? Capturing the complexity of health trajectories of older adults



The aim of this thesis was to evaluate how well people are aging, taking the complexity of their health status into account. Despite its positive nature, population aging represents a public health challenge that could be alleviated by maintaining good health during older age. To this aim, we verified temporal trends of disability in older Swedish adults between 1991-2010 taking into account occurrence and number of years of life lived with disability. We also developed a health assessment tool (HAT) for older people by using four clinical indicators (physical function, cognitive function, morbidity, and disability) and detected age-related variation and individual health trajectories over time. Finally, we proposed a novel approach to monitor older individuals' health changes through reference health curves that can help delineate ad-hoc public health and care actions.

YLVA KÖHNCKE 2017

Photo: Max-Planck Institute for Human Development®

Lifestyle, cognitive aging, and brain correlates



How do different lifestyles relate to differences in cognitive aging? On average, we tend to get a bit worse in cognitive performance (processing speed, memory, and other cognitive abilities) as we age, even if cognitive decline stays below the extent of what we see in dementia. However, there are large differences between persons in how we age cognitively. The aim of this thesis was to investigate lifestyle factors that are related to between-person differences in cognitive as well as structural and molecular brain integrity.

NINA BECKER 2017

Photo: Yvonne Brehmer

Inter-individual differences in associative memory: structural and functional brain correlates and genetic modulators



We know that memory declines in aging, which impacts the everyday lives of older adults as well as their independence. The decline of associative memory, for example remembering a face-name combination, where one left the car keys, or which medication to take at which time, has a particular influence on our everyday lives. However, there are pronounced individual differences in associative memory, leaving some adults with relatively intact, and others with severely deficient associative memory. The underlying sources of these individual differences remain unclear. In this thesis, the aim was to identify the neural underpinnings of individual differences in associative memory, with special regard to brain structure, function, and neurochemistry.

BEATA FERENCZ 2017

Photo: Maria Yohuang

Genetic and lifestyle influences on memory, brain structure, and dementia



This doctoral thesis investigated genetic, inflammatory, and lifestyle influences on cognition, brain structure, and dementia. The influence of TOMM40 polymorphisms (Study I), a genetic risk score based on PICALM, BIN1 and CLU polymorphisms (Studies II, III), and inflammatory cytokines (Study IV) were assessed, as well as potential interactions with physical activity (Studies II-IV). All studies were based on the Swedish National study on Aging and Care in Kungsholmen (SNAC-K), including a subsample that had participated in magnetic resonance imaging (MRI).

CHARLOTTA NILSEN 2018

Photo: Maria Yohuang

Do psychosocial working conditions contribute to healthy and active aging? Studies of mortality, late-life health, and leisure



The growing demographic challenge posed by an aging population makes finding predictors of health in old age increasingly important. This thesis investigated long-term associations between midlife psychosocial working conditions and late-life health and leisure and examined whether sense of coherence in midlife modified the association between psychosocial working conditions and all-cause mortality. The studies were based on individually linked data from the Swedish Cause of Death Register and two Swedish longitudinal surveys, the Level of Living Survey (LNU) and the Swedish Panel Study of Living Conditions of the Oldest Old (SWEOLD).

ALEXANDER DARIN-MATTSSON 2018

Photo: Maria Yohuang

Set for life? Socioeconomic conditions, occupational complexity, and later life health



Life expectancy has increased in the western parts of the world and more people reach old age. Some groups of people have benefitted more from the increase in life expectancy and have better health than others. Because of biological, psychological, behavioral, and social factors over the life course, adverse health accumulates in later life. The overall aim of this thesis was to investigate the relationships between socioeconomic conditions, the complexity level of peoples' work (measured as occupational complexity), and health in late life by studying 1) the association between complexity of work during midlife and later life health and 2) health inequalities in late life attributable to differences in socioeconomic position. All studies used individually linked data from LNU and SWEOLD.

EMERALD G. HEILAND 2018

Photo: Maria Yohuang

Cardiovascular risk factor profiles in the development and progression of physical limitation in old age: a population-based study



Preservation of independence has been reported to be highly desired by older adults, even more than longevity. However, subclinical cardiovascular pathology can threaten a healthy older adult's maintenance of physical function. Therefore, the aim of this thesis was to investigate the role and potential neuropathological mechanisms of cardiovascular disease-related risk factors in the development of physical limitation and disability in older adults. Data were taken from the Swedish National study on Aging and Care in Kungsholmen (SNAC-K) for the initial three studies and from the embedded SNAC-K MRI sub-study for the final study.

ANNA MARSEGLIA 2018

Photo: Selma Wolofsky, NVS/KI

The impact of diabetes on cognitive aging and dementia



The impact of prediabetes and diabetes on different stages of cognitive function during aging remains unclear. This thesis aimed to investigate the impact of prediabetes and of diabetes on cognitive aging—from cognitive deficits, through cognitive decline, to dementia—, explore underlying cerebral mechanisms and identify factors that may protect older adults with diabetes from dementia. The four studies in this thesis were based on data from SNAC-K, the SNAC-K brain magnetic resonance imaging (MRI) study, and the Swedish Adoption/Twin Study of Aging (SATSA).

LINNEA SJÖBERG 2018

Photo: Maria Yohuang

Using a life-course approach to better understand depression in older age



The aim of the thesis was to explore the prevalence of depression, and to identify risk factors, secular changes, and consequences of depression in late adulthood from a lifecourse perspective. The four studies in this thesis were based on data from the H-70 study, SNAC-K, and the Kungsholmen Project (KP). Overall, results showed that the importance of psychosocial factors in relation to depression risk and the postponement of dementia onset, emphasizes the importance of establishing preventive strategies aimed at increasing social interactions among older adults.

GEORGE SAMRANI 2018

Photo: Maria Yohuang

Interference control in working memory: neurobehavioral properties and age differences



This doctoral thesis aimed to investigate the basic processes of interference control in working memory. We sought to unravel some of the underlying mechanisms of interference control by examining brain correlates, while also trying to understand the differences that arise with advancing adult age. The studies in this thesis are based on data collected from several experiments and follow-up data from the Betula study. The data in this doctoral thesis contribute new insight into interference control in working memory.

DOMINIKA SEBLOVA 2019

Causal effects of education on cognition: how do we generate evidence?



Education is associated with many aspects of life, including health. For example, there is hope that improved education may help to reduce the burden of dementia, which is a large public health challenge for which treatment is lacking. However, such hopes assume causality of the relationship between education and dementia. The primary aim of this doctoral thesis was to examine the relationship between formal education and cognition (i.e. early-life cognition, cognitive decline and neuropathological disturbances to cognition in form of dementia) during the life-course. The secondary aim was to discuss how we can generate evidence on causal relationships and infer causation in epidemiology. This thesis adopted a plurality and triangulation of evidence approach with regards to arriving at causal conclusions. The individual studies employed diverse designs in the exploration of links between education, cognition and dementia.

RASMUS BERGGREN 2019

Photo: Maria Yohuang

Cognitive development and educational attainment across the life span



The aim of this thesis was to explore the effects of language learning on brain structure and cognitive function. Another aim was to study to what extent educational attainment alters the rate of cognitive decline in old age. These different strands of research are united through the concept of brain plasticity, which is the brain's ability to change its structural configuration in response to new experiences. The studies in this thesis are based on behavioral data and brain imaging data from experiments conducted in this doctoral project, as well as data from the Betula study. One of the studies consists of a systematic review and meta-analysis of longitudinal studies within the area of education and age-related decline in episodic memory performance.

DAVIDE L. VETRANO 2019

Photo: Lucas Morin

Impact of cardiovascular and neuropsychiatric multimorbidity on older adults' health



Multimorbidity, the presence of two or more chronic diseases in one person, is common in older people, and associates with a number of negative outcomes. In this thesis, we propose a methodology to assess and measure multimorbidity in older individuals. We use it to describe the longitudinal evolution and prognosis of multimorbidity clusters, and to investigate the extent to which clusters of cardiovascular and neuropsychiatric multimorbidity impact and interact with physical function. Data are from SNAC-K, a population-based study including 3,363 community-dwelling and institutionalized individuals aged \geq 60 years.

JOHAN REHNBERG 2019

Inequalities in life and death: Income and mortality in an ageing population



Income serves as an indicator of success relative to others and provides individuals with resources that strengthen their ability to face challenges and benefit from opportunities. Out of all social determinants of health, income is one of the strongest predictors of health outcomes. The positive association between income and health in the working-age population is well established; those with higher income tend to have better health. Less is known about the association between income and health among older people. The aim of this thesis was to investigate the association between income and mortality across ages, with a focus on later life. The studies in this thesis are based on data from Swedish national registers, and survey data (LNU and SWEOLD) linked to data from administrative registries.

KUAN-YU PAN 2019

Impact of psychosocial working conditions on health in older age



Work takes up a large proportion of time in our adult lives, thus possibly making it an important determinant of health. This doctoral thesis aimed to investigate the impact of psychosocial working conditions on health in older age, including metabolic and cognitive health, and disability. Psychosocial working conditions were defined in accordance with the job demand-control model and classified into four scenarios: high strain (high demands, low control), low strain (low demands, high control), passive job (low demands, low control), and active job (high demands, high control). The four studies in this thesis were based on data from SNAC-K.

LUCAS MORIN 2019

Photo: Davide Vetrano

Too much, too late? Drug prescribing for older people near the end of life



The burden of drugs prescribed to older people at the end of life has recently drawn increasing scrutiny. Growing evidence suggests that patients with life limiting diseases and poor prognosis are prescribed drugs that may do more harm than good or treatments that have little chance of achieving their benefit during the patients' short remaining lifespan. The overall aim of this thesis was to evaluate the quality of drug prescribing in older adults near the end of life. Three of the four studies in this thesis are based on routinely collected administrative and healthcare data with national coverage in Sweden. The findings from this thesis confirm that a large proportion of older people are most likely overtreated at the end of life, which exposes them to unnecessary risks.

BÁRBARA AVELAR PEREIRA 2019

Photo: Maria Yohuang

Multimodal imaging: functional, structural, and molecular brain correlates of cognitive aging



Aging is associated with a decline in many (but not all) cognitive abilities. Although it remains largely unknown how changes in brain integrity relate to cognitive deficits, these changes are likely expressed across interrelated functional, structural, and molecular layers. This complexity calls for a multimodal imaging approach in age-related mind-brain research. Hence, in this thesis, different imaging modalities were combined in order to study the neural basis of cognitive aging. A primary focus in this thesis was functional connectivity, a measure of how well different brain areas communicate with each other, but changes in white-matter integrity and molecular properties were also investigated.

STINA EK 2019

Photo: Maria Yohuang

Predictors and consequences of injurious falls among older adults: a holistic approach



The field of research on falls among older adults is well studied. Despite this, there are some knowledge gaps that need to be addressed: 1) research studying injurious falls, as opposed to any falls; 2) knowledge on sex differences, and specific risk profiles for injurious falls; 3) development of an effective screening tool for community-dwelling older adults, that can detect people at risk of first-time falls, who may be targeted by preventive interventions; and 4) what factors influence the risk of losing independence, in a long-term perspective, after an injurious fall. The purpose of this thesis is to fill these gaps through the following aims: to detect risk profiles of injurious falls among older adults, to enable early detection of those at risk, and to examine the long-term consequences of fall injuries on everyday function. Data from (SNAC-K) was used.

LIEKE DE BOER 2019

Photo: Maria Yohuang

Dopamine, decision-making, and aging: neural and behavioral correlates



Good decision-making involves being able to select the best alternative from a range of options and adjust one's preferences based on what is happening in the environment. As humans get older, their ability to do this changes. Age-related changes in decision-making ability result from changes in brain structure and function, such as the deterioration of the brain's dopaminergic system in old age. In this thesis, a sample of 30 older and 30 younger participants was used to investigate age-related differences in neural and behavioral correlates of value-based decision-making, which involves making decisions that can result in rewards and punishments. Such decisions are known to rely on dopaminergic functioning.

MOZHU DING 2019

Photo: Mike Lei Zhang

The role of atrial fibrillation in cognitive aging: A population-based study



The role of atrial fibrillation in brain and cognitive aging (e.g., cognitive decline and dementia) is still unclear. In this doctoral thesis, we aimed to investigate the temporal trends and potential determinants of dementia incidence, the occurrence of atrial fibrillation and the pattern of use of antithrombotic drugs, the association of atrial fibrillation with cognitive decline and dementia, and the association of atrial fibrillation with various structural brain abnormalities among older adults. Data were derived from KP, SNAC-K, and the SNAC-K MRI sub-study.



Additional achievements

Career advancements: new positions/titles

- Neda Agahi, Associate Professor of Public Health Science at KI, 2017
- Yvonne Brehmer, Associate Professor of Psychology at KI, 2017
- Erika Jonsson Laukka, Associate Professor of Psychology at KI, 2018
- Marc Guitart-Masip, Associate Professor of Neuroscience at KI, 2018
- Pär Schön, Associate Professor of Social Work at SU, 2019

Awards

• Laura Fratiglioni awarded Karolinska Institutets Grand Silver Medal, 2018, with the motivation

"Laura Fratiglioni is one of the leading international researchers in epidemiology of aging. She is awarded the medal for her outstanding contributions to Karolinska Institutet in science, doctoral education and leadership and innovation. With her strong clinical and scientific background, Laura Fratiglioni is often sought out as an expert in aging and she has strongly contributed to the international profile of KI in this field. Her work has contributed to the use of epidemiologic methods in aging research. Thereto, Laura Fratiglioni is devoted to communicating her research findings to the general public."

- Kristina Johnell Outstanding Female Academic (AcademiaNet), The Robert Bosch Stiftung and Nature Publishing Group, Germany, 2017
- Johan Fritzell and Roger Keller Celeste's paper "Do socioeconomic inequalities in pain, psychological distress and oral health increase or decrease over the life course? Evidence from Sweden over 43 years of follow-up" was awarded the 2019 Aubrey Sheiham AWARD for Distinguished Research in Dental Public Health Sciences

Appointments to commissions of trust outside KI

ARC researchers were appointed to different commissions of trust outside of KI, such as: members of the Swedish Ethical Review Authority and other boards in Sweden; acted as peer reviewers for international and national funding agencies, including the Swedish Research Council; participated in scientific advisory boards, committees, boards and several EU networks and consortia; and served as invited lecturers and chairs of several national and international conferences.



Laura Fratiglioni receives the Karolinska Institutet Grand Silver Medal 2018.



Impact

Impact

Impact

Scientific impact

The major scientific impact is provided by the publications of the studies in peer-reviewed journals (see chapter Research for a summary of the major findings). Further, ARC researchers participate in numerous research networks and have an extensive network of collaborators both nationally and internationally. We organize several symposia and workshops and frequently attend national and international conferences. A selection of these activities is presented.

- Two workshops were held within the project "Sino-Sweden Research Network on Aging: exploring the differential impacts of biomedical and environmental factors on cognitive aging across cultures". This project was initiated by Dr. Chengxuan Qiu in 2017 as an attempt to bridge the knowledge gap between cultures and strengthen the existing network on aging research. The first workshop took place at ARC in October 2017, and the second workshop was held in May 2019 in Beijing, China. Around ten researchers from ARC attended the workshops.
- ARC, SU and the University of Exeter Medical School organized the International Symposium "Multimorbidity research at the cross-roads: developing the evidence for clinical practice and health policy" in Stockholm, Nobel Forum, May 21 2018, in collaboration with the Journal of Internal Medicine (JIM) and the International Network for Research on Multimorbidity "Threads & Yarns". See: https://www.multimorbidity2018-stockholm.se/
- The inaugural OPPEN workshop was held in May 8-9 017 at ARC. The Optimizing geriatric Pharmacotherapy through PharmacoEpidemiology Network (OPPEN) is a consortium of researchers working in the field of geriatric pharmacoepidemiology. Five research groups from Australia, Belgium, Finland, Italy and Sweden presented their research and explored opportunities for collaboration.
- ARC organized several conferences and two junior researcher workshops within the Social Inequalities in Ageing (SIA) program during 2017-2019. SIA: Health, care and institutional reforms in the Nordic welfare model is a comprehensive five-year Nordic research program financed by NordForsk. The program is led by professor Johan Fritzell. The program consists of researchers from all Nordic countries.



Stockholm Tokyo Workshop on aging

- Many ARC researchers were involved in The Swedish Meeting for Alzheimer Research at KI, November 20, 2019. This meeting was organized by the Center for Alzheimer Research (CAR), a hub for all research with relevance for Alzheimer's disease and other dementias at Karolinska Institutet, of which ARC is one of the founders.
- ARC researchers attended the International Association of Gerontology and Geriatrics European Region Congress 2019 (IAGG-ER) in Gothenburg, Sweden, May 23-25. ARC contributed with several seminars, talks, posters, and two exhibition stands (ARC and NEAR).
- ARC researchers attended the Nordic Congress in Gerontology in Oslo, Norway, May 2-4, 2018. ARC was well-represented with more than thirteen oral presentations, three symposiums, ten posters, and an exhibition stand.

Societal impact

ARC is involved in a range of outreach activities with the purpose of sharing knowledge and promoting understanding and awareness of aging research in the public domain. Here we highlight some of these activities and events organized with the aim of informing the public, policy makers and society at large.

• ARC participated in Järvaveckan 2019. Järvaveckan is the second largest arena for discussing current political issues in Sweden along with Almedalen. It is an initiative to reduce the distance between elected politicians and citizens. In collaboration with the Stockholm Gerontology Research Center and the Swedish Dementia Center we organized a seminar about dementia and mental ill health in the elderly, and shared an exhibition stand where visitors could talk to researchers, test their grip strength and sense of smell (tests used in SNAC-K), and participate in a survey study about how it is to age in Stockholm.

Exhibition area at Järvaveckan. Photos: Marie Helsing Västfjäll



Opening ceremony of the International symposium on Brain, Health, and Aging in Beijing

Photo: Suhao Wang

• ARC hosted state visitors from Canada on February 21 in 2017. ARC was visited by Her Excellency Sharon Johnston from Canada and Her Majesty the Queen of Sweden. The visit took place in conjunction with the state visit by the Governor General and his wife to Sweden at the invitation of His Majesty the King of Sweden. The research conducted at ARC and the work of the Swedish Dementia Centre were presented.



State visitors at ARC *Photo: Yanan Li*

- ARC researchers participated in FORTE Talks 2019. Forte Talks is a venue for the exchange of knowledge between researchers, decision-makers, practitioners, users and other stakeholders who are interested in human health, working life and welfare. Linnea Sjöberg, scientific communicator within NEAR, talked about her research on depression among the elderly and how the National E-infrastructure for Aging Research (NEAR) can broaden our knowledge on the subject. Associate professor Anna-Karin Welmer talked about her research on prevention of injurious falls among older adults.
- ARC and the Swedish National Pensioners' Organization (PRO) jointly organized an open seminar on the conditions for equal access to health and social care for the oldest old people on March 8 in 2018. Three ARC researchers presented their research on the topic.
- An information meeting for SNAC-K participants took place on October 17, 2018. The SNAC-K

participant day is held every third year as an opportunity for participants in the study, as well as their relatives, to hear about study results and listen to current findings by some of the leading researchers in the field of aging research. Between talks, the audience had the opportunity to meet and interact with researchers from ARC, SNAC-K, the Stockholm Gerontology Research Center, and the Swedish Dementia Centre.



Anna-Karin Welmer meets with visitors at the SNAC-K participant day. *Photo: Maria Yohuang*

- Another example of outreach activities include dissemination of results from a study of differences in mental health problems among older people, written by researchers at ARC on behalf of the Public Health Agency of Sweden. The results were published in a report in 2019 and presented at seminars and videorecorded conferences intended for policy makers and practitioners. The results showed that the prevalence of mental health problems is common among older adults and varies substantially between subgroups of the older population.
- On behalf of Region Stockholm and the Center for Epidemiology and Social Medicine (CES),

researchers at ARC together with the Stockholm Gerontology Research Center (Stiftelsen Stockholms läns Äldrecentrum) compiled a report on the health and living conditions of those aged 65+ in Stockholm county. The most important results were launched in a short video, and the results have been presented for politicians and policy makers in the Stockholm Region on several occasions. The report describes the distribution of these factors within different population groups and its development over time (2002-2018).

• Our collaborators at the Stockholm Gerontology Research Center and Swedish Dementia Centre have established systems for reaching audiences outside the scientific community. Many of the researchers at ARC participate regularly in conferences and courses for care providers, politicians, other decision makers, and interest groups. ARC contributes to the Swedish-language magazine Äldre i Centrum, based at the Stockholm Gerontology Research Center. This national magazine on aging research covers health and disease in aging, presenting important happenings in the field.

An Arts and Science collaborative project between ARC and Stockholm School of Photography (Fotoskolan STHLM)

It is often said that "a picture is worth a thousand words", and the world of research is indeed largely dominated by words. As a way of complementing these words, we teamed up with Stockholm School of Photography (Fotoskolan STHLM) to create new and relevant pictures of older people to be used by ARC for research communications. We quickly realized that we had started a sort of experimental project where two widely different disciplines and perspectives, photography and research, would have the opportunity to highlight the issue of aging in a new way. Through combining the subjectivity of photography with the objectivity of research we formed a true Arts and Science collaboration.

Twenty photography students were invited to ARC and attended lectures and discussions concerning aging, inequalities in aging, and ageism. Their task was to incorporate their newfound knowledge with their own perspectives and finally give their personal interpretation of who an older person in Sweden may be today.



The conditions were that they would follow individuals, who should be at least 75 years of age, during their everyday lives, and the photos would be taken in color. We secured representations of each socioeconomic position, dependency status, living condition and Swedish/ non-Swedish background. The students focused primarily on portraits, but also interactions and activities of different sorts with five key values in mind; authenticity, recognition, surprise, existentialism and warmth.

The results were way above expectations for both us and the teachers at Fotoskolan STHLM as the photographers contributed a more in-depth and broad range of pictures than we could ever have imagined. The project was completed with a 3-week open exhibition at Folkuniversitetet which included a selection of photos and lectures by researchers from ARC talking about the collaboration and about aging research. We are grateful to the students, to the amazing people who agreed to be photographed and to Fotoskolan STHLM. We hope that this collaboration can be an inspiration for other Arts and Science projects in the future. All portraits in this report are taken by the students of Fotoskolan STHLM.

Clinical and public health impact

Here we highlight some of the activities aimed to influence the clinical best practices in areas related to ARC's research.

By using the computerized techniques we developed for analyzing drug utilization data from the Swedish Prescribed Drug Register, we regularly assist the National Board of Health and Welfare and the Swedish Association of Local Authorities and Regions (SALAR, SKR) in their regular comparisons of the quality of health care. These measurements have also played a major role in the successful initiative to improve drug use in older people. This initiative was a part of the agreement between the government and SALAR to support long-term improvement work, that focuses on improving the quality and cohesiveness of the care of the most frail elderly people and even though this initiative ended in 2014, the monthly measurements continues, as they are appreciated among both the counties and municipalities. Since 2000 we have developed a computerized decision support system (miniQ) to facilitate prescribing and drug utilization reviews in eldercare. The system, which is web-based, has three interlinked components: miniQ for physicians and nurses, SeniorminiQ for patients and relatives, and Monitor which provides support for pharmacological experts. miniQ is implemented in several counties in Sweden. Moreover, during 2016-2018 it formed the basis of an EIT Health project aiming at adapting the system for other European countries, starting with UK and Spain (www.eithealth.eu/mini-q). As a result of this project, a spinoff company has been founded in Spain, which continues with this venture. In 2019 miniQ was also awarded by the Royal Swedish Academy of Engineering Sciences (IVA) by being included in their "100-lista" (https://www.iva.se/projekt/research2business/100listan).

Our longstanding research in the area of geriatric pharmacology and pharmacoepidemiology and participation in the development of national indicators for drug therapy in the elderly have likely played an important role in the reported continuous improvement in the quality of drug use in elderly people since 2005 (Socialstyrelsen 2019).



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(Folkhälsomyndigheten)	Goljes minne S & E
Alzheimerfonden	The Solstickan Foundation
Triton Advisers (Sweden) AB	Tore Nilssons stiftelse f.med.forskning
King Gustaf V and Queen Victoria's Foundation	Ahréns stiftelse

Publications

Publications

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Appendix

Board members

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Ongoing projects at ARC (in alphabetical order)

- Integrated care for older people with complex health problems. How does it affect health, health care utilization and health equity?, Janne Agerholm, PI
- Cognitive aging: from observational studies to intervention, Lars Bäckman, PI
- Cognition, brain, and aging (COBRA), Lars Bäckman, PI
- Does our healthcare system truly fit older people? Impact of multidimensional health trajectories on the use of medical and social care services, Amaia Calderón-Larrañaga, PI
- Phenotypes of healthier aging: the role of environmental, behavioral, and biological factors in health trajectories, Amaia Calderón Larrañaga, PI
- Pushed to the edge of society: Social exclusion among older women and men in Sweden, Lena Dahlberg, PI
- Mental health in old age: the role of social disadvantages throughout the life course and across birth cohorts, Serhiy Dekhtyar, PI
- Patient-centered IT-support for quality and safety of drug use in older adults: The QS-project, Johan Fastbom, PI
- Evolving gender differences in health & care across cohorts (FUTUREGEN), Stefan Fors, PI
- Aging through life: identifying new pathways for living longer and healthier, Laura Fratiglioni, PI
- Disentangling complexity of health in aging: a new research environment to pave the road for individual medicine, Laura Fratiglioni, PI
- NEAR: The National E-infrastructure for Aging Research in Sweden, Laura Fratiglioni, PI
- Not all older adults develop dementia: exploring underlying compensatory mechanisms related to healthy brain aging, Laura Fratiglioni, PI
- The body-mind connection: exploring the biological mechanisms underlying the effects of somatic health on brain aging, Laura Fratiglioni, PI

- The Swedish National study on Aging and Care in Kungsholmen (SNAC-K): Follow-up data collection, Laura Fratiglioni, PI
- Does inequality increase among older persons in Sweden? A multidimensional perspective, Johan Fritzell, PI
- European Social Policy Network Programme, Johan Fritzell, Swedish PI
- Health and mortality in older Europeans a matter of cash and care? Johan Fritzell, PI
- Inequality dynamics over the life course: family and policy influences, Johan Fritzell, PI
- Social inequalities in ageing (SIA): health, care, and institutional reforms in the Nordic welfare model, Johan Fritzell, PI
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- Longitudinal trajectories of olfactory abilities: What predicts old-age olfactory memory decline? Erika Jonsson Laukka, PI
- IronAge, Grégoria Kalpouzos, PI
- Psychosocial working conditions and late-life physical functioning: What role do gender, socioeconomic position, work-life balance, and coping mechanisms play? Ingemar Kåreholt, PI

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- Sino-Sweden Network for Aging Research: differential impacts of biomedical and environmental factors on cognitive aging across cultures, Chengxuan Qiu, PI
- The role of cerebral small vessel disease in cognitive aging, Chengxuan Qiu, PI
- Can a healthy physical and social environment compress the period of disability in older adults? Debora Rizzuto, PI

- Brain functional connectome across the human lifespan: links to white matter degeneration, dopamine depletion, and cognitive decline (DyNAMiC), Alireza Salami, PI
- •Why do older people seek emergency care? Causes, circumstances and explanations, Pär Schön, PI
- Immunization, frailty and healthy aging: a scoping review, Davide L. Vetrano, PI
- How does physical activity preserve cognition in aging? Rui Wang, PI
- Social Health And Reserve in the Dementia patient journey (SHARED), Anna-Karin Welmer, PI
- Thinking, moving, and falling: early detection of fall-prone phenotypes as targets for primary interventions—a translational study, Anna-Karin Welmer, PI
- Identifying compensatory mechanisms against dementia in diabetes, Weili Xu, PI

Number of publications by year

YEAR	ORIGINAL ARTICLES	REVIEW ARTICLES	REPORTS	book Chapters	PHD Theses	other pub.	IN TOTAL
2017	99	10	4	3	4	2	122
2018	116	15	3	4	6	2	146
2019	140	16	5	2	10	8	181
	355	41	12	9	20	12	449

International forum

2017

Kirk Erickson, Professor, University of Pittsburgh, US. Aging, exercise and brain plasticity. March 16.

Amélie Quesnel-Vallée, Associate Professor, McGill University, Canada. The development of health inequalities across generations. June 15.

Kim Beernaert, post doc, Vrije Universiteit Brussel. Improving comfort around dying in elderly people: a cluster randomized controlled trial. September 14.

Lars Nyberg, Professor, Umeå University. Brain maintenance: studies from the Betula project. October 27.

2018

Martin Hyde, Associate Professor, Centre for Innovative Ageing, Swansea University. Trapped between Ageism and Austerity? Problematising the problem of the older worker. March 15.

Susanne Jaeggi, Associate Professor, UC Irvine. Enhancing brain and cognition through cognitive training. March 27.

Luigi Ferucci, Scientific Director NIA, Longitudinal Studies Section. Aging beyond description: the example of sarcopenia. May 23.

Geert Jan Biessels, Professor, UMC Utrecht. Diabetes, cognitive ageing and dementia. May 29.

Anne B. Newman, Professor, University of Pittsburg. Healthy aging – Impact of Cardiovascular Disease. June 5.

Emanuele Marzetti, Assistant Professor, Geriatrics Teaching Hospital "Agostino Gemelli", Rome; and **Riccardo Calvani**, Post doc, Catholic University of the Sacred Heart, Milan. Bio-gerontology and Translational Medicine: How Can We Reach "Optimal Longevity? September 4.

John T O'Brien, Professor, University of Cambridge. Can imaging changes be detected 20 years before symptom onset in dementia? September 27.

2019

Jennifer Weuve, Associate Professor, School of Public Health, Boston University. Racial disparities in dementia risk. March 21.

Albert Roso, Statistician Foundation University Institute for Primary Health Care Research Jordi Gol i Gurina, Barcelona; and **Davide Vetrano**, PhD Student ARC, KI/ SU. Longitudinal development of MM clusters. April 2.

Stephanie Studenski, Professor, University of Pittsburgh School of Medicine. Mobility and aging. May 14.

Mariana Virtanen, Professor, Department of Public Health and Caring Sciences, Uppsala University and Finnish Institute of Occupational Health, Helsinki and Turku, Finland. Working conditions and health: recent evidence from large cohort studies. June 4.

Greg Arling, Professor, School of Nursing, Purdue University. Promoting care transitions from nursing facility to community: Maximizing consumer choice while achieving cost savings. June 13.

Gagan S. Wig, Associate Professor, Center for Vital Longevity, School of Behavioral and Brain Sciences, University of Texas at Dallas. Brain network aging. September 17.

Hanneke E. M. den Ouden, Assistant Professor, Radbound University, Netherlands. Maladaptive biases in motivated action: computations, brains and psychopathology. October 2.

Manuel Montero Odasso, MD, PhD, Gait and Brain Lab, Parkwood Institute and University of Western Ontario. There is something in the way you walk. Lessons learnt from the Gait and Brain Study. October 24.

Kristine Yaffe, Professor, University of California San Fransisco. Sleep disturbances and accelerated cognitive aging. December 11.

Guest researchers

2017

Federica Prinelli, Post doctoral fellow, Institute of Biomedical Technologies, CNR, Italy. At ARC: January 16 to February 3. Host: Weili Xu.

Miriam Haaksma, PhD student, Radboud University, Netherlands. At ARC: January-October. Hosts: Debora Rizzuto, Amaia Calderon Larrañaga and Laura Fratiglioni.

Terese Høj Jørgensen, Assistant Professor, University of Copenhagen, Denmark. At ARC: February-May. Hosts: Stefan Fors and Johan Fritzell.

Caterina Trevisan, PhD student, Università di Padova, Italy At ARC: February-November. Hosts: Debora Rizzuto and Anna-Karin Welmer.

Petra Ulmanen, researcher, Socialhögskolan, Stockholm University. At ARC: spring 2017. Hosts: Carin Lennartsson and Pär Schön.

Laura Mónica Pérez Baztan, MD, Parc Sanitari Pere Virgili Hospital, Barcelona. At ARC: March 1 to May 31. Host: Amaia Calderon Larrañaga.

Ross Andel, Professor, University of South Florida, USA. At ARC: May 15-29. Host: Ingemar Kåreholt.

Isabel Bauman, researcher at LIVES, Schwitzerland. At ARC: May 15 to July 15. Host: Neda Agahi.

Benjamin Shaw, Professor, University at Albany, USA. At ARC: May 31 to June 10. Host: Neda Agahi.

Amélie Quesnel-Vallée, Associate professor, McGill University, Canada. At ARC: June 10-17 and October 15-21. Host: Johan Fritzell.

Theresa Müller, master's student, University of Cologne, Germany. At ARC: August-December. Supervisor: Erika Jonsson Laukka. **Rui She,** PhD student, Chinese University of Hong Kong (CUHK), China. Exchange program between KI and CUHK. At ARC: September 5 to November 30. Supervisor: Chengxuan Qiu.

Yongxiang Wang, Post doctoral fellow, Shandong Provincial Hospital affiliated to Shandong University, China. At ARC: September 25 to December 20. Host: Chengxuan Qiu.

Alberto Zucchelli, MD, Brescia, Italy. At ARC: November 2017 to May 2018. Hosts: Davide Vetrano and Debora Rizzuto.

2018

Roger Keller Celeste, professor, Universidade Federal do Rio Grande do Sul, Brazil. At ARC: January 31to March 31, Host: Johan Fritzell.

Emily Loughlin, PhD Student, National University of Ireland, Irland. ROSEnet Short Term Scientific Mission. At ARC: February 7-17. Supervisor: Lena Dahlberg

Simon Englund, master's student, KI. At ARC: January-May. Supervisor: Debora Rizzuto

Marguerita Saadeh, master's student, Public Health program KI. At ARC: January-June. Supervisor: Amaia Calderon Larrañaga.

Klara Johanna Lohkamp, master's student, Radboud University, The Netherlands. At ARC: June 4 to November 30. Supervisors: Chengxuan Qiu and Mozhu Ding.

Amélie Quesnel-Vallée, Associate Professor, McGill University, Canada. At ARC: June 11-17. Host: Johan Fritzell.

Linda Enroth, Post doc, Tampere University, Finland. At ARC: September 2018 to February 2019. Host: Stefan Fors and Johan Fritzell.

2019

Wu Wei, post doc, Hubei University of Chinese Medicine, China. At ARC: March 2019 to March 2020. Host: Laura Fratiglioni and Debora Rizzuto.

Rownak Jahan Archie, master's student, KI. At ARC: January to June. Supervisors: Chengxuan Qiu and Mozhu Ding.

Ottavia Ferraro, PhD student, University of Pavia, Italy. At ARC: February-July. Supervisor: Debora Rizzuto.

Laura Salonen, PhD student, University of Turku, Finland. At ARC: spring 2019. Supervisor: Johan Fritzell.

Susanne Jaeggi, Professor, University of California, Irvine, USA. At ARC: April 11 to May 16. Host: Lars Bäckman.

Amélie Carrère, PhD student, INED, France. At ARC: April 23 to May 19. Supervisor: Lucas Morin.

Qiqi Wang, PhD student, Chinese Center for Disease Control and Prevention (China CDC), Beijing, China. At ARC: August 31 to November 28. Supervisors: Chengxuan Qiu and Yajun Liang.

Abigail Dove, master's student, University of Helsinki, Finland. At ARC: August-December. Supervisor: Anna Marseglia.

Caterina Trevisan, PhD student, Geriatric Unit, Department of Medicine, University of Padova, Italy. At ARC: August 2019 to January 2020. Supervisor: Anna-Karin Welmer.

Alessandra Marengoni, Associate Professor, University of Brescia, Italy. At ARC: August 2019 to July 2020. Host: Laura Fratiglioni.

Andreja Speh, MSc doing a one-year research stay, University of Ljubljana, Slovenia. At ARC: August 2019 to August 2020. Supervisor: Erika Jonsson Laukka.

Katharina Allers, PhD student, Carl von Ossietzky University of Oldenburg, Germany. At ARC: August-November 2019. Host: Lucas Morin.

Maria Forslund, PhD student, Swedish Institute for Social Research, Stockholm University. At ARC: October 2019 to summer 2020. Host: Johan Fritzell.

Ju Yui Lee, Professor, Namseoul University, Korea. At ARC: November 18 to December 13. Hosts: Johan Fritzell and Pär Schön.







Photos: Sara Eng, Linda Ydemar and Veronica Tybell

Aging Research Center

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