Contents

4 Message from the director
5 Introduction
7 Organization
8 Organization and leadership
12 Collaboration around the world
14 Guest researchers
17 Research
19 Research infrastructure
20 Scientific production in numbers
21 Research – major findings in brief
33 Education
41 Additional achievements
42 Career advancements
42 New appointments at KI
43 Appointments to commissions of trust outside KI
43 Awards
45 Scientific outreach
46 Clinical and societal impact
47 Communication and dissemination of research findings
48 Selection of outreach activities and events
50 ARC in the media
53 Finance, funding, and future plans
57 Appendix
58 Publications
72 International forum
74 Guest researchers
75 Overview of number of employees per sector and per level

Production: Aging Research Center
Cover photos: Copyright Grafvision 2013 (used under license from Shutterstock.com) and Fred Froese, Irina Afonskaya, and CREATISTA 2013 (used under license from iStockphoto.com).
Message from the director

Two years have passed since our last report, two intensive years rich in exciting scientific findings, implementation of new research lines, and further expansion of our center. At moments like this, it is important to pause, look back, and consider our achievements. I have had the pleasure of leading ARC since 2007, and as with previous biennial reports, on this occasion I am pervaded by a feeling of pride and happiness. No matter which parameters we look at, we are doing our job well. We produce high-quality research, have an impact on society, and—I believe—contribute to better health for old people. In just the last two years, we have accomplished a great deal. We have completed several studies published in high impact journals, consolidating our national and international profile in the field of aging research. We have followed several PhD students up to completion of their graduate programs. We have employed two new professors and new lecturers, opened a new lab, and developed larger national and international networks. Finally, our budget has grown substantially.

In 2000, when ARC was first established, we were a small group of enthusiastic researchers highly motivated to build a new center in Sweden to increase our opportunities for internationally competitive science. In the last decade and a half, we have actively participated in the development of the research field and have grown along with it. We have invested in a serious effort to recruit and train a new generation of top-level scholars who are passionate about aging research. At the same time as our mid-career researchers are becoming leaders in their fields, the mean age at ARC is growing younger—a good sign for the future of ARC and the future of aging research in Sweden.

Organizational and in terms of personnel, ARC has matured as we have grown. We have modified our internal organization to keep pace with our expansion and have made concrete, consistent efforts to involve the new generation of aging researchers in the workings and administration of the center, because they are ARC’s future.

Finally, last but not least, in spite of our growth—ARC now has almost 90 employees—we have preserved a warm and friendly atmosphere. When you come to our center, you will find hard workers who stay at their computers even late into the evening, and you can often hear discussions and challenging questions, but also lots of laughs. We are convinced that our social atmosphere, accumulated research experience, and growing expertise will help us achieve our future goals and increase our impact in the scientific and clinical communities as well as in society.

Laura Fratiglioni  
Director of ARC

The Aging Research Center (ARC) was established in 2000 by Karolinska Institutet (KI) and Stockholm University. It is a “Center of Excellence” supported by two consecutive grants from the Swedish Research Council for Health, Working Life and Welfare (Forte).

ARC is a physical center that shares premises with its closest collaborators, the Stockholm Gerontology Research Center (Äldescentrum, supported by Stockholm City and the Stockholm County Council) and the Swedish Dementia Centre (Svenskt Demenscentrum, supported by the Swedish National Board of Health and Welfare). This close proximity facilitates the sharing of research findings with an audience beyond academia. Together with the two other centers, ARC supports the aging research magazine, Äldre i Centrum.

ARC is internationally renowned for its research on the health status of older adults, trends and inequality among old people, brain aging, and prevention of dementia. The research activities are characterized by:

1. A focus on health in aging, the goal of which is preventing, postponing, or decreasing morbidity and disability in old age.
2. A multidisciplinary approach that includes medicine, social gerontology, psychology, and epidemiology.
3. Creation of large databases from population-based studies on aging and health.
4. Access to other large databases on aging via national and international collaboration.
5. Integration of epidemiological and social science studies with clinical and molecular work.
7. Special attention to neuroscience with focus on neural correlates of cognitive functions and prevention of brain aging.
8. Implementation of intervention studies to prevent cognitive decline, dementia, and multimorbidity.

Since January 2008, the research environment has been strengthened by the creation of the Graduate Research School on Health and Aging, which is also supported by Forte. The school uses the competencies of partners at multiple universities across Sweden to give PhD students a theoretically and methodological-ly multidisciplinary background.

The Aging Research Center (ARC) was established in 2000 by Karolinska Institutet (KI) and Stockholm University. It is a “Center of Excellence” supported by two consecutive grants from the Swedish Research Council for Health, Working Life and Welfare (Forte).

ARC is a physical center that shares premises with its closest collaborators, the Stockholm Gerontology Research Center (Äldescentrum, supported by Stockholm City and the Stockholm County Council) and the Swedish Dementia Centre (Svenskt Demenscentrum, supported by the Swedish National Board of Health and Welfare). This close proximity facilitates the sharing of research findings with an audience beyond academia. Together with the two other centers, ARC supports the aging research magazine, Äldre i Centrum.

ARC is internationally renowned for its research on the health status of older adults, trends and inequality among old people, brain aging, and prevention of dementia. The research activities are characterized by:

1. A focus on health in aging, the goal of which is preventing, postponing, or decreasing morbidity and disability in old age.
2. A multidisciplinary approach that includes medicine, social gerontology, psychology, and epidemiology.
3. Creation of large databases from population-based studies on aging and health.
4. Access to other large databases on aging via national and international collaboration.
5. Integration of epidemiological and social science studies with clinical and molecular work.
7. Special attention to neuroscience with focus on neural correlates of cognitive functions and prevention of brain aging.
8. Implementation of intervention studies to prevent cognitive decline, dementia, and multimorbidity.

Since January 2008, the research environment has been strengthened by the creation of the Graduate Research School on Health and Aging, which is also supported by Forte. The school uses the competencies of partners at multiple universities across Sweden to give PhD students a theoretically and methodological-

Laura Fratiglioni
Director of ARC

Photo: Tore Bellander

Photo: Tore Bellander

---

Introduction

The Aging Research Center (ARC) was established in 2000 by Karolinska Institutet (KI) and Stockholm University. It is a “Center of Excellence” supported by two consecutive grants from the Swedish Research Council for Health, Working Life and Welfare (Forte).

ARC is a physical center that shares premises with its closest collaborators, the Stockholm Gerontology Research Center (Äldescentrum, supported by Stockholm City and the Stockholm County Council) and the Swedish Dementia Centre (Svenskt Demenscentrum, supported by the Swedish National Board of Health and Welfare). This close proximity facilitates the sharing of research findings with an audience beyond academia. Together with the two other centers, ARC supports the aging research magazine, Äldre i Centrum.

ARC is internationally renowned for its research on the health status of older adults, trends and inequality among old people, brain aging, and prevention of dementia. The research activities are characterized by:

1. A focus on health in aging, the goal of which is preventing, postponing, or decreasing morbidity and disability in old age.
2. A multidisciplinary approach that includes medicine, social gerontology, psychology, and epidemiology.
3. Creation of large databases from population-based studies on aging and health.
4. Access to other large databases on aging via national and international collaboration.
5. Integration of epidemiological and social science studies with clinical and molecular work.
7. Special attention to neuroscience with focus on neural correlates of cognitive functions and prevention of brain aging.
8. Implementation of intervention studies to prevent cognitive decline, dementia, and multimorbidity.

Since January 2008, the research environment has been strengthened by the creation of the Graduate Research School on Health and Aging, which is also supported by Forte. The school uses the competencies of partners at multiple universities across Sweden to give PhD students a theoretically and methodological-ly multidisciplinary background.
ARC envisions a world in which all people can age with dignity and security through improvements in health, equal access to the best social and medical services, and full integration in society.

ARC’s mission is to understand the biomedical and psychological aspects of the aging process in relation to social and physical contexts across the entire lifespan. Our ultimate goal is to improve the health and well-being of older individuals by meeting the challenges and embracing the opportunities presented by the aging population.
ARC is a center within KI; it is part of the Department of Neurobiology, Care Sciences and Society (NVS). It is led by a board that includes representatives from Forte, Karolinska Institutet, Stockholm University, and the Stockholm Gerontology Research Center as well as other Swedish universities.

The responsibility for scientific, organizational, and financial issues, including those related to staff, external contractors, and changes in administrative staff, is shared by the members of the Steering group, which is led by ARC’s director. ARC’s steering group consists of ARC’s director, Laura Fratiglioni; the Division Head; Kristina Johnell; the Deputy Head of Division, Jonas Persson; senior representatives from each sector; and three junior research representatives. This group meets once a month. Daily decisions and actions regarding promotion, finances, staff, and work environment are made by the Executive group.

ARC has a yearly planning day (ARC day) where both scientific updates are presented and organizational issues are discussed. The sectors are also presenting new research findings, discuss collaboration, and socialize on retreats which are organized regularly. At the ARC Junior Researcher Group retreat, graduate students and post-docs meet every year to work on collaboration, give updates on the latest research, and practice their presentation skills.

ALL AT ARC

Members of the Aging Research Center.
SECTOR MEDICINE

Back row: Kristina Johnell (Head of Division), Johan Fastbom, Weili Xu, Lucas Morin, Anna-Karin Welmer, Laura Fratiglioni (Director), Linda Rettenwander, Anna Marsaglia, Francesca Mangiafico, Hu-Xin Wang, Rui Wang, and Barbara Caracciolo.

Front row: Gioia Santore, Krister Håkansson, Debora Rizzuto, Emerald Heiland, and Mozhu Ding.
The sector is led by: Laura Fratiglioni, Johan Fastbom, Kristina Johnell, and Miia Kivipelto.

SECTOR PSYCHOLOGY


Front row: Cecilia Stenfors, Goran Papenberg, Lars Backman, Erika Jonsson Laukka, and Jonas Persson (Deputy Head of Division). The sector is led by: Lars Backman and Martin Lövdén.

SECTOR SOCIAL GERONTOLOGY


Front row: Johan Fritzell, Carin Lennartsson, Ingemar Kåreholt, Marti Parker, och Lena Dahlberg.
The sector is led by: Johan Fritzell, Carin Lennartsson, and Marti Parker.

ADMINISTRATIVE AND TECHNICAL STAFF

Vanessa Suthat, Kimberly Kane, Lena Ragert-Blomgren, Johanna Bylund, Cecilia Annerholm, Alexandra Ek, Maria Wahlberg, and Maria Yohuang.

Please note that not all members of staff were present when the photos were taken.
Collaboration around the world

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

EU consortia where ARC researchers are involved:

- EIT Health, a node in the EU granted KIC network – Knowledge Innovation Communities
- The European Study of Cohorts for Air Pollution Effects (ESCAPE)
- The European Prevention of Alzheimer’s Dementia (EPAD)
- Healthy Ageing Through Internet Counselling in the Elderly (HATICE)
- EU Joint Programme – Neurodegenerative Disease Research (JPND)
- Multidimensional Prognostic Indices (mPI-age)
- New dietary strategies addressing the specific needs of the elderly population for healthy ageing in Europe (NU-AGE)
ENRICO MOSSELLO  
MD, Research Unit of Medicine of Ageing, Department of Experimental and Clinical Medicine, University of Florence

“I was at the Aging Research Center for 3 months after a lucky meeting and a warm invitation from Professor Laura Fratiglioni. The idea was to analyze epidemiological data gathered in Stockholm to better understand the research question I had as a clinical researcher and medical doctor practicing psychogeriatrics: what is the effect of background personality on aging-related health outcomes? My stay in Stockholm was truly engaging. Under the guidance of Professor Laura Fratiglioni and Hui-Xin Wang and working in cooperation with Almira Osmanovic-Thunström and Sara Angleman, I directly experienced how data are gathered and analyzed in a large epidemiological study. I also had a chance to improve my ability to perform statistical analysis and to present them in a scientific paper. I enjoyed the extraordinary organization of the research setting, the lovely welcome from all colleagues, the stimulating discussions mixing clinical issues and research methodology, and the pleasant stay in the city.”

BARBARA WIMMER  
PhD student, Monash University

“From the beginning of June to the end of October 2014, I visited the ARC as a guest PhD student from Monash University, Melbourne, Australia. Under the supervision of Associate Professor Kristina Johnell, I had the chance to investigate various aspects of medication regimen complexity in the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K), including factors associated with medication regimen complexity in older people and medication self-administration problems in older people in Sweden. The very friendly and supportive atmosphere at ARC, the interdisciplinary composition, the diversity and high quality of presentations and continuing education, and an amazing warm and light summer were highlights of my stay. Very special thanks to all who made my time in Stockholm a great experience!”

ROSS ANDEL  
Associate Professor, School of Aging Studies, University of South Florida

“I visited ARC between June 8 and 18, 2014. During my stay, I met with several collaborators working at ARC (e.g., Dr. Kåreholt), as well as those from elsewhere but working at ARC at the same time as I was (e.g., Professor Silverstein from the University of Syracuse). In addition, I scheduled multiple meetings with my doctoral students at ARC. Finally, I gave a presentation entitled “Sugar and Cognition: Why Sweetening Your Life May Make Your Brain Sour” in which I discussed some of my recent findings regarding the influence of blood glucose on cognitive aging using Sweden-based data. As every year, I immensely enjoyed my time at ARC. I enjoy the setup where a great number of researchers are seated within a small area, thus facilitating discussions and collaboration.”

MARYAM ZIAEI  
PhD student, School of Psychology, University of Queensland

“I came to ARC to visit Associate Professor Jonas Persson and continue working with him on one of my PhD projects, which focuses on emotion–cognition interactions in young and older adults. During my visit I also started new collaborations and learned more about methods for analyzing fMRI data. Also, and importantly, I received very constructive feedback on my ongoing work. The friendly, welcoming, and inclusive environment of ARC helped me make new friends with researchers in the aging field and share my experience with them. I am hoping to continue my collaboration with researchers at ARC and visit the center again in the near future.”

Guest researchers – highlights

ARC has guest researchers from all over the world. In this section, the experiences of a selection of our guest researchers are highlighted. A complete list of guest researchers from 2013 to 2014 is included in an appendix at the end of the report.

Photo: Veronica Caleri

Photo: Kate Petri

Photo: Reza Bonyadi

Photo: John Smith
“I visited ARC between January 1 and February 28, 2014. During my stay, I worked together with Professor Fritzell in the social gerontology group on a project studying inequalities in oral health over the life course. My collaboration with Johan started at the State University of Rio de Janeiro in 2008. At ARC I also organized and taught a 2-week course on structural equation modelling. Students from both ARC and CHESS (Stockholm University), attended the course.

This was my first visit to ARC, and I was very impressed by the nice environment and the warm and productive atmosphere. It was notable that professors, researchers, and PhD students in the social gerontology group worked close together. This kind of working environment facilitates exchanges of ideas and insights, and I plan to continue research collaborations and student exchanges between ARC and my university.”

ROGER KELLER CELESTE
Senior Lecturer, Department of Preventive and Social Dentistry, Universidade Federal do Rio Grande do Sul

ÂKE WAHLIN
Professor in Gerontology, licensed psychologist, Institute of Gerontology, School of Health Sciences, Jönköping University

“In 2012 and 2013 I was on a 1-year sabbatical. Between December 1, 2012, and June 31, 2013, I was kindly invited to work as visiting professor at ARC. For me it was a happy reunion because I had been an employee at ARC between 1990 and 2003. During my stay, I was generously taken care of by Lars Bäckman’s research group. During this time I worked mainly with my BioAge projects and also wrote the application for a professorship in gerontology. As a result of that successful application I have been employed at Jönköping University since July, 2013.”
Research

In this section, a selection of research findings from the past two years will be briefly presented. This section also contains information about research infrastructure, scientific production, and data sets. Researchers from ARC continue to produce a high number of published papers, and many of them are published in high impact journals. Results from the ongoing population-based Swedish National study on Aging and Care in Kungsholmen (SNAC-K), and an ongoing intervention study, the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) will be presented. During the past two years, a new experimental laboratory for studies on cognitive intervention and neural plasticity (Hjärnlabbet; the Brain Lab) has been founded. Several new projects have also been initiated, including a project on Cognition, Brain and Aging (COBRA) and a project that investigates accumulation of iron in the brain, and its implications for cognitive functions and aging. Initial results from these projects will be described. Much research at ARC relies on information from large databases, and new data was collected in the longitudinal Swedish Panel Study of Living Conditions of the Oldest Old (SWEOLD).

Research infrastructure at ARC

ARC plays a major role in large ongoing studies of aging, including SNAC-K, SWEOLD, and the Swedish Centenarian Survey (part of the Five Country Oldest Old Project, 5-COOP). Information from these databases forms the basis of many of our most important research findings. In the SNAC-K project, ARC has also started a population-based magnetic resonance imaging study, SNAC-K MRI. The af Jochnick Center initiated and participates in the groundbreaking COBRA project.

ARC collaborates closely with researchers responsible for other large ongoing studies: the SNAC-K Care System Study; the Kungsholmen Project; Cardiovascular Risk Factors, Aging and Dementia (CAIDE); the European Dementia Prevention Initiative; FINGER; the Betula Project; Dementia in Swedish Twins; Healthy Aging Through Internet Counselling in the Elderly; Multimodal Preventive Trials for Alzheimer’s Disease: Towards Multinational Strategies (MIND-AD); the Swedish Level of Living Survey; and the Luxemburg Income Study.

At ARC we use various national registers, including the Swedish Prescribed Drug Register, the National Patient Register, and the Cause of Death Register. Located at the National Board of Health and Welfare, the Swedish Prescribed Drug Register is one of the largest pharmacoepidemiological databases in the world.
Scientific production in numbers

Number of articles, books, book chapters, reports, and PhD theses are reported below by research area.

<table>
<thead>
<tr>
<th>Research area</th>
<th>Original articles</th>
<th>Review articles</th>
<th>Book chapters</th>
<th>Reports</th>
<th>PhD theses</th>
</tr>
</thead>
<tbody>
<tr>
<td>A  Longevity, morbidity, and functioning</td>
<td>38</td>
<td>3</td>
<td>2</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>B  Treatment and care of elderly persons</td>
<td>18</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>C  Health trends and inequality</td>
<td>29</td>
<td>1</td>
<td>7</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>D  Brain aging</td>
<td>95</td>
<td>13</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>E  Miscellaneous</td>
<td>17</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 1. Number of articles, books, book chapters, reports, and PhD theses reported by research area.

Research – major findings in brief

A complete list of references cited in this section is provided in the appendix.

Research area 1: Longevity, morbidity, and functioning

Despite its intrinsic positive nature, the aging of the population poses challenging questions, such as how we can achieve not only longer but also healthier lives. Our goal is to increase knowledge regarding the complex picture of health in older adults, to describe their health status, and to monitor health trajectories during aging. We take many dimensions of health into account, including medical conditions, medication, perceived health, physical functioning, mobility, and well-being.

Paths toward healthy aging

As the population ages, elderly people are becoming an increasingly important group that merits special attention with regard to health and social issues. Lifestyles affect survival chances at all ages, but the consequences of poor lifestyle behaviors may differ between elderly people and young adults. In a systematic review, we summarized the evidence regarding the impact of lifestyle behaviors on survival among elderly people (Rizzuto et al. 2014). The benefits of healthy lifestyles (e.g., no smoking, normal weight, physical activity) and social support are still present in older adults. A healthy lifestyle, even at old age, leads to better physical function and decreased susceptibility to disease, which is one of the key factors to longevity. Although several specific determinants of human longevity have been identified, the underlying social and biological pathways remain to be clarified. It is clear that none of the factors identified to date is necessary or sufficient to determine how each individual will age; people may achieve exceptional longevity in multiple ways by engaging in different combinations of healthy behaviors. The mechanisms behind longevity are likely to involve the complex interplay among demographic, physiological, behavioral, and biological factors and their association with different health outcomes. Moreover, not only do biological, social, and psychological factors contribute to health in aging, but they are also active across the whole lifespan (Figure 2).

Longer telomeres (located at the ends of the chromosomes) have been associated with a longer lifespan. We investigated the association between a polymorphism (T/C) of a telomere gene (hTERT) and longevity in two cohorts of older adults, one from the Kungsholmen Project and the other from SNAC-K (Kalpouzos et al. 2014). In both cohorts, female T/T carriers aged 75 years or older lived 2 to 3 years longer than the female C/C carriers. This effect, possibly due to a synergistic effect between genetic background and the lifelong exposure to endogenous estrogen, was not present in men or younger old people.
Social conditions and health behaviors at middle age affect late-life health. The likelihood of living a long and healthy life is, in part, shaped by social conditions experienced throughout the life course. We have investigated the relationship between earlier life environmental conditions and late-life health. First, we examined trajectories of social engagement from midlife to old age and late-life disability. We found that both decreasing levels of social activities and continuously low levels of social activities are associated with increased risk of disability (Agahi et al. 2013). Second, we analyzed how changes in smoking habits over a long period were associated with progression to health problems from midlife to old age. We found that smokers, and even former smokers, who survived into old age, appear to be at an increased risk for impaired mobility, musculoskeletal pain, and psychological distress, which can diminish quality of life and increase care needs (Agahi & Shaw 2013; Andel et al. 2014). Finally, we explored the associations between physical and psychosocial work environment in midlife and health in late life. The results show that both poor psychosocial and physical work environments in midlife are associated with an increased likelihood of psychological distress, musculoskeletal pain, and physical impairment during old age (Nielsen et al. 2014). This finding highlights the detrimental long-term health consequences of work-related stress.

Previous research suggests that vascular risk factors and related vascular diseases impair functional independence in older adults. Data from SNAC-K showed that the aggregation of multiple vascular risk factors or related cardiovascular diseases are associated with an increased likelihood of mobility limitation, and that the association may vary by age (Andel et al. 2014). This finding highlights the importance of understanding how vascular risk factors are partially mediated by atherosclerosis of large cerebral and peripheral arteries (Welmer et al. 2014).

Research area 2: Treatment and care of elderly persons

The research in geriatric pharmacoepidemiology at ARC aims to understand and improve drug treatment in older people. This work focuses on the quality and inequality of older people’s drug therapy, drug treatment in persons with dementia, and monitoring drug use over time. We develop analytical methods for studying drug use and for reviewing drug treatment in older patients. We also contribute to the development of indicators for assessing the quality of drug use and to information technology solutions to help prescribers make optimal decisions. We collaborate closely with the Swedish National Board of Health and Welfare.

With regard to health and social care services for the elderly population, we focus on how people’s needs are met. We also investigate the social policy implications of increasing longevity and the increasing number of elderly persons with ill-health and complex health problems in societies worldwide.

Quality of medication use in elderly people

In collaboration with researchers involved in the Swedish Dementia Registry, we found that patients who use anti-dementia drugs of the cholinesterase inhibitor type are treated with less antipsychotics and anxiolytics than patients who do not take cholinesterase inhibitors. Our results suggest that treatment with cholinesterase inhibitors may reduce the behavioral disturbances characteristic of patients with Alzheimer disease (Fereishtehnejad et al. 2014).

In collaboration with researchers from Australia, we found that older hospitalized persons with high medication regimen complexity are more likely than those with lower level of education to be prescribed psychotropic drugs by psychiatrists and geriatricians than those with lower level of education (Wasteson et al. 2014).

We have presented a hypothetical economic model of disease-modifying treatment for people with Alzheimer disease, which shows that such a treatment would lead to high costs for society, both because of the costs of the treatment itself and the prolonged survival of people who are treated (Sköldunger et al. 2013).

In a collaborative project with researchers from Sahlgrenska University hospital, we found that the number of drugs increased by two per person 3 months after transition from ordinary prescriptions to multi-dose drug dispensing (Wallerstedt et al. 2013). This increase was accompanied by a decrease in the quality of drug use and a future lower rate of change in drug use (Figure 3).

In a project at the Swedish National Board of Health and Welfare, we compiled data from scientific studies and Swedish registers about the prevalence and nature of adverse drug reactions that led to hospital admissions of elderly people (Socialstyrelsen 2014). The most important finding is that the majority of hospitalizations due to adverse drug reactions are caused by a limited number of drugs that result in a limited number of symptoms or disorders, many of which are preventable. This suggests that instruments may be developed to detect and prevent adverse drug reactions leading to hospitalizations.

Figure 3. The proportion of patients who had potentially harmful drug treatment according to indicators of prescribing quality. Longitudinal results for 10,922 individuals at 3-month intervals before and after the transition to multi-dose drug dispensing (index date) (adapted from Wallerstedt et al. 2013).

To be prescribed psychotropic drugs by psychiatrists and geriatricians than those with lower level of education (Wasteson et al. 2014).
Why do socioeconomic inequalities in health persist in old age?

Socioeconomic inequalities in health are remarkably robust across countries, over time, and across numerous health indicators, even in people of advanced age (Fritzell 2014). In the SNAC-K study, we found that a higher level of education was associated with better performance in tests of balance, timed chair stands, and walking speed in people aged 60 to 60. Further analyses suggested that a higher level of education was associated with better gap strength among female manual workers and with better balance and walking speed among non-manual workers (Welmer et al. 2013). Using data from SWEOLD, we have shown that older women had more health problems than older men and that people with a lower level of education had more health problems than people with a higher level of education; the disparities were observed in all age groups and across a wide range of health indicators (Figure 5; Fors et al. 2013; Fors & Thorslund 2015).

Health inequalities are shaped by life-long processes. Thus, it is critical to understand the issue of health inequalities from a life course perspective. We conduct cross-national, comparative research highlighting socioeconomic differences in mobility and cognitive impairment across individuals. A higher level of education, living with somebody, and female gender were associated with better diet quality across the four countries (Irz et al. 2014). Our research also revealed that socioeconomic differences in mobility and cognitive impairment among older people in Sweden could partly be attributed to social gradients in smoking and obesity (Fors et al. 2013). Finally, findings from the US older population suggest that behavioral risk factors such as smoking and physical inactivity contribute to socioeconomic inequalities in health (Shaw et al. 2014).

A potential explanation for socioeconomic inequalities in late-life health focuses on the role of health-related behaviors. Analyzing the financial, social, and demographic determinants of diet quality among older people in four European Union countries (the United Kingdom, Italy, Sweden, and Finland), we found that diet quality was low on average and heterogeneous across individuals. A higher level of education, living with somebody, and female gender were associated with better diet quality across the four countries (Irz et al. 2014). Our research also revealed that socioeconomic differences in mobility and cognitive impairment among older people in Sweden could partly be attributed to social gradients in smoking and obesity (Fors et al. 2013). Finally, findings from the US older population suggest that behavioral risk factors such as smoking and physical inactivity contribute to socioeconomic inequalities in health (Shaw et al. 2014).
Research area 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-year-olds? 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/or physical training or changes in diet? Several factors typically interact to cause faster cognitive decline and dementia, and some factors can protect against cognitive deterioration.

Genetic influences on brain functioning become stronger with increasing age and decreasing brain resources. Heritability studies have documented that genetic influences on cognitive performance and decline increase in old age. Given these associations, we investigated the effects of common genetic variations on brain integrity and cognitive functioning in older adults without dementia. Our cross-sectional and longitudinal data suggest that effects of genetic variations on cognition become stronger as people age (e.g., Ghisletta et al. 2014), whereas genetic effects in younger adults are smaller or undetectable. Furthermore, we documented that genetic effects in old age are stronger when carrying two or more disadvantageous genotypes, which may result in interactive genetic effects on cognition (Papenberg et al. 2014). These patterns support the notion that age-related declines in brain resources may magnify effects of genes on cognition. Extending these patterns to the neural level in a functional imaging study, we found lower performance in updating of long-term memories for older carriers of a genetic predisposition associated with less dopamine D2 receptors in the striatum (Pantzar et al. 2014). In contrast, no genetic effects were observed in non-depressed individuals carrying both risk alleles (associated with Alzheimer’s disease) on memory for past events (Ferenczi et al. 2014). In another study on depression in old age, we found that memory-related genetic variations affected memory for past events only in older adults with depression. Individuals carrying both risk alleles performed the worst on tests of memory (Pantzor et al. 2014). In contrast, no genetic effects were observed in non-depressed individuals, again suggesting that genetic effects are most easily detected at suboptimal levels of brain functioning.

Despite increasing evidence in favor of magnification of genetic effects in aging, we did not find evidence for this pattern in a larger study of older adults, likely because many lifestyle and individual-difference factors may overshadow genetic effects (Laukka et al. 2013). Indeed, our data suggest that once additional factors are taken into account, it may be easier to disclose genetic effects in old age. We showed that more physical activity circumvents negative effects of carrying disadvantageous genotypes (associated with Alzheimer disease) on memory for past events (Ferenczi et al. 2014). In another study on depression in old age, we found that two memory-related genetic variations affected memory for past events only in older adults with depression. Individuals carrying both risk alleles performed the worst on tests of memory (Pantzor et al. 2014). In contrast, no genetic effects were observed in non-depressed individuals, again suggesting that genetic effects are most easily detected at suboptimal levels of brain functioning.

Taken together, several studies from our lab suggest that effects of common genetic variations on brain functioning may become stronger with increasing adult age or may be most easily detected in populations characterized by lower brain resources. In this way, genetic effects contribute to the increased between-person differences in cognitive and brain aging.

Vascular burden and psychological stress undermine brain integrity
Effects of aging on the structural integrity of the brain have been extensively studied for many years. However, the factors that contribute to the deterioration of structural integrity remain to be found, and longitudinal assessments are still sparse. At ARC, the large database from the SNAC-K population study contains structural neuroimaging data. The database includes measurements of gray and white matter volume and assessments of microstructural and macrostructural white matter integrity.

In our exploration of the factors that contribute to loss of brain integrity in aging, we found that old age, genetic susceptibility (e.g., APOE ε4), and increased burden of vascular risk factors (e.g., hypertension, diabetes) are associated with brain pathology. Specifically, we observed that a marker of cerebral small vessel disease (white matter hyperintensities) was associated with reduced brain tissue volume. This association was independent of the aging process, genetic susceptibility, and vascular risk factors (Wang et al. 2014). Using diffusion tensor imaging, we also investigated the role of vascular risk factors in microstructural white matter integrity. We showed that the aggregation of heavy alcohol consumption, hypertension, diabetes, and current smoking is detrimental to white matter integrity, and that this effect is more pronounced among APOE ε4 carriers (Wang et al. 2015). We paid special attention to the medial temporal lobe because it is particularly vulnerable to aging and found that negative life events influence the volumes of hippocampus and amygdala. The strongest effects were observed for events experienced in adolescence and old age (Gerritsen et al. 2015). We are currently investigating whether lifestyle factors and inflammation influence brain integrity.

We also investigated the relationships between gray matter and white matter deterioration and cognitive decline. We first showed that among the cognitive domains explored in SNAC-K, only perceptual speed was related to microstructural white matter indices, and solely in participants older than 78 years (Laukka et al. 2013). We further demonstrated a longitudinal relationship between microstructural white matter indices and perceptual speed in the older participants. Decline in perceptual speed was associated with integrity of the corticospinal tract (Figure 7; Lövdén et al. 2014).

Figure 7. On the left, the corticospinal tract is shown in dark blue on the brain map. On the right, the graph displays the relationship between change over 2.5 years in integrity of the corticospinal tract (mean percentage, which is an index of white matter integrity) and change in perceptual speed performance in participants in the Swedish National Study on Aging and Care (Lövdén et al. 2014).

Figure 6. Brain activation in the left caudate nucleus during long-term memory updating. Older A1-carriers (A1) had significantly less activation in this region than younger adults and older non-carriers (adapted from Persson et al. 2014).
Finally, using diffusion tensor imaging data from SNAC-K, we showed that reduced integrity of white matter microstructure was associated with exacerbated global cognitive decline (Figure 8, Wang et al. 2015).

The strong effect of vascular burden and metabolic disorders in brain structural changes has been confirmed also by other studies of the CAIDE MRI subsample and the participants in the AGES-Reykjavik Study. In the CAIDE subsample, middle hypertension, but not body mass index or cholesterol, was associated with thinner cortex in various brain regions and thinner cortex in various brain regions and 2) smaller gray matter volume, but only if the coronary heart disease had started at least a decade prior to the MRI examination (Vuorinen et al. 2014). In the AGES-Reykjavik Study of 4206 elderly persons, diabetes was strongly related to cerebral microbleeds, cortical and subcortical infarcts, more white matter lesions, less gray matter, and more global atrophy. Diabetes was also associated with poorer performance on tests of executive function and processing speed. Such deleterious effects of diabetes on cognition were mediated by the structural brain abnormalities (Qu et al. 2014).

Additionally, a study on serum homocysteine (a sensitive marker of folate and vitamin B12 status) reinforced the hypothesis that vascular mechanisms play a role in brain pathological alterations. Findings from prospective studies on the role of homocysteine in Alzheimer disease have been mixed. Post-mortem and MRI data from the population-based Vantaa 85+ Study (n=265, 103 had post-mortem MRI) showed that elevated homocysteine levels are associated with more neurofibrillary tangles, especially in persons who had a dementia diagnosis and cerebral infarcts. MRI data revealed that higher levels of homocysteine were associated with more severe medial temporal lobe atrophy and more severe periventricular white matter hyperintensities (Hoooshmand et al. 2013).

Tracing the progression from physical impairment and subjective cognitive impairment to dementia It is still not clear whether subtle physical impairment or cognitive impairment represents the first sign in the path leading to dementia. Using the 6-year follow-up data from SNAC-K on 2998 individuals aged 60+ years, we found that slower walking speed or decline in walking speed (a sign of physical impairment) is associated with an increased likelihood of incident dementia. However, we further found that processing speed (a cognitive measure) could partly account for the association between slower walking speed and increased risk of dementia (Widmer et al. 2014). These results suggest that slowing of walking speed may occur secondary to slowing of processing speed in the path leading to dementia.

In a Swedish Twin Registry study of 11379 individuals aged 50+ years, chronic morbidity, especially multimorbidity, was associated with both subjective cognitive impairment and cognitive impairment without dementia. Multiple mechanisms may be involved in these associations. A twin-correlation matched-case-control analysis suggested that genetic and early-life environmental factors may partially account for the association between chronic diseases and cognitive impairment without dementia but not for the association between chronic disease and subjective cognitive impairment (Caracciolo et al. 2013).

Role of vitamins in late-life cognitive impairment and Alzheimer disease We found that elevated serum levels of different vitamin E forms are associated with reduced risk of cognitive impairment in older adults, and the association is modulated by concurrent blood cholesterol concentration. This finding suggests that various vitamin E forms might play a role in cognitive impairment (Mangialasche et al. 2013). In the multicenter AddNeuroMed study of 253 persons (81 patients with Alzheimer disease, 86 patients with mild cognitive impairment, and 86 cognitively intact), we investigated whether a combination of MRI with plasma vitamin E measures could help us distinguish between healthy controls and persons with either mild cognitive impairment or Alzheimer disease (Mangialasche et al. 2013). In addition, we explored whether this combined measure was useful in predicting conversion from mild cognitive impairment to Alzheimer disease after one year. Finally, in a memory clinic-based study of 75 patients (29 with subjective cognitive impairment, 28 with mild cognitive impairment, and 18 with Alzheimer disease), we studied the relationships among plasma vitamin D, cerebrospinal fluid biomarkers of Alzheimer disease, structural brain volumes, and cognitive impairment. We found that lower levels of vitamin D were related to increased likelihood of cognitive impairment. Vitamin D levels were also associated with the Alzheimer disease phenotype, including cerebrospinal fluid levels of beta-amyloid1-42 and brain volumetric measures (Hoooshmand et al. 2014).

What are the major risk and protective factors for cognitive impairment and dementia? This research line is primarily based on the longitudinal databases available at ARC, but in addition, we have developed extensive international collaboration, especially with researchers in the Nordic countries and the United States. In the last 2 years we have been able to confirm the relevance of the following factors for dementia: Metabolic disorders. By analyzing reimbursement registra-
life that included several self-reported, modifiable risk factors (e.g., education, smoking, alcohol consumption, diabetes, leisure activities) was highly predictive of late-life dementia (Exalto et al. 2014; Anstey et al. 2014). This provides a simple tool to identify people at risk of dementia so that intervention can begin early. Finally, we have shown that high levels of education, increased leisure-time activities, or maintaining vascular health could diminish the risk of dementia due to the APOE ε4 allele, which demonstrates that genetic risk for dementia can be modified (Ferrari et al. 2013).

Prevention of cognitive decline and dementia: first results from a population-based intervention study

Previous research has identified several potentially modifiable risk or protective factors for dementia. It is critical to use this information to develop interventions that will delay disease onset (Imtiaz et al. 2014). Indeed, current evidence from multidisciplinary research supports the hypothesis that unhealthy lifestyles and cardiovascular burden play a major role in age-related cognitive decline and dementia, especially when they occur in middle age (Lövdén et al. 2013; Solomon et al. 2014; Qiu et al. 2015). Promoting healthy lifestyles and proper management of cardiovascular risks have been the major strategies for reducing the risk or delaying the onset of cognitive impairment and dementia. FINGER is a multicenter randomized control trial involving 1260 persons aged 60–77 years who are at risk of cognitive decline. The multidomain intervention includes nutritional guidance, physical exercise, cognitive training, social stimulation, and management of metabolic and vascular risk factors (Kivipelto et al. 2013; Ngandu et al. 2014). The primary outcome is change in global cognition as measured with the comprehensive neuropsychological test battery. The first results from FINGER suggest that a multidomain intervention can improve or maintain cognitive functioning in at-risk elderly people from the general population (Ngandu et al. 2015). A 7-year follow-up is planned to evaluate the effects of the multidomain intervention on the incidence of dementia and Alzheimer disease.

Can we maintain cognitive functioning in old age by increasing neurocognitive plasticity?

The studies on this topic at ARC focus on understanding plasticity, that is, reactive changes in the brain caused by alterations in experiential demands from the environment. In other words, how are brain and cognition in younger and older age influenced by experience, such as cognitive stimulation, education, and retirement? And what are the brain mechanisms behind the effects of stimulation on cognitive performance in aging? We approach these issues both through intervention (training) studies and with multivariate statistical modeling of data from longitudinal and population-based studies such as SNAC-K. In recent years, our greatest focus has been on examining effects of cognitive training on brain and cognition. One study on genetic influence showed that carriers of the val allele of the COMT polymorphism, which is associated with different levels of the neurotransmitter dopamine in prefrontal cortex, had lower baseline performance and larger performance gains from working memory training than carriers of the met allele (see Figure 9, Bellander et al. 2014). These results are an example of how genes (COMT) and experience (training) together shape behavior (cognitive performance). Other work has demonstrated that adults can show effects of cognitive training that last up to 2 years (Schmiedek et al. 2014). Beginning in 2014, we will expand our research activities on this topic and will conduct several large intervention studies that examine the combined effects of cognitive training, non-invasive brain stimulation, and pharmacological interventions on cognitive performance in aging. To this, we have expanded our lab facilities. A 200 m² area (Hjärrlandet) is now available to collect data for these studies.

In our population-based databases, epidemiological, clinical, and cognitive data are integrated with neuroimaging and neuropathological data, and we are thus able to explore brain mechanisms linking psychosocial, vascular, and nutritional factors to cognitive deterioration in aging.

Preliminary results from the Cognition, Brain, and Aging project (COBRA)

COBRA is a 10-year project with three measurement occasions separated by 5 years. ARC, Umeå University, and the Max Planck Institute in Berlin collaborate in the project. The study sample (n = 182) ranges from 63–67 years of age at baseline. The assessment battery includes PET-derived markers of dopamine D2 receptor densities, structural MRI (gray and white matter changes), functional MRI (networks activated during working memory and resting-state networks), perfusion, a comprehensive cognitive battery (episodic and working memory, speed, implicit learning), a questionnaire on lifestyle properties (physical, mental, and social), and blood sampling for genetics and biomarkers (Figure 10). The chief goal of COBRA is to relate age-related cognitive changes to changes in the brain parameters assessed. Of particular interest is to examine which of the candidate neural correlates of cognitive decline first displays signs of change in old age. Likewise, we seek to determine whether one change in one brain variable is associated with subsequent changes in other brain measures and thus acts as a primary mechanism of age-related decline in brain and cognition. Awaiting longitudinal data, we are focusing on associations between the brain and cognitive data and how these links may be affected by lifestyles. Preliminary findings suggest that all classes of variables examined in COBRA have good measure properties. Further, analyses show associations between the dopamine markers and cognitive performance and links among dopamine, functional activation patterns, and cognition.

Iron in the brain: a new project

In 2014, we initiated a new line of research on the deleterious effects of accumulation of iron in the brain on gray matter volume, neural activity, and cognition in aging. A pilot study, conducted in 2014, including 45 healthy younger and older adults, yielded promising results (presented at a conference in 2014). The age-related accumulation of iron in the striatum was associated with less activity in this specific region of the brain when performing a motor-imagery memory task. It was also associated with worse memory performance. The project is currently growing into a longitudinal protocol covering the entire adult life span.
Education
Courses

Undergraduate (first cycle) courses
ARC is responsible for the undergraduate course “Society and health” (6 credits) and for the aging section (1.5 credits) of the “Developmental psychology” course, both part of the psychology program at KI. The first course has an epidemiological and a sociological perspective and gives the students the opportunity to learn about health inequalities in different contexts. The second course includes lectures on the effects of healthy and pathological aging on a selection of psychological, medical, and social domains.

Master’s (second cycle) courses
ARC researchers are responsible for and involved in several courses and supervise master’s projects. ARC is responsible for the course “Health inequalities in the older population” (4.5 credits) in the master’s program “Population health: societal and individual perspectives” at Stockholm University. The course takes place every second year and has a life course approach with a specific focus on health inequalities at older ages. ARC is also responsible for “Geriatric epidemiology”, a course for the Master program in public health epidemiology at KI. The aim of the course is to provide an overall picture of worldwide population aging and the opportunities and challenges it poses. The course also illustrates the application of modern epidemiological approaches to studying the most common health problems in aging and to critically evaluating the epidemiological literature in aging research.

Doctoral (third cycle) courses
Researchers at ARC are responsible for the doctoral-level course “Application of epidemiological methods in aging research.” The course offers the opportunity to learn epidemiological methods and their applications to research on aging. Different epidemiological methods are presented, and after the course, the students understand the importance of epidemiological approaches in research on aging and health and have an updated understanding of the epidemiology of common geriatric disorders such as Alzheimer disease and Parkinson disease.

“Life-course epidemiology” (4.5 credits) was held at the University of Gothenburg in 2014. The course was arranged by both the EpiLife and the ARC research schools (see below) in collaboration with the Centre for Ageing and Supportive Environments in Lund and Swedish Brain Power, the national network on neurodegenerative diseases. The course, which included both doctoral and postdoctoral students, focused on how factors at different stages of life may affect later health and functional outcomes. The course covered epidemiological and statistical methods related to the life course approach and several health topics presented from a life-course perspective.

In February 2014 ARC guest researcher Roger Keller Celeste held an advanced intensive course (3 credits) in "Structural Equation Modelling using Mplus".

Swedish National Graduate School for Competitive Science on Ageing and Health (SWEAH)
Our specialized knowledge about a number of aging research issues also led several researchers to teach in courses at different levels at KI and other universities. At the international level, we participated in organizing and teaching “The summer school of modern methods in biostatistics and epidemiology,” organized by the Harvard School of Public Health in the United States and the Department of Medical Epidemiology and Biostatistics, KI, which was held in Treviso, Italy. We also helped organize and teach the “International course of Neuroepidemiology,” organized by the University of Palermo in Italy and the Mayo Clinic in the United States. This course was held in Erice, Italy.

Since fall 2014 ARC has been a collaborator in SWEAH. SWEAH’s mission is to develop efficient and creative cooperation among Swedish higher education institutions and relevant national and international partners. The school has received 3 years of funding from the Swedish Research Council, with the possibility to extend funding for an additional 5-year period. 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.

Since fall 2014 ARC has been a collaborator in SWEAH. SWEAH’s mission is to develop efficient and creative cooperation among Swedish higher education institutions and relevant national and international partners. The school has received 3 years of funding from the Swedish Research Council, with the possibility to extend funding for an additional 5-year period. 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.
The graduate research school started in 2008, and in 2012 we successfully reapplied to Forte for continued funding for 2013 through 2015. Six groups and centers participate in the school: ARC; the Division of Occupational Therapy and Alzheimer’s Disease Research Center, KI; the Centre for Ageing and Supportive Environments, Lund University; Swedish Brain Power (a national network); and EpiLife, Gothenburg University. The idea behind the graduate school is to use the partners’ respective competencies as the basis for a graduate school in aging research at a national level with substantial multidisciplinary interaction. The goal is to cover the different scientific disciplines related to older people both from a theoretical and a methodological point of view. In this way, the school seeks to provide PhD students with the opportunity to access various courses and other educational activities within multiple scientific areas, giving them the advantage of a multidisciplinary perspective during their development as researchers.

The school offers courses (see above), seminars, workshops, and international forums to doctoral students in aging research in Sweden. The 1-hour weekly scientific seminar should be relevant to aging research. The seminar program is prepared at the beginning of each semester. Both senior researchers and PhD students lecture at the seminars, providing opportunities for the students to engage in scientific discussions across disciplines and to form contacts with outside researchers that can lead to future collaboration. The number of seminars has varied between 20 and 30 a year.

During 2013 and 2014 the research school arranged two workshops and one advanced course. The first workshop was “Data Management and Graphics using STATA” and the second, “Linear mixed and structural equation modelling on longitudinal brain data.”

ARC has also hosted several senior researchers who are internationally recognized as authorities in their field. Each researcher has presented his or her major findings, opinions, and future perspectives in a 2-hour meeting (international forum) open to all students and other researchers at KI. Eleven forums were held during 2013 and 2014. Examples include:

- **Professor Vern L. Bengtson, Edward C Roybal Institute on Aging, School of Social Work, University of Southern California**, gave a lecture on the topic “New trends in the theory of aging.”
- **Professor Sally Braithwood, University of Southampton**, lectured on “Using simulation and modelling to improve social care systems: the UK experience.”
- **Professor Agnes Flöel, NeuroCure Clinical Research Center, Charité**, gave a lecture on “Lifestyle interventions and noninvasive brain stimulation for the aging brain.”
- **Professor Marja Jylhä, School of Health Sciences, University of Tampere**, gave a lecture on “What do older people know about their health and how? Self-rated health at the crossroads between biology, psychology, and the social world.”
- **Professors Jo C Phelan and Bruce G Link, Columbia University, Mailman School of Public Health**, lectured on “Social conditions as fundamental causes of health inequalities: theory, evidence, and policy implications.”
- **Professor Naftali Raz, Institute of Gerontology, Wayne State University**, lectured on the topic “Fine structure and heavy metal: getting closer to our aging brain.”
- **Professor Jinglong Wu, Biomedical Engineering Laboratory, Graduate School of Natural Science and Technology, Okayama University**, lectured on “New devices for human brain mapping and early detection of Alzheimer disease.”

Since 2011, the graduate school has collaborated with Tampere School of Public Health. The aim of the collaboration is to increase the number of available courses and other activities of interest in the fields of aging research and public health for the doctoral students at both universities. A workshop was arranged in Tampere in 2012 and in Stockholm in 2014. The primary aim of the workshops is to give PhD students the opportunity to present their research, get feedback on their work, and give feedback on other research projects. The students also had the opportunity to develop networks and learn about other dissertation projects. Senior researchers from both institutes took part in the workshops.

The graduate school has the opportunity to pay course fees and travel and lodging costs for students who take relevant courses at universities other than their own. ARC had a total of 29 doctoral students 2013 and 2014 and four defended their theses.
PhD theses defended in 2013 and 2014

BRITT-MARIE SJÖLUND

Britt-Marie Sjölund’s thesis examined physical functioning in older adults using data from the Kungsholmen Project, the Nordanstig Project, and the SNAC-Nordanstig study. The aim was to identify potentially modifiable factors. The results of the thesis show that older adults in the rural population were more disabled in ADL than older adults in the urban population. The studies in the thesis also found that older women were more disabled in ADL than men. Diseases and other health conditions found to have a negative influence on ADL were cognitive impairment, cardiovascular diseases, multimorbidity, musculoskeletal diseases, and depression. Being physically active earlier in life, in old age, or both was associated with being less ADL disabled in old age.

BRITT-MARIE SJÖLUND is now working as senior lecturer at the University of Gävle, Faculty of Health and Occupational Studies, Department of Health Caring Sciences.

JONAS WASTESSON
Unequal drug treatment: age and educational differences among older adults.

Jonas Wastesson’s thesis aimed to investigate whether drug treatment is unequally distributed among older adults on the basis of age and socioeconomic position. Wastesson used nationwide Swedish registers (the Swedish Prescribed Drug Register, the Patient Register, the Social Services Register, and the Education Register) to carry out large-scale studies of drug treatment (e.g. osteoporosis drugs and psychotropics) among people aged 75 years and older in Sweden. The results of the thesis highlight that older age and lower educational level are associated with suboptimal drug treatment. This suboptimal drug treatment can include under- and over-prescription of drugs, limited access to medical specialists, and limited access to more newly developed drugs.

JONAS WASTESSON is now working as a postdoc at the Max-Planck Odense Center on Biodemography of Aging, University of Southern Denmark.

BABAK HOOSHMAND
The impact of homocysteine and B vitamins on Alzheimer’s disease, cognitive performance and structural brain changes.

Low levels of vitamin B12 and folate and high values of homocysteine (a known cardiovascular and cerebrovascular risk factor) are common conditions in elderly people. The overall aim of this thesis was to investigate the association of vitamin B12, folate, and homocysteine with cognition and structural brain changes. Data from well known Swedish and Finnish population-based studies were used to investigate the research questions. Results of this project indicated that lower B12, elevated total homocysteine, and lower folate levels are involved in late-life cognitive impairment and structural brain changes. Health professionals should consider regularly assessing vitamin B12 and folate status in elderly people. Adequately timed and powered well-planned randomized controlled trials are needed to determine the impact of B-vitamin supplementation on preventing cognitive decline and dementia-related pathology.

BABAK HOOSHMAND is now working as a radiology resident at Munich University Hospital.

DEBORA RIZZUTO
Living longer than expected: protective and risk factors related to human longevity.

The overall aim of Debora Rizzuto’s thesis was to detect the most relevant factors that lead to longer survival after age 75. The major research questions were: What is the impact of the most common chronic diseases in elderly people on the survival of elderly people? What effects do lifestyles and social environment have on lifespan? Does the most important component of longevity lie in our genes? The data used in the thesis were from the Kungsholmen Project. Findings underscored the malignant nature of dementia, especially for women, because of the long period individuals lived with the severe disease stages. The findings also suggest that the benefit of a healthy lifestyle, healthy behavior, and social support probably last a lifetime. Moreover, allelic variations in APOE, APOC, and ICE genes were associated with a higher mortality rate, but the combined effect of genetic-environmental joint exposures may lead to the attenuation of the mortality rate, indicating that people with genetic susceptibility may reduce their initial mortality rate by modifying their lifestyle. Therefore, efforts to encourage smoking cessation, physical activity, and social engagement should be continued long into late life.

DEBORA RIZZUTO is now working as a postdoc at ARC.

Photo: Frida-Lo Dieckhoff
Photo: Ove Wall
Photo: Muriel Hooshmand
Photo: Giola Santoni
Additional achievements
Career advancements

New appointments at KI

- Laura Fratiglioni elected as teacher representative on the Board of KI in 2014 as well as the Board of Research, 2012-2014 and 2015-2017.
- Laura Fratiglioni member of the Recruitment Committee.
- Kristina Johnell, Head of Division from January 1, 2014.
- Kristina Johnell is a member of the Nomination Assembly at KI.
- Kristina Johnell is a steering group member for the Center for Alzheimer research at KI.
- Kristina Johnell and Marti Parker are members of the Academic Center for Gerodontics.
- Miia Kivipelto is team leader for the Neurogeriatric-clinical trials unit at New Karolinska Solna, a project within KI to develop campus Solna.
- Jonas Persson, Deputy Head of Division from January 1, 2014.

ARC researchers are partners in the newly established Center for Alzheimer Research at KI. There was a kick-off on March 3 and a meeting on November 3, 2014.

Apointments to commissions of trust outside KI

- ARC researchers were appointed members of the Ethical Review Board; acted as peer-reviewers for international and national funding agencies, including the Swedish Research Council, participated in several EU networks and consortia; and served as invited lecturers at chairs of several national and international conferences.

Awards

- Yvonne Brehmer received funding to start an Otto Hahn Group on Associative Memory in Old Age at the Max Planck Institute for Human Development in Berlin.
- Laura Fratiglioni was awarded with the Bengt Winblad Lifetime Achievement Award at the Alzheimer’s Association International Conference in 2013.
- Miia Kivipelto received the Skandia Lennart Levi Prize 2013 for her research into dementia and Alzheimer disease.
- Bengt Winblad received KI’s “Stora Silvermedaljen” in 2013.
- Goran Papenberg received the Otto Hahn medal for his dissertation.
- Chengxuan Qiu received the International Society of Behavioral Medicine Contributions to International Collaborations Award in 2014.
- Pär Schön won the best poster award at the Nordic Congress of Gerontology in 2014.
- Laura Fratiglioni was awarded the Premio Enrico Greppi prize by the Italian Geriatric and Gerontology Society.
- Miia Kivipelto was voted “Best PI at KI” by the KI Postdoc Association.
Scientific outreach
Clinical and societal impact

Clinical impact

Our major clinical impact over the last two years has been in the area of drug use in elderly people and can be summarized as follows:

- 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, SKL) in their annual 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 is 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 persons.

- Since 2000 we have developed a computerized decision support system (miniQ) to facilitate prescribing and drug utilization reviews in eldercare. The system, which is now 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 has now been implemented in more than 650 health care units in 16 counties in Sweden.

- Quality of drug use in elderly people. 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 a role in the recently reported improvement in the quality of drug use in elderly people since 2005 [Socialstyrelsen 2014].

Societal impact

ARC’s aim is to inform stakeholders about the results of our research by participating in the public debate about issues relevant to aging research.

ARC’s outreach to society has increased:

- During 2013 and 2014, ARC researchers frequently took part in national news programs on television and radio, including on the educational radio station (UR) and popular morning breakfast shows.

- We have noticed an increase in the demand for teaching and participating in conferences, including outside academia. As well as informing local and county councils and pensioners’ organizations, and participating in Almedalsveckan (an important weekly-long Swedish political forum).

- During 2013, Stefan Fors was a member of a reference group for a project commissioned by the Swedish organization Mind. The purpose of the project was to develop an aggregate measure of psychological health and to compare psychological health in different geographical areas in Sweden and in different countries in Europe. The measure was named the “Mind-index”, and results based on the index were published in 2013 (comparing European countries) and in 2014 (comparing counties in Sweden) by Mind.

Communication and dissemination of research findings

ARC has been involved in organizing several symposia. ARC researchers participate in numerous research networks and have an extensive network of collaborators both nationally and internationally. ARC researchers are also involved in many teaching activities, such as seminars, international forums, and journal club meetings.

During the spring of 2013, ARC’s new website, http://ki-su-arc.se/, was launched. Brochures about ARC were published in 2013 in both English and Swedish.

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.

Several ARC researchers took part in Almedalsveckan in 2013 and 2014, Almedalsveckan is an annual forum in Sweden for politicians from all the major political parties. ARC researchers have also hosted visits from national and international politicians and policy makers, including delegations from Canada, China, and South Africa. During a visit by representatives of Forte to ARC in fall 2014, ARC underscored the importance of aging research in Sweden and worldwide.
Selection of outreach activities and events

- The af Jochnick brothers, co-founders of the af Jochnick Center for the Cognitive Neuroscience of Aging, visited ARC in June 2013 and September 2014 for updates on research findings.

- SNAC-K data collection staff, participants, and Professor Laura Fratiglioni participated in the documentary film Forska för livet (“Research for life”) by Folke Rydén, Marianne Gustavsson, and Lisa Belfrage.

- There was a press seminar on a SNAC report, with Laura Fratiglioni present. The seminar led to several news articles in the media.

- ARC was one of the exhibitors at the 22nd Nordic Congress of Gerontology (22 NKG) held in Gothenburg on the 25-28 of May 2014, and ARC researchers also held symposia and poster presentations. The theme of this year’s congress was “age well.”

- In December 2014, members of ARC presented their research at the breakfast seminar in the spirit of Alfred Nobel at Stockholm University. The seminar was organized by Stockholm Business Regions and Stockholm University, and the theme of this year’s seminar was aging.

- Forte Talks, a conference held March 25-26, 2014, was organized by Forte as a forum for discussion between researchers, policy makers, and care users. ARC contributed presentations and posters and was an exhibitor at the conference.

- The vice-chancellors of KI and Stockholm University visited ARC in September 2014 for an update on ARC’s latest research findings and future plans.

- In 2014 Forte released a report on aging and memory written by three ARC researchers: Martin Lövdén, Johan Fastbom, and Stefan Fors. Information in this report was also discussed in a seminar held in Stockholm in October 2014.

- In December 2013, Miia Kivipelto contributed to discussions at an international summit meeting on dementia held in London. Health and science advisers, world-leading experts, and senior industry figures gathered to discuss and agree on an international approach for future dementia research.

- Marti G Parker, Bettina Meinow, Hanna Berndt, Louise Sundberg, Stefan Fors were nominees for 2014’s “best original article of the year” in Lakartidningen (the Swedish Medical Journal). Their article was about the Swedish Centenarian Survey – A study of Swedish 100 year olds health and functional status.

- Miia Kivipelto was a panelist during the Nobel Week Dialogue in 2014. This event gathers Nobel Laureates, world-leading scientists, experts, and thought leaders for a panel discussion on the topic of aging.
### ARC in the media

<table>
<thead>
<tr>
<th>Media</th>
<th>Number of appearances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newspapers</td>
<td>50 articles and/or press items in newspapers such as Dagens Nyheter, Svenska Dagbladet, Göteborgsposten, and the New York Times.</td>
</tr>
<tr>
<td>Magazines</td>
<td>12 articles in magazines such as Focus; Medicinsk Vetenskap; SPRF; Medlemsnämnden för Sveriges Pensionärs Riksförbund; Icon; Dagens Samhälle; and Der Spiegel.</td>
</tr>
<tr>
<td>Television</td>
<td>25 TV appearances and/or references on programs such as Aktuellt and Nyhetsmorgon</td>
</tr>
<tr>
<td>Radio</td>
<td>10 interviews on Swedish radio.</td>
</tr>
<tr>
<td>Internet</td>
<td>Four research results received a great deal of attention on the Internet: Martin Lövdén and Lars Backman’s study on how physical activity affects the memory in 60-year olds, Martin Lövdén’s study on how older adults perform on cognitive tasks compared to younger adults, Chengxuan Qiu’s study on decreased incidence of dementia, and Mia Kivipelto’s study on how our lifestyle affects risk of dementia (FINGER).</td>
</tr>
</tbody>
</table>
Finance, funding, and future plans
Income

Summary of major financial resources in 2013 and 2014.

List of external funders

Major funders (in alphabetical order)
- European Union
- Jochnick Foundation
- Swedish Research Council for Health, Working Life and Welfare (Forte)
- The Swedish Research Council (Vetenskaprådet)

Other funders (in alphabetical order)
- Alzheimer Foundation, Sweden (Alzheimerfonden)
- Dementia Fund (Demensfonden)
- Emil and Wera Cornell Foundation
- Gamla tjänarinnor Foundation
- Gun and Bertil Stohne Foundation
- Hierta-Retzius Scholarship Fund
- Hjärnfonden
- French National Institute of Health and Medical Research
- King Gustaf V and Queen Victoria’s Foundation
- Nordic Research Councils for the Humanities and the Social Sciences (NOS-HS)
- Ragnhild and Einar Lundström Memorial Foundation
- Sigurd and Elsa Golje Memorial Foundation
- Stockholm County Council/ALF
- Sweden’s Central Bank’s Jubilee Fund (Riksbankens Jubileumsfond)
- Söderström/Kongigska Foundation
- The National Board of Health and Welfare (Socialstyrelsen)
- The Royal Swedish Academy of Sciences
- The Swedish Foundation for Humanities and Social Sciences (Riksbankens Jubileumsfond)
- The Swedish Society of Medicine
- The Wallenberg Foundations

*Indirect costs paid to Karolinska Institutet.
Future plans

ARC plays an important role in addressing future challenges related to the aging of populations. Our major focus for the future is to ensure sustainable growth of research at ARC. We strive to maintain high-quality research with a great impact on science, the health care system, and society at large. These goals will be achieved by providing a challenging, multidisciplinary, and creative research environment with many opportunities for national and international networking. This kind of environment is essential for attracting talented doctoral students and postdocs and continuing to attract guest researchers. We will also expand our collaboration with the two other aging research centers in Sweden—the Centre for Ageing and Supportive Environments at Lund University and the Centre for Ageing and Health at the University of Gothenburg—to make joint efforts to further strengthen Swedish aging research. Our educational objectives include continued work with graduate-level (third cycle) education, particularly within the framework of the Graduate School in Aging Research, in collaboration with the Centre for Ageing and Supportive Environments. We will also continue our endeavors within various undergraduate (first cycle) and master’s (second cycle) programs. ARC has successfully grown in recent years, and this requires development of new organizational strategies. Three younger researchers have joined the Steering Group to enhance the opportunities for involvement of the younger faculty. We also place special focus on our future research leaders who are in the process of forming their own research groups. Postdocs and doctoral students have also established ARC Juniors, a group that will continue to organize retreats and seminars to facilitate the exchange of multidisciplinary research ideas and networking. Finally, we also plan to announce new positions at all levels of the organization.

Kristina Johnell
Head of Division

Photo: Stefan Zimmerman
Appendix

Publications

Original articles

A. Longevity, morbidity and functioning


konsekvenser av sjukdom – Exemplet stroke.
Social Work in Public Health.
– Previous violence, socioeconomic position, and
Trygged S, Hedlund E, Kåreholt I. Living in danger
Health.
Socioeconomic inequalities in health after age 50:
Eur J Ageing
Shaw BA, Agahi N. Smoking and physical inactivity
immigrant groups in Sweden: The contribution of
working conditions.
and health after retirement – exploring the role of
association between mid-life socioeconomic position
and health after retirement – exploring the role of
881.
Rostilla M, Frittell J. Mortality differentials by
Shaw BA, McGeever K, Grobert E, Agahi N, Fors S.
Socioeconomic inequalities in health after age 50:
101:52-60.
Thorslund M, Wastesson J, Agahi N, Lagergren M,
Trygged S, Hedlund E, Kåreholt I. Brain aging
Trygged S, Hedlund E, Kåreholt I. Valdeutsatta
kvinnor av långtida negativa ekonomiska
konsekvenser. Socialmedicinsk Tidskrift. 2013;
Trygged S, Hedlund E, Kåreholt I. Women
Wattesson JW, Ringbäck Weitfoft G, Johnell K.

D. Brain aging


Appendix

Book chapters

A. Longevity, morbidity and functioning


B. Treatment and care of elderly persons


C. Health trends and inequality


D. Brain aging


Doctoral dissertations

A. Longevity, morbidity and functioning

B. Treatment and care of elderly persons


D. Brain aging
## International forum

<table>
<thead>
<tr>
<th>Date</th>
<th>Speaker</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 23</td>
<td>Sally Brailsford, Professor, University of Southampton</td>
<td>Using simulation and modelling to improve social care systems: the UK experience</td>
</tr>
<tr>
<td>April 25</td>
<td>Marja Jylhä, Professor, School of Health Sciences, University of Tampere</td>
<td>What do older people know about their health and how? Self-rated health at the crossroads between biology, psychology and the social world</td>
</tr>
<tr>
<td>May 8</td>
<td>Naftali Raz, Professor, Institute of Gerontology, Wayne State University, Detroit</td>
<td>Fine Structure and Heavy Metal: Getting Closer to our Aging Brain</td>
</tr>
<tr>
<td>Sept 26</td>
<td>Sudha Seshadri, Professor of Neurology, Boston University School of Medicine, Senior Investigator, the Framingham Study</td>
<td>Overview of neurological research in the Framingham Heart Study and CHARGE consortium, Genetics of Alzheimer Disease, Challenges in Identifying Biomarkers for Alzheimer Disease</td>
</tr>
<tr>
<td>Oct 10</td>
<td>Kenneth Hugdahl, Professor, University of Bergen</td>
<td>Auditory hallucinations in schizophrenia: From cognition to brain systems</td>
</tr>
<tr>
<td>Nov 12</td>
<td>Azita Emami, Professor, Dean of Nursing, University of Washington, Seattle</td>
<td>Diversity among eldercare providers</td>
</tr>
</tbody>
</table>

## Biology of Aging

<table>
<thead>
<tr>
<th>Date</th>
<th>Speaker</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct 3</td>
<td>Angel Cedazo Minguez, Associate Professor, Neurogenetics, KI, Center for Alzheimer Research</td>
<td>Towards debunking myths and understanding risks for Alzheimer disease</td>
</tr>
<tr>
<td>Oct 20</td>
<td>Nancy Pedersen, Professor, Department of Medical Epidemiology and Biostatistics, KI</td>
<td>Where genes come into theories of (neuro)biology of aging</td>
</tr>
<tr>
<td>Dec 17</td>
<td>Thomas Nyström, Professor, Department of Chemistry &amp; Molecular Biology, University of Gothenburg</td>
<td>The biology of aging and the search for aging factors using model systems</td>
</tr>
</tbody>
</table>
Guest researchers

2013
- Åke Wahlin, Professor, Stockholm University. At ARC: 1 December 2012 to 31 August 2013. Host: Lars Backman.
- Marja Jylha, Professor, University of Tampere. At ARC: 22–26 April. Host: Mats Thorslund.
- Benjamin Shaw, Professor, University at Albany. At ARC: 15–26 April. Host: Neda Agahi.
- Naftali Raz, Professor, Wayne State University. At ARC: 8–13 May. Host: L Backman.
- Hiram Beltrán-Sánchez, PhD, Harvard University. At ARC: May.
- Steven Zari, Distinguished Professor, Penn State University and Adjunct Professor, Högskolan i Jönköping. At ARC: 20–21 May. Host: Ingemar Kåreholt.
- Merrill Silverstein, Professor, University of Southern California. At ARC: May–June. Host: Mats Thorslund.
- Ross Andel, Associate Professor, University of South Florida. At ARC: 10–19 June. Host: Ingemar Kåreholt.
- Kuo-Chen Huang, MD, PhD, National Taiwan University. At ARC: 21 June–11 September. Host: Marti Parker.
- Anna Marseglia, Psychologist, Institute of Neuroscience, Padua, Italy. At ARC: August–December. Hosts: Wei Li and Laura Fratiglioni.
- Kuo-Chen Huang, National Taiwan University. At ARC: 21 June–11 September. Host: Marti Parker.
- Danijela Gnjidic, University of Sydney. At ARC: 2–13 September. Host: Kristina Johnell.
- Mario Meloni, MD, resident in Neurology in Italy. At ARC: December 2013 to June 2014. Hosts: Laura Fratiglioni and Barbara Caracciolo.

2014
- Roger Keller Celeste, CD, MSc, PhD, Chefe do Departamento de Odontologia Preventiva e Social Faculdade de Odontologia. At ARC: 20 January to 20 March. Host: Johan Fritzell.
- Anna Laveskog, PhD student, Neuroradiologist Karolinska University Hospital. At ARC: 28 April–13 June. Host: Chengxuan Qiu.
- Maryam Ziaei, PhD student, University of Queensland. At ARC: 14 April–1 May. Host: Jonas Persson.
- Ross Andel, Associate Professor, University of Southern California. At ARC: August. Host: Ingmar Kåreholt.
- Merrill Silverstein, Professor, University of Southern California. At ARC: May–June. Host: Mats Thorslund.
- Barbara Wimmer, PhD student, Monash University. At ARC: 1 June–31 October. Host: Kristina Johnell.

Overview of number of employees per sector and per level

<table>
<thead>
<tr>
<th>Sector Medicine N=29</th>
<th>Sector Psychology N=29</th>
<th>Sector Social Gerontology N=26</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Professors</td>
<td>3 Professors</td>
<td>4 Professors</td>
</tr>
<tr>
<td>3 Senior lecturers</td>
<td>2 Researchers</td>
<td>1 Senior lecturer</td>
</tr>
<tr>
<td>2 Research associates</td>
<td>4 Research associates</td>
<td>3 Researchers</td>
</tr>
<tr>
<td>7 Post docs</td>
<td>6 Post docs</td>
<td>9 PhD students</td>
</tr>
<tr>
<td>11 PhD students</td>
<td>3 Research assistants</td>
<td>3 Post docs</td>
</tr>
<tr>
<td>1 Scientific coordinator</td>
<td>1 Research assistant</td>
<td>5 PhD students</td>
</tr>
<tr>
<td>1 Research assistant</td>
<td></td>
<td>1 Scientific coordinator</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 Project manager</td>
</tr>
</tbody>
</table>

Database group
- 2 database managers

Administrative group
- 3 administrative staff
- 2 coordination, communication
In close collaboration with

Aging Research Center
Karolinska Institutet/Stockholm University
Gävlegatan 16
S-113 30 Stockholm
Phone: +46 8 690 5823
Fax: +46 8 690 6889
www.ki-su-arc.se