2011 – 2012

Biennial Report

ARC
AGING RESEARCH CENTER

Karolinska Institutet

Stockholms universitet

CONTENTS

Introduction

The Aging Research Center (ARC) was established in 2000 through a joint effort of Karolinska Institutet (KI) and Stockholm University. It is a "Center of Excellence" supported by two consecutive grants from The Swedish Council for Working Life and Social Research (Forskningsrådet för Arbetsliv och Socialvetenskap or FAS). In 2011 ARC was evaluated by FAS and received very positive feedback.

ARC is a physical center that shares premises with its closest collaborators, the Stockholm Gerontology Research Center (Äldrecentrum, 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 the walls of academia. Together with the two other centers, ARC supports the aging-research magazine *Äldre i Centrum* (www.aldrecentrum.se).

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 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 cognitive aging via national and international collaboration.
5. Integration of epidemiological and social studies with clinical and molecular work.
6. Special attention to neuroscience with focus on neural correlates of cognitive functions and prevention of brain aging.
7. 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 National Graduate School for Aging Research, which is also supported by FAS. The school uses the competencies of partners at multiple universities across Sweden to give PhD students a theoretically and methodologically multidisciplinary background.

Organization and leadership

ARC is a center within KI; it belongs to the Department of Neurobiology, Care Sciences and Society (NVS). It is led by a **Governing Board** that includes representatives from FAS, KI, Stockholm University, and the Stockholm Gerontology Research Center as well as other Swedish universities (**Figure 1**).

Governing Board

2011

Picture: Stefan Zimmerman

2012

Picture: Maria Yohuang

Members

Bo Malmberg, Professor, SU* (Chair)

Nancy Pedersen, Vice Dean, KI (Deputy Chair)**

Cecilia Magnusson, Associate Professor, KI

Lars Nyberg, Professor, Umeå University

Marta Szebehely, Professor, SU

Anne Ekdahl, Swedish Geriatric Association

Gabriel Romanus, Former Member of Parliament

Sven-Erik Wånell, Director, Stockholm Gerontology Research Center**

Måns Rosén, Director, The Swedish Council on Technology Assessment in Health Care**

Adjunct members

Kerstin Tham, Chair, NVS**

Laura Fratiglioni, Director, ARC

Bengt Winblad, Co-director, ARC

Marti Parker, Head of Division, ARC**

Ylva Ekendahl, Head of Economy Dept, NVS**

Members

Bo Malmberg, Professor, SU (Chair)

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Barbro Westerholm, Member of Parliament

Marta Szebehely, Professor, SU

Anne Ekdahl, Swedish Geriatric Association**

Gabriel Romanus, Former Member of Parliament

Chatrin Engbo, Director, Stockholm Gerontology Research Center**

Måns Rosén, Director, The Swedish Council on Technology Assessment in Health Care

Adjunct members

Kerstin Tham, Chair, NVS**

Laura Fratiglioni, Director, ARC

Bengt Winblad, Co-director, ARC

Kristina Johnell, Acting Deputy Head of Division, ARC**

Miia Kivipelto, Deputy Head of Division, ARC

Ylva Ekendahl, Head of Economy Dept, NVS**

Figure 1. ARC Governing Board, 2011 and 2012. *SU=Stockholm University. **Not present when the photograph was taken.

The role of the board is to ensure professional administration of the center and compliance with the specific goals of the center. During 2012, some board members ended their mandate, and new members joined as reported in **Figure 1**. The board met four times each year, and at each meeting, the ARC director reported on activities and financial issues. The board provided advice concerning the organization of ARC and the promotion of aging research.

The responsibility for scientific, organizational, and financial issues, including those related to staff and external contractors, as well as changes in administrative staff, is shared by the members of **Steering Committee** (**Figure 2**), which is led by ARC's director. This committee meets once a month. Daily decisions, actions regarding promotion, finances, staff, and work environment are made by the **Executive Group** (**Figure 2**).

Steering Committee

2011

Picture: Stefan Zimmerman

L Fratiglioni, B Winblad*, L Bäckman, M Thorslund, A Herlitz, J Fastbom, M Parker*, M Kivipelto, K Johnell (during winter as Acting Deputy Head of Division during M Kivipelto's parental leave)

2012

Picture: Maria Yohuang

L Fratiglioni, B Winblad*, L Bäckman*, M Thorslund, A Herlitz, J Fastbom*, M Parker, C Lennartsson (from spring as substitute for M Parker), M Kivipelto, K Johnell (through spring as Acting Deputy Head of Division during M Kivipelto's parental leave)

Executive Group

L Fratiglioni, Director

M Parker, Head of Division

B Winblad, Deputy Director

M Kivipelto, Deputy Head of Division

K Johnell, Acting Deputy Head of Division

Figure 2. Leadership at ARC, 2011 and 2012. *Not present when the photograph was taken.

Sector Medicine

2011

Laura Fratiglioni, Professor

Johan Fastbom, Associate Professor

Miia Kivipelto, Associate Professor

1.5 Researchers   1.5 Research associates
5 Postdocs   4.5 PhD students
4 Research assistants

2012

Laura Fratiglioni, Professor

Johan Fastbom, Professor

Miia Kivipelto, Professor

2 Researchers   0.5 Lecturers
0.5 Research associates 5.5 Postdocs
6.5 PhD students   3 Research assistants

Sector Medicine, December 2011. Picture: Stefan Zimmerman

Sector Psychology

2011

Lars Bäckman, Professor

Agneta Herlitz, Professor

1.5 Senior researchers   2.5 Research scientists
1.5 Postdocs   5 PhD students
0.5 Research assistants

2012

Lars Bäckman, Professor
Martin Lövdén, Researcher

2 Researchers   2 Research associates
2.5 Postdocs   4.5 PhD students
0.5 Research assistants   0.5 Research engineers

Sector Psychology, December 2011. Picture: Stefan Zimmerman

Sector Social Gerontology

2011

Mats Thorslund, Professor

Marti Parker, Associate Professor

3 Senior researchers   3 Postdocs
4 PhD students   2.5 Research assistants

2012

Mats Thorslund, Professor

Marti Parker, Professor

4 Researchers   4 Postdocs
3 PhD students   4 Research assistants
0.5 Project administrators

Sector Social Gerontology, December 2011. Picture: Stefan Zimmerman

Figure 3. ARC is organized into three sectors.*

Each sector is headed by at least two senior researchers and includes researchers, guest researchers, postdocs, and PhD students in the respective area. All research activities are implemented by project groups. This ensures multidisciplinary collaboration among the three sectors. Project groups typically consist of a senior researcher, one or two postdocs, and a group of PhD students. The groups are economically independent; research costs and salaries for PhD students and postdocs are derived from project grants. ARC provides premises, IT support, and data from the databases.

The Data Management Group creates and organizes the databases of the Kungsholmen and SNAC-K projects, provides data to researchers upon request, and ensures quality and safety of the databases. The Administrative Group provides support in the areas of office management, personnel, finance and budget, coordination, and information (**Figure 4**).

Administrative and Technical Staff

2011
Data Management Group
2 Database managers
1 Statistician
2.5 Staff for SNAC-K data collection

Administrative Group
4.5 Administrative staff

2012
Data Management Group
2 Database managers
1 Statistician
2.5 Staff for SNAC-K data collection
1 Research engineer in brain imaging

Administrative Group
5.5 Administrative staff

Administrative and Technical Staff, December 2011. Picture: Stefan Zimmerman

Figure 4. Administrative and Technical Staff at ARC.*

*Please note that not all members of staff were present when the sector pictures were taken.

Databases
Databases from ongoing projects since 2000

PROJECT AND WEBSITE *Project leader*	DESCRIPTION **& 2011–2012** ACTIVITIES
SNAC-K population study www.snac.org *Laura Fratiglioni*	A population-based project started in March 2001 as a part of the Swedish National study of Aging and Care (SNAC). Baseline data collection was completed in 2004: 3363 participants, 60+ years old, were extensively examined. A codebook can be downloaded from the home page. The examination includes a nurse interview, a clinical examination by physicians, and psychological testing. The third follow-up of the older cohorts and the second follow-up of the younger cohorts ended in 2012. Baseline examination of a new cohort of 60-year-olds was also completed in 2012. **Figure 5** shows the project's data collection staff.
SNACK-MRI study www.aldrecentrum.se/snack *Lars Bäckman*	In collaboration with the Division of Geriatric Medicine, Department of NVS, KI, we have implemented a population-based magnetic resonance imaging (MRI) study within the SNAC-K project. A random sample of 555 persons underwent structural MRI and diffusion tensor imaging (DTI) at baseline. A total of 347 persons have been to the first follow-up and 100 to the second. During 2011–2012, a sample of 57 persons from the new cohort of 60-year-olds was examined with MRI.
SNACK care system study www.aldrecentrum.se/snack *Mårten Lagergren*	Together with the SNAC-K population study and in the same geographical area, the Stockholm Gerontology Research Center has implemented a parallel study focusing on care utilization by old people. The study started in February 2001 and encompasses all persons 65+ years who have social care or receive long-term home health care or rehabilitation. Results have been presented at several meetings and summarized in reports by the Stockholm Gerontology Research Center.

Figure 5. SNAC-K data collection staff.   Picture: Lena Noalt

New databases created 2011–2012

PROJECT AND WEBSITE *Project leader*	DESCRIPTION **& 2011–2012** ACTIVITIES
5-COOP *Marti Parker* **SCS**100 **Swedish Centenarian Study**	The Swedish sample of the Five Country Oldest Old Project (5-COOP) is a random sample of persons born between July 1911 and June 1912. The sample (n=320) was about one third of the centenarians living in Sweden in 2011. A total of 274 of these persons were interviewed. The study is the first nationwide survey of Swedish centenarians. Variables include subjective and objective health indicators, social network and background, cognition, well-being, and use of medical and social services. Similar studies are being carried out in Denmark, France, Switzerland, and Japan, providing the opportunity to study health status in relation to the level of mortality selection.
Neuroimaging databases www.ki-su-arc.se *Martin Lövdén*	At ARC we have collected functional and structural neuroimaging (MRI and PET) data in several smaller-scale projects that address specific issues in the cognitive neurosciences of aging. These projects have dealt with the functional, neurochemical, and structural neural correlates of forgetting, working memory, episodic memory, emotional aspects of memory, cognitive variability, and learning-related changes following language acquisition and cognitive training.

Continuation of projects started before ARC

PROJECT AND WEBSITE *Project leader*	DESCRIPTION **& 2011–2012** ACTIVITIES
The Kungsholmen Project www.kungsholmenproject.se *Bengt Winblad*	A cohort of 2368 persons, 75+ years old and living in a central area in Stockholm, was clinically examined on five occasions during 1987–2000. In 1995, the project expanded to include a rural population (*Nordanstig*). The database includes 12-year long follow-up data and offers information on aging from a multidisciplinary perspective. By the end of 2012, the project had led to more than 45 PhD theses. Hospital register data and death certificates are collected continuously.
SWEOLD www.sweold.se *Mats Thorslund*	Nationally representative samples derived from a panel study (the Swedish Level-of-Living Survey) of adults that began in 1968. Survivors from the panel (77+ years, n≈550) were interviewed in 1992, 2002, and 2004. Longitudinal data from the Level-of-Living Survey are also available for 1974, 1981, 1991, 2000, and 2010. Each wave of the survey is nationally representative, providing useful estimates of health and other living conditions in the older population. A new wave of data collection was carried out in 2010/2011. The dataset was complemented with an additional sample of 335 persons. This was done to enhance the original sample and create the opportunity for detailed cross-sectional analyses of the oldest old.

Other major collaborative projects

PROJECT AND WEBSITE *Project leader*	DESCRIPTION & 2011–2012 ACTIVITIES
CAIDE www.uef.fi/caide/home *Miia Kivipelto*	The National Institute for Health and Welfare, Helsinki; the Department of Neurology, University of Eastern Finland; and ARC collaborate on the Cardiovascular Risk Factors, Aging and Dementia study (CAIDE). A random sample of 2000 individuals was invited for a re-examination in 1998; 1449 people participated. A second re-examination was conducted in 2005–2008; 909 people participated.
FINGER http://www.thl.fi/en_US/web/en/project?id=22356 *Miia Kivipelto*	The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) takes place in Finland and involves the National Institute for Health and Welfare; the University of Helsinki; the University of Oulu; the University of Eastern Finland; and KI. The aim of this ongoing, two-year, multi-center, multi-domain intervention study is to prevent cognitive impairment, dementia, and disability in 60–77 year-olds at increased risk of dementia.
The Betula Project www.betula.su.se *Lars-Göran Nilsson*	A sample of 3500 persons aged 35–80 years living in Umeå, Northern Sweden, has been assessed every fifth year since 1988 with regard to multiple cognitive, biological, and social variables. New cohorts have been included at each wave to estimate the size of test-retest effects. About 4700 persons have been assessed. A sixth wave will take place 2013–2015.
HARMONY http://ki.se/ki/jsp/polopoly.jsp?l=en&d=13903&a=30105 *Margaret Gatz and Nancy Pedersen*	HARMONY is an international collaboration involving the Department of Medical Epidemiology and Biostatistics and ARC at KI, the University of Gothenburg, and the University of Southern California. At baseline, 14,435 twins underwent a screening test, and 1557 persons were clinically examined. Linkages with the National Patient Register and the Cause of Death Register are made on a regular basis, most recently with diagnoses through 2010.

National Registers

At ARC we use various national registers, including the Cause of Death Register by Statistics Sweden, the National Patient Register, and the more recently launched Swedish Prescribed Drug Register. Located at the National Board of Health and Welfare, the Swedish Prescribed Drug Register represents one of the largest pharmacoepidemiological databases in the world.

The register was introduced in July 2005 and contains individual-based data for all prescribed and dispensed drugs (both ordinary prescriptions and multi-dose dispensed drugs) in Sweden. Data are continuously collected from Swedish pharmacies. Variables include detailed drug data (e.g., drug identification code, date of dispensing, amount of drug dispensed, dosage, and prescriber specialty) and age, sex, and geographical place of residence of the patients.

Research outcomes

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

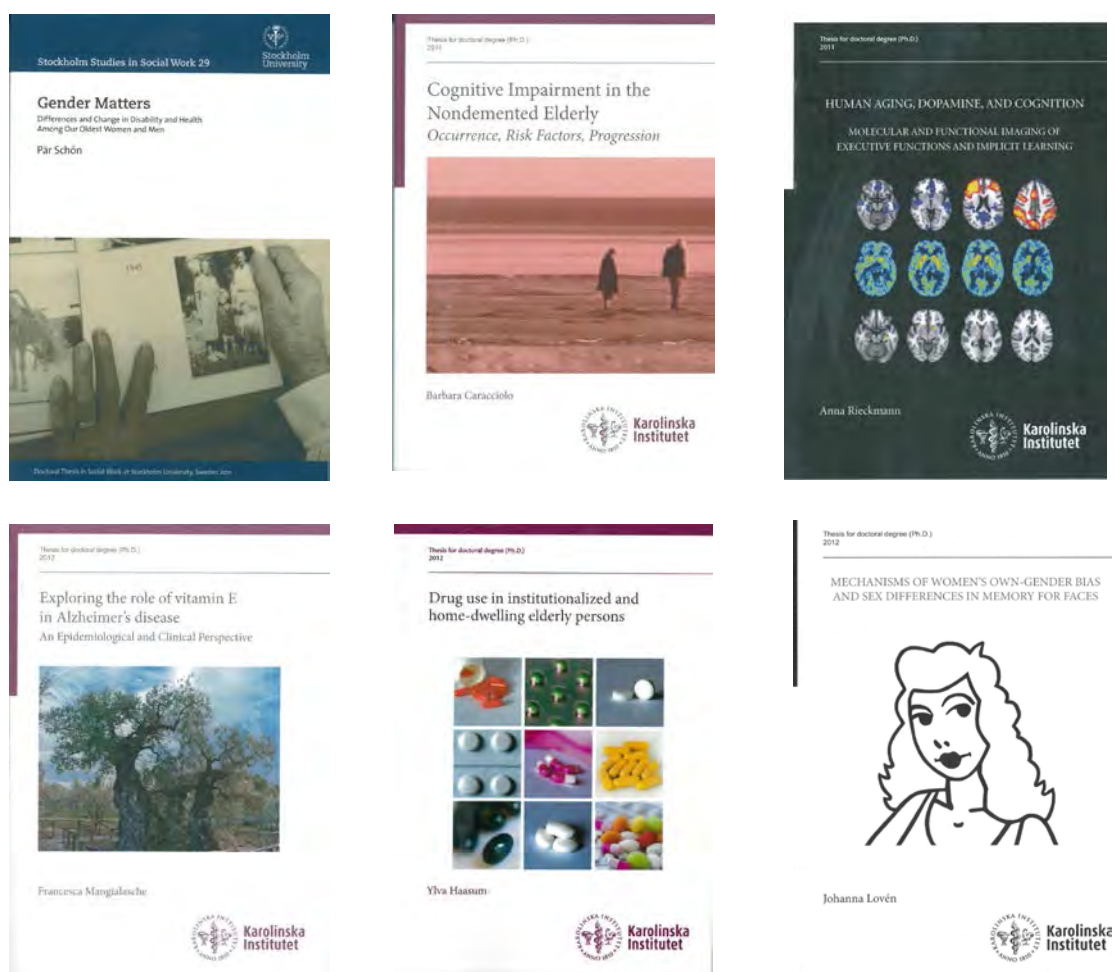| RESEARCH AREA	ORIGINAL ARTICLES	REVIEW ARTICLES	BOOKS	BOOK CHAPTERS	REPORTS	PHD THESIS
A Longevity, morbidity, and functioning	18	2	1	1	–	–
B Treatment and care of elderly persons	19	–	–	4	8	1
C Health trends and inequality	13	–	–	5	2	2
D Brain aging	101	16	–	5	1	3

Figure 6. PhD theses defended at ARC, 2011 and 2012.

Research findings

Please note that references are listed in the APPENDIX.

RESEARCH AREA 1: LONGEVITY, MORBIDITY, AND FUNCTIONING

1. Social determinants of health and function in later life: a life-course approach

The likelihood of living a long and healthy life is, in part, shaped by social conditions experienced throughout the life course. Using nationally representative survey data linked to information from the Swedish National Cause of Death Registry, we showed that those who reported having grown up in a broken family (without one or both biological parents) were at a higher risk of dying before reaching old age (before the age of 70) than those who reported having grown up with both biological parents. Similarly, an increased risk of premature mortality was also observed among those who were unmarried, rather than married or cohabiting, in midlife (ref. #41). In an ongoing study, based on nationally representative longitudinal survey data, we are exploring the associations between physical and psychosocial work environment in midlife and health during old age. Preliminary results show that both poor psychosocial and physical work environment in midlife are associated with an increased likelihood of psychological distress, musculoskeletal pain, and physical impairment during old age. Moreover, poor psychosocial work environment, but not physical work environment, is associated with higher rates of poor global self-rated health and cognitive impairment during old age.

2. Multimorbidity: occurrence, risk factors, and consequences

Based on a systematic review of the literature, we summarized the scientific evidence concerning occurrence, causes, and consequences of multimorbidity (the coexistence of two or more chronic diseases) in elderly people (ref. #152). Findings from the review showed that the prevalence of multimorbidity in older persons ranges from 55% to 98%. In cross-sectional studies, older age, female gender, and low socioeconomic status are factors associated with multimorbidity. These findings are also confirmed by longitudinal studies. The major consequences of multimorbidity are disability and functional decline, poor quality of life, and high health care costs. The results found on multimorbidity and mortality risk were inconsistent.

The few studies already available on multimorbidity have focused on quantifying the phenomenon. Despite some conceptual differences, the common denominator in all the definitions is the number of chronic diseases occurring concurrently. However, patients are more than the sum of their diseases, and the use of a quantitative definition fails to catch the patterns of disease, potentially leading to inadequate care management. It would be beneficial for advancements in the field to develop analytical methods to describe how and why diseases co-occur in the population, to detect the biological mechanisms and to explore specific pathways leading to disease clusters (ref. #7).

3. Leisure-time activities, social network, and health

Studies concerning the effect of different types of leisure activities on various cognitive domains and on delaying the age of dementia onset are limited. We explored this topic using two different cohorts. In a cohort of 1463 Chinese adults aged 65+ years, followed up after 2.4 years, a high level of mental activity was related to significantly less decline in global mental function, language, and executive function. Physical activity was related to less decline in episodic memory and language, and social activity was associated with less decline in global cognition (ref. #14). In a Swedish study including 1375 dementia-free Swedish community dwellers with good cognitive function (mean age=81.2), 388 persons developed dementia over a nine-year period.

Age at onset of dementia was significantly older in persons who had higher levels of participation in mental, physical, or social activity. A dose-response pattern was found. The difference in mean age at dementia onset between the inactive group and the most active group was 17 months (ref. #118). We have also studied the association between long-term trajectories of social engagement and late-life disability. Preliminary results suggest that middle-aged individuals with continuously high levels of social interactions over a 34-year period leading up to old age have a lower risk of disability in late life than those with continuously low and medium levels of social activities or decreasing levels.

4. Predictors of survival after life expectancy

The oldest verified person ever is Jeanne Calment, who died in 1997 at the age of 122 years and 164 days. When someone lives so long, it makes us wonder what the secret is. Does it lie in the genes? What makes the difference? Is it important where people live or the way they live? Is it something they do or do not do? In our research we explore the role of health, lifestyle, and social environment on the probability of reaching a very advanced age. Findings from our studies suggest that survival after 75 was associated with health status, lifestyle, genetic factors, and a combination of those factors (ref. #8, #130). Dementing and cardiovascular disorders were the major causes of shorter life after living four years on average with the disease. In addition, people with dementia lived half of

this period in moderate/severe disease phases. People with healthy lifestyles and rich social networks lived about five years longer than people with high-risk profiles. These associations, although attenuated, were also found in individuals aged 85 years and older and those with chronic diseases (**Figure 7**). Finally, preliminary results showed that allelic variations in four genes (*APOC1*, *APOE*, *IDE*, and *PI3K*) were associated with a higher mortality rate, but these effects were counteracted by healthy lifestyle. This suggests that people with genetic susceptibility may reduce their initial mortality rate by modifying their life habits. Further, the benefits from smoking cessation, increased physical activity, and social engagement continue into late life.
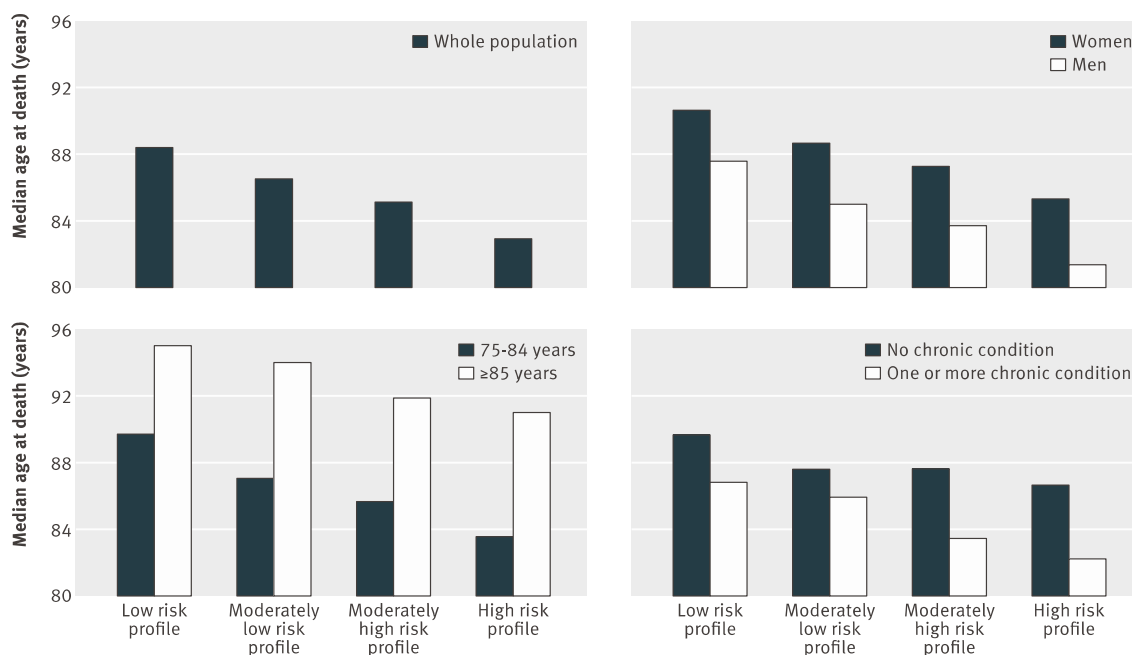
Figure 7. Median age at death in four risk groups according to combinations of modifiable factors among the entire population, men and women separately, of older adults (75–84 years) and oldest old adults (≥85 years), and by status of chronic conditions (ref. #8).

RESEARCH AREA 2: TREATMENT AND CARE OF ELDERLY PERSONS

5. Qualitative and quantitative aspects of formal and informal care

From 2011 to 2013, ARC, in cooperation with the Stockholm Gerontology Research Center, has been commissioned by the Swedish government to evaluate 19 local developmental projects for integrated health and social care services and ten collaborative networks for the care of older people across Sweden. This evaluation has highlighted the coordination problems that are common between local authorities and the providers of health and social care services for older people with complex health problems and severe care needs. These problems result from a lack of communication and coordinated care planning between the agencies responsible for eldercare. There are also boundary disputes between the service providers regarding responsibility for care provision and funding (ref. #190). One example of evaluation work carried out in 2011–2012 was the evaluation of a local developmental project for integrated health and social care organization for the oldest old in a municipality north of Stockholm (with 56,000 inhabitants). The project aimed to establish a unique integrated structure for the funding, organization, and delivery of care services to older people with severe care needs. The results showed that improved discharge planning and a safe return from the hospital to the home setting resulted in fewer readmissions than previously. Because of better integration of the care systems, the number of "bed-blockers"; i.e., those patients whose medical treatment is complete, has also decreased (ref. #192).

6. Quality of drug use in elderly persons: improvement and maintenance

During 2011–2012 a number of studies based on the Swedish Prescribed Drug Register and SNAC-K were carried out.

6a. By record linking data from the Swedish Prescribed Drug Register and the National Social Services Register, we were able to compare the quality of drug use in institutionalized and home-dwelling elderly people. About one third of the institutionalized elderly people were exposed to potentially inappropriate drugs and/or drug combinations—almost three times more often than home-dwelling elderly people. Institutionalization was also found to be a risk factor for inappropriate drug use, even when taking age, sex, and comorbidity into consideration (ref. #21).

6b. The Swedish Prescribed Drug Register provides the opportunity to study relatively small patient groups. In one study we examined drug use in Swedish centenarians (ref. #34). In comparison with nonagenarians and octogenarians, the centenarians (n=1672) were found to have high use of analgesics, hypnotics/sedatives, and anxiolytics. This reflects either a palliative approach to drug treatment in centenarians or that pain and mental health problems increase in extreme old age. In addition, centenarians appeared to be prescribed cardiovascular drug therapy according to less strict guidelines than nonagenarians and octogenarians.

6c. In recent studies based on data from SNAC-K, we verified whether some medical conditions in elderly people were undertreated. We detected a clear undertreatment of osteoporosis in elderly people with dementia (ref. #22). We then examined the influence of education on osteoporosis treatment, using record-linked data from the Swedish Prescribed Drug Register, the Swedish Patient Register, and the Swedish Education Register (ref. #35). The use of osteoporosis drugs is associated with higher education, thus confirming previous findings from our group that indicate socioeconomic inequalities in drug use in elderly people.

6d. In collaboration with researchers at Sahlgrenska University Hospital, we investigated the association between multi-dose drug dispensing and quality of drug treatment in elderly people using data from the Swedish Prescribed Drug Register and the Vega database, which is comprised of information on both in- and outpatient care. Even after adjustment for age, sex, disease burden, and type of residence, the results clearly showed that use of multi-dose drug dispensing is associated with poorer quality of drug use, as measured with five different indicators (ref. #30).

7. Economic aspects related to prevention, treatment, and care of elderly persons

7a. Costs of treatment and care for dementia. Eldercare, and in particular treatment of people with dementia, generates high societal costs throughout the care system. For disorders such as dementia that affect people over long periods of time, it is difficult to collect data over the whole course of the disease. Therefore there is a strong argument for simulation studies. We use simulation studies to verify whether a treatment that can modify the disease course could be beneficial for the individuals and at the same time reduce the societal burden. In a first study (ref. #31) we show an uneven distribution of dementia costs at different disease stages. Social care services are responsible for those people with the most severe problems and the highest care costs. Then, using Markov modeling, we reported that giving dementia-specific treatment would benefit individuals, but that the societal cost would rise. This rise would mainly be accounted for by an increase in longevity of one year for people undergoing the treatment. The rise in societal costs is considered to be within acceptable limits, as the cost of the treatment per Quality Adjusted Life Year (600,000 SEK) is under the level required for the treatment to be considered cost-effective by society (ref. #32).

7b. Cost-effectiveness of potential dementia preventive intervention programs starting at midlife. We have estimated the cost-effectiveness of a potential dementia prevention program using the CAIDE Dementia Risk Score and a Markov model adapted to Swedish conditions (ref. #151). The prevention program consisted of two main components, a health promotion program and pharmacological treatment of cardiovascular risk factors. Figures on costs and mortality were obtained from literature or databases. The multi-domain preventive intervention was less costly and resulted in better dementia-related outcomes than "usual care," supporting the conclusion of cost-effectiveness.

7c. Occurrence and cost of brain disorders in the European Union. In a collaborative European project, the 12-month prevalence and disability burden of a broad range of mental and neurological disorders in the European Union (EU) were estimated based on a stepwise multi-method approach. The findings showed the true size of the burden from "disorders of the brain" was considerably larger than expected, as brain disorders represent the largest contributor to the all-cause morbidity burden as measured by disability-adjusted life years (DALYs) in the EU (ref. #116). Furthermore, the total cost of disorders of the brain in Europe in 2010 was estimated at €798 billion. Direct costs constituted the majority of costs, whereas the remaining 40% were indirect costs associated with patients' production losses (**Figure 8**). On average, the estimated total cost for each person with a brain disorder in Europe ranged between €285 for headaches and €30,000 for neuromuscular disorders (ref. #74).
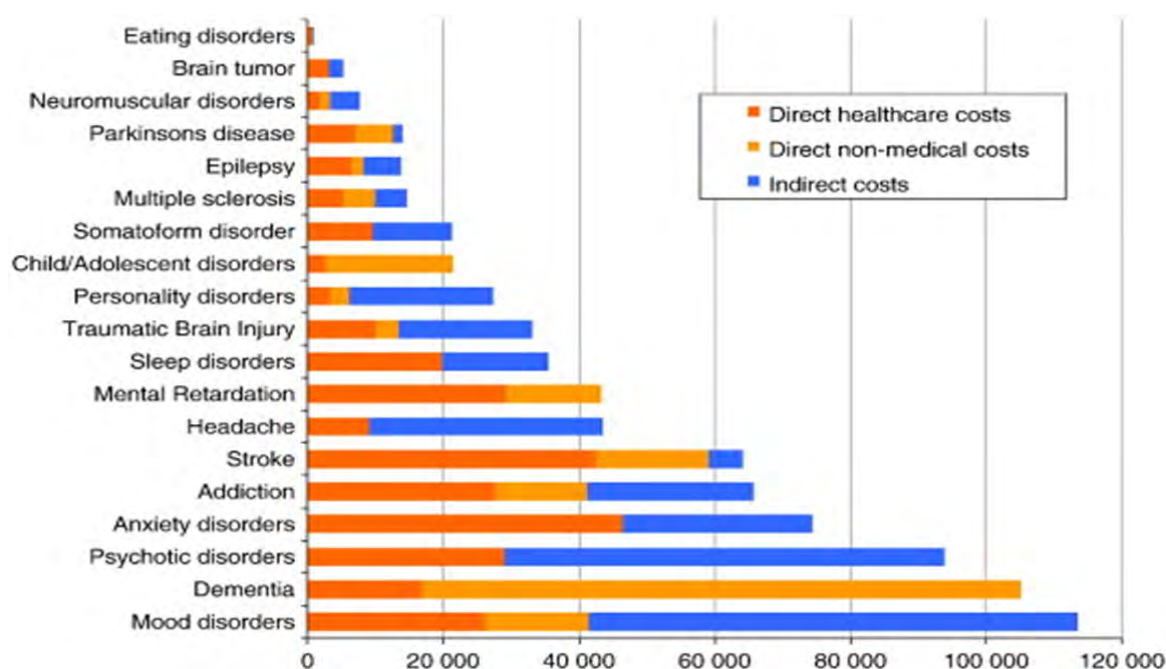
Figure 8. Total societal cost (health care, non-medical, and indirect costs) related to different brain disorders (€PPP million, 2010; ref. #74).

RESEARCH AREA 3: HEALTH TRENDS AND INEQUALITY

8. Understanding health trends

A crucial public health question is whether increases in life expectancy have been accompanied by increasing or decreasing prevalence rates of health problems among the oldest persons in the population. We have explored health trends among the oldest old (ages 77+) in Sweden during the period 1992–2011. The study is based on nationally representative survey data (SWEOLD) and encompasses many indicators of health and physical function. The preliminary results showed increases in prevalence rates of pain, psychological problems, and impaired mobility and decreased lung function during the period. Self-rated health and physical function remained unchanged. However, despite the increases in health problems, the proportion of the oldest old reporting that they need help with their basic activities of daily living decreased during the period. On average, older women have more health problems than older men, but the development over time is similar.

Finally, data from the Kungsholmen Project and the SNAC-K study showed that the prevalence of dementia remained stable from 1987–1989 and 2001–2004 in central Stockholm, Sweden, whereas the survival of patients with dementia increased (**Figure 9**; ref. #125). The results suggest that the incidence of dementia might have decreased over the last two decades of observation in this region. This study has significant implications for forecasting the societal burden of dementia and suggests that better prevention and treatment of vascular disease may be responsible for such dementia risk decline.
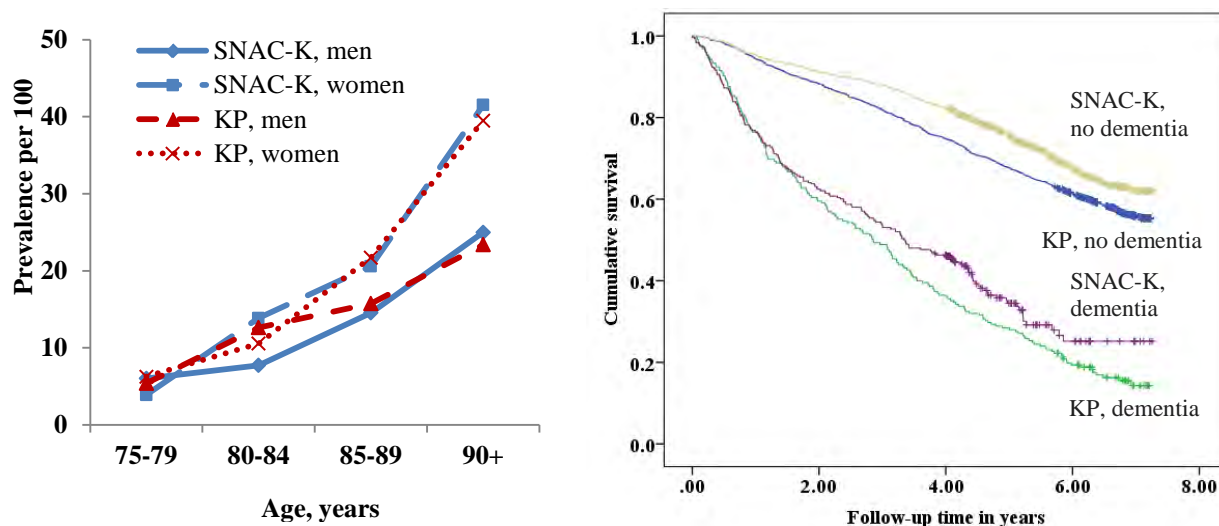
Figure 9. Age- and sex-specific prevalence (left) and the Kaplan-Meier survival curves (right) of people with dementia in the Kungsholmen Project (1987–1994) and SNAC-K (2001–2008) (ref. #125).

9. Inequalities in health

Although it is now well established that socioeconomic inequalities in health and mortality prevail into very old age, the patterns and etiologies of these health inequalities are still largely unexplored. In recent studies based on population data from Sweden and Finland, we have shown that education is significantly associated with physical and cognitive functioning as well as with rheumatoid arthritis. Individuals with lower education are more likely to have all of these conditions than individuals with higher education (ref. #5, 143). Health inequalities during old age are likely shaped by lifelong processes. Thus, in order to understand these inequalities, it is necessary to apply a life-course perspective. Using datasets comprising longitudinal survey and registry data, we have explored the association between socioeconomic conditions during different stages of the life course and mortality. The results showed that social class in childhood and adulthood were both independently associated with premature mortality (i.e., before the age of 70) (ref. #41). Similarly, income in midlife and income during retirement were both independently associated with mortality during retirement (ref. #42). The mechanisms generating late-life health inequalities are opaque. However, in a new study we have shown that socioeconomic differences in smoking and obesity could partly explain the socioeconomic inequalities in mobility and cognitive impairments observed among elderly Swedes (ref. #43). Yet another study found that older individuals with higher education were more likely to participate in health-enhancing exercise than individuals with lower education (ref. #9).

10. Biological and social aspects of gender differences in cognition, health, and longevity

Gender differences in old age are the result of the lifetime accumulation of biological and social factors (ref. #179). Paradoxically, women outlive men in all countries of the world, yet they report higher morbidity at all ages than men. Using data from the Human Mortality Database, we have shown that in most low-mortality countries, the gender gap in life expectancy has gone through three phases: 1) stable, 2) increasing, and 3) decreasing gender differences. All but two countries have gone through these phases (although starting at different times) (ref. #48), which suggests changes in gender-related social factors. We have also investigated various indicators of health and function among the oldest old and found that gender differences prevail in the highest age groups (ref. #47, 199). Furthermore, when it comes to musculoskeletal pain, results suggest that time spent in pain in relation to total life expectancy has increased in later cohorts (ref. #199), more so for women than for men. Our register-based studies of medication use have shown that older women are prescribed more hypnotics and sedatives than older men (ref. #25). Our research on sex differences in cognition builds on our previous results that women have an advantage in verbal episodic memory tasks and on face recognition tasks. Recent results have shown that women remember female faces with greater efficiency than male faces, but this advantage is diminished when attention is divided (ref. #45).

RESEARCH AREA 4: BRAIN AGING

Cognitive aging

11. Cognitive functions in normal aging

Cognitive performance declines in healthy aging. Longitudinal studies performed over the last two decades have shown that mean age-related changes accelerate after the age of 65. Changes are most pronounced in fluid abilities such as processing speed, working memory, and episodic memory. Our recent studies have continued to refine the description of cognitive changes in healthy aging and aimed at explaining the individual differences in these changes, using data from the SNAC-K study and from complementary smaller-scale data collections. We have reported that age differences in cognitive performance at baseline in the SNAC-K study are most pronounced for processing speed and episodic memory performance (ref. #92). In addition, we demonstrated that single genetic polymorphisms can only explain small portions of the individual differences in these cognitive abilities in old age (ref. #92). Other studies have revealed that individuals displaying more moment-to-moment fluctuations in cognitive performance are also those individuals who are forgetting more (ref. #119). In addition, we have discovered that day-to-day fluctuations in cognitive performance are linked to fluctuation in negative affect (ref. #58). Moreover, we have reported that the finding that negative information is better remembered also holds for older adults (ref. #72). Thus, our research has continued to refine the understanding of the aging cognitive system, linking performance across domains of cognitive functioning and time scales and relating it to genetics and emotion.
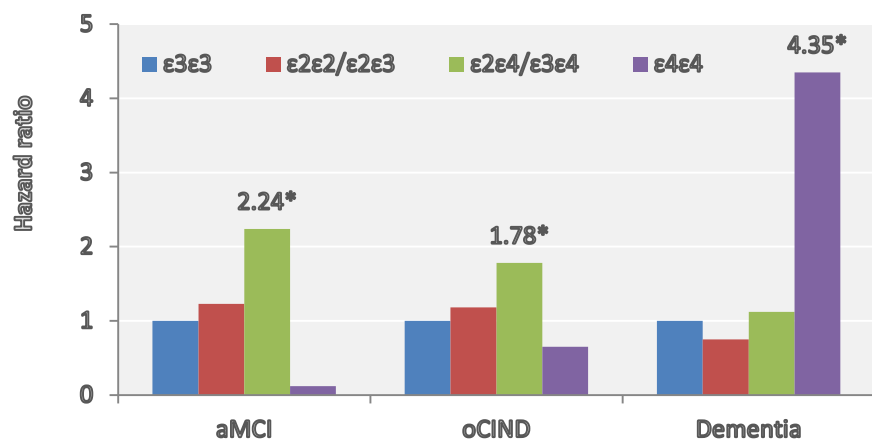
12. Mild cognitive impairment/Secondary dementia prevention

Cognitive impairment in non-demented elderly persons, often labeled mild cognitive impairment (MCI), is one of the strongest predictors of dementia. It has been estimated that on a yearly basis, 6.8% of people with MCI progress to dementia. A total of 4.9% of people with MCI develop Alzheimer's disease (AD) within three years. If prevention of cognitive deterioration and dementia is to be effectively pursued, we must understand the extent of MCI in the population, its underlying mechanisms, and the likelihood that it will progress toward more severe stages of cognitive decline. Three research lines have been developed:

12a. Mild cognitive impairment: occurrence and risk factors. Using information from the nationwide Swedish Twin Registry on 11,926 dementia-free and cognitive impairment no dementia (CIND)-free individuals, it has been estimated that one out of four Swedes (25%) aged 65 years or older have some degree of cognitive impairment (ref. #64). In twin pairs with discordant CIND status, formal education was the only environmental factor that could explain the differences in

outcomes (ref. #64). This finding confirms the protective value of education on cognitive decline, independent of genetic background and early life environment. In another study based on the same cohort of Swedish twins, mental, musculoskeletal, respiratory, urological, and endocrine diseases were all significantly associated with increased odds of CIND (ref. #65). Co-twin analyses showed that genetic and early-life environmental factors partially explained the association between CIND and chronic diseases. In a study based on the Kungsholmen cohort, we also found that being in a low mood almost tripled the risk of developing MCI within three years (ref. #63). Further, low mood seems to have a more prominent role in the early, rather than in more advanced, stages of cognitive decline. Finally, people carrying one APOE ε4 allele are at increased risk of both amnestic MCI and global MCI (ref. #150; **Figure 10**). Low mood interacts with the APOE ε4 allele so that cognitively healthy elderly people with both risk factors have a 12-fold increased risk of developing MCI within three years (ref. #63).

Figure 10. Multi-adjusted hazard ratio of amnestic mild cognitive impairment (aMCI), other domain cognitive impairment, no-dementia (oCIND), and dementia according to APOE genotypes (ref. #150).

12b. Preclinical dementia and natural evolution of mild cognitive impairment. In the Kungsholmen Project, it was observed that people in the preclinical stage of AD deviated from the normal aging curve earlier than people in the preclinical stage of vascular dementia. Those in the preclinical stage of AD deviated up to nine years before diagnosis, and those with vascular dementia deviated up to six years before diagnosis. However, once people with preclinical vascular dementia started to decline, they deteriorated at a faster rate than people with preclinical AD (ref. #91). Data regarding two different cohorts of 70-year-olds from the Kungsholmen and the H70 projects indicated that decline in cognitive test results occurred 5 to 10 years before dementia diagnosis. The onset occurs earlier for fluid cognitive abilities (such as memory and speed) than crystallized abilities (such as verbal abilities), but acceleration after onset is faster for the latter. Finally, among the 160 persons age 75+ from the Kungsholmen Project with incident MCI, low mood three years before the detection of MCI was an effective predictor of progression to dementia three years after the diagnosis of MCI. This finding suggests that low mood may be an early sign of initial cognitive deterioration rather than a "true" risk factor for or consequence of MCI (ref. #63). We also found that people with MCI who carried two APOE ε4 alleles (ε4 homozygotes) progressed substantially faster to dementia than people with MCI who were not APOE ε4carriers; those with two ε4 alleles developed dementia more than three years earlier (ref. #150). On the other hand, accelerated progression from MCI to AD and dementia occurs when white matter lesions at MRI examination co-occur with vascular diseases or vascular risk factors (ref. #67).

12c. Pre-MCI. The research focus here shifted from MCI to earlier syndromes of cognitive impairment, namely, pre-MCI. The most-studied sign of this early phase is subjective cognitive complaints, the subjective feeling of deterioration in one's own cognitive capabilities, also known as subjective cognitive impairment or SCI. Longitudinal studies support the idea that a proportion of people who will later develop dementia pass through a stage when cognitive decline is not yet evident, but there is a subjective perception of it. The prevalence of SCI was unknown until recently, when we used information from the Swedish Twin Registry on nearly 12,000 dementia- and MCI-free individuals to estimate that 39% of Swedish people aged 65 years and older present with SCI (ref. #64). The same study showed that SCI and MCI have distinct sociodemographic profiles. One important question about both SCI and MCI is to what extent they are determined by genetic background and early life environment (genes and family environment). Caracciolo et al. (ref. #64) found that at the SCI and MCI stage, adult life environment is more important than genetic and familial background factors in discriminating people who perform well and perceive themselves as functioning optimally from those with signs or symptoms of initial cognitive deterioration. Similarly to people with CIND, those with subjective cognitive complaints are more likely to be affected by chronic diseases. Indeed, SCI was found to be associated with most chronic diseases, suggesting that general rather than specific mechanisms underlie the association. Also, in this case, adult life environment rather than genetic background and early life environment appears to be prominent in explaining the association between SCI and chronic disease.

Risk factors for dementia

13. The role of vascular risk factors in brain pathology

Numerous studies have linked APOE ε4 and vascular factors to dementia, including AD. In the Kungsholmen Project, we found that APOE ε4 is a major risk factor for MCI (ref. #150), AD, and dementia, but not all carriers of ε4 develop dementia. Indeed, we identified some factors that may modify the risk of dementia due to ε4: high education, active participation in leisure activities, and maintaining vascular health (**Figure 11**; ref. #71). A further study supported this last finding, as we found that education counteracted the risk due to APOE (ref. #144).

Several reports have linked midlife obesity to dementia in late life. We found that both overweight and obesity at midlife independently increase the risk of dementia, AD, and vascular dementia. Genetic and early-life environmental factors may contribute to the midlife high adiposity-dementia association (**Figure 12**) (ref. #148).

Figure 11. Multi-adjusted hazard ratio (HR) of dementia by APOE ε4 in relation to education, vascular risk factors, and leisure activity score. In orange: people with low education, high vascular burden, and low activity score; in blue: people with high education, low vascular burden, and high activity score (ref. #71).
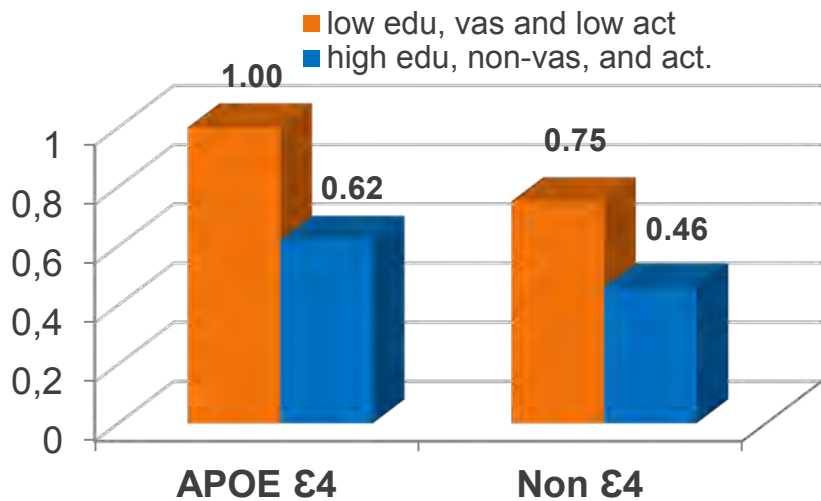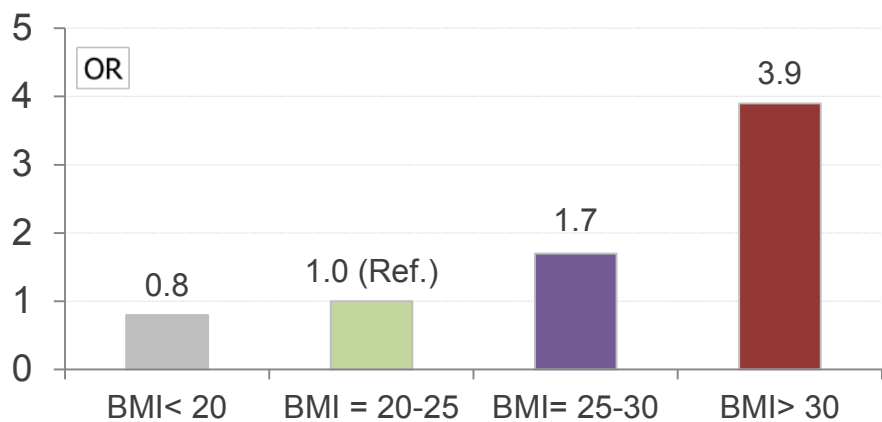

Figure 12. Odds ratio (OR) of overweight (body mass index [BMI] 25–30) and obesity (BMI>30) at midlife for dementia in late life (ref. #148).

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Finally, in the SNAC-K MRI sample (n=523, age ≥60 years, 59.3% women), we investigated the association between vascular factors and pathological changes in the brain. We found that as the number of vascular risk factors increased, the volume of the hippocampus and entorhinal cortex decreased significantly (ref. #124). These associations were evident only among men, suggesting that in men, the medial temporal lobe is more vulnerable to cardiovascular risk factors than in women. In the AGES-Reykjavik Study (n=4205, mean age 76 years, 58% women), cerebral microbleeds had a prevalence of 11.3% and were not associated with age-related macular degeneration, a finding that does not support the hypothesis that amyloid deposits in the retina and the brain are correlated (ref. #123).

14. Risk factors in middle age, cognitive decline, and dementia

14a. Changes in blood pressure from midlife to late life in relation to dementia risk and cognitive decline. Elevated blood pressure (BP) has been associated with increased risk of dementia in several studies, but the impact of hypertension seems to be age-dependent. In the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study in Finland, we previously linked midlife hypertension to higher dementia risk two decades later. We are now continuing these studies by focusing on the relation between patterns of change in BP during three decades after midlife and dementia, and by using data from the more recent second CAIDE follow-up in addition to data from the first follow-up. Preliminary results show that compared to people without substantial decline in BP from midlife until 30 years later, CAIDE participants with a decline of more than 15 mmHg in systolic BP or more than 15 mmHg in diastolic BP had a significantly increased risk of developing dementia. A possible explanation for the relation between decreasing BP and dementia may be the effect of dementia-related diseases on brain areas involved in BP regulation (i.e., the insula). A bidirectional relation could thus be hypothesized: midlife hypertension increases the risk of dementia-related pathological processes, and once such processes start they can in turn affect BP regulation. In addition, we found that elevated systolic or diastolic BP in midlife was related to poorer psychomotor speed in late-life and that declining diastolic BP between midlife and first follow-up (20 years) was related to worsening of executive functioning between first and second follow-up (work in progress).

14b. Changes in blood pressure from midlife to late life and structural magnetic resonance imaging findings. In the CAIDE MRI population, midlife hypertension was related to more severe white matter lesions, as was long-term hypertension during 20 years after midlife. Decreasing BP after midlife was also associated with white matter lesions even after controlling for antihypertensive treatment. In contrast, lipid-lowering drugs had a protective effect against white matter lesions (ref. #141). In addition, midlife hypertension was related to a thinner cortex 28 years later in several brain areas, including the insular, frontal, and temporal cortices. In elderly people with thinner insular cortices, there was a continuous decline in systolic BP and an increase in pulse pressure after midlife, whereas in elderly people with thicker insular cortices, the decline in systolic BP started at older ages, paralleled by a decline in pulse pressure (ref. #142, 2013; **Figure 13**).

Figure 13. Significant differences in late-life cortical thickness between people with and without hypertension in midlife (warmer colors indicate thinner cortex) (ref. #142).
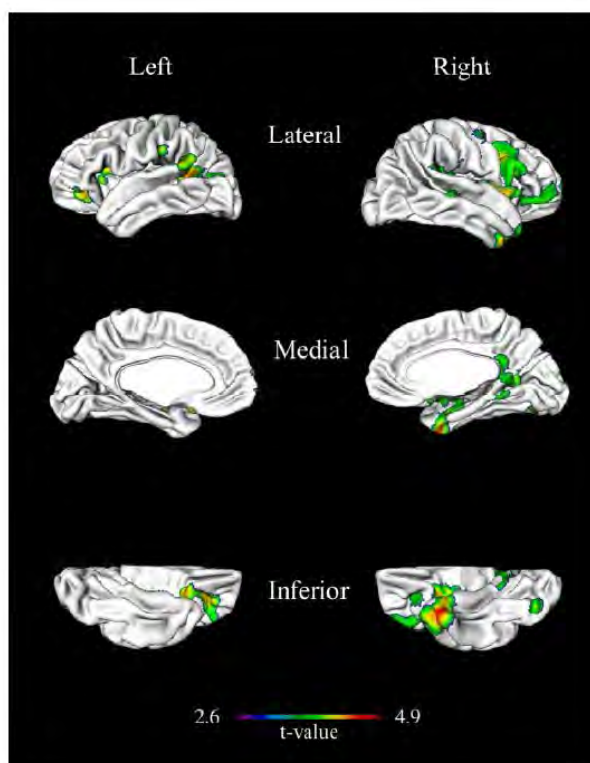
14c. Overweight/obesity and hypercholesterolemia. In the CAIDE MRI population, midlife overweight or obesity was related to more severe white matter lesions two decades later. Long-term (20 years) overweight or obesity also increased the risk of more severe white matter lesions (ref. #141). However, we did not find any associations between body mass index, cholesterol, or the APOE ε4 allele and cortical thickness in this group of elderly people (ref. #142).

14d. Inflammation. The association between rheumatoid arthritis or arthritis and dementia/AD has been investigated in several studies; the hypothesis has been that the chronic inflammatory component of rheumatoid arthritis may promote/facilitate neurodegeneration. In the CAIDE study, we investigated the association between self-reported joint disorders (rheumatoid arthritis and other joint disorders) in midlife and cognitive status 21 years later (ref. #143) and found an increased risk of cognitive impairment or dementia if any joint disorder was present at midlife.

15. Brain reserve and dementia risk

Studies on the possible modifying effect of education on the APOE-dementia association are limited. We tested the hypothesis that education may decrease the risk of dementia associated with APOE ε4. The study used pooled data from three major population-based studies in northern Europe, which included a total of 3436 participants aged 65+: the Kungsholmen Project and the Gothenburg Birth Cohort studies in Sweden and the CAIDE project in Finland. Both APOE ε4 (carriers of one ε4: OR 2.5, carriers of two ε4: OR 3.7) and lower education (<8 years) were independently associated with significant decreased risk of dementia. An interaction between education and APOE ε4 was observed. APOE ε4 allele carriers who had low education were at higher risk of dementia; the risk diminished if they had higher education (ref. #144).

16. Psychological stress and dementia risk

16a. Occupation-based psychological stress. Work stress can influence the risk of dementia even after retirement, as data from ARC researchers have demonstrated. Wang et al. (ref. #145) found that a low level of job control was associated with a doubled risk of dementia and AD, but levels of job demands were not associated with an increased risk of dementia. When the two dimensions were combined into a four-category job strain model, both high job strain (low control/high demands) and passive strain (low control/low demands) were related to higher risk of dementia and AD than active job strain (high control/high demands). The findings suggest that lifelong work-related psychosocial stress was associated with increased risk of dementia and AD in late life, independent of other known risk factors (ref. #145).

16b. Late-life psychological stress. Although life after retirement is generally considered to be a peaceful period of life, many psychological challenges may occur as well, such as changes in working routines, loneliness, loss of autonomy, death of loved ones, and deterioration in health, all of which may lead to psychological stress. A project at ARC aims to investigate i) the prevalence of stress in the SNAC-K population and ii) to what extent higher stress levels are a risk factor for cognitive aging, dementia, and worse health in older adults. During the third phase of SNAC-K (2007–2010), the perceived stress scale and measurement of blood cortisol were introduced into the longitudinal design to measure stress levels in older adults. During 2011, stress levels of 1656 community dwelling, 66–96 year-old adults participating in the third phase of SNAC-K were analyzed. Results are forthcoming.

17. Diet and antioxidant hypotheses for neurodegeneration

17a. Vitamin E complex. We are examining various nutrients in relation to age-related cognitive impairment and AD. In collaboration with the University of Perugia in Italy, we are investigating the antioxidant vitamin E, which includes eight natural compounds, four tocopherols and four tocotrienols. Most research on vitamin E in relation to dementia and AD has primarily focused only on α-tocopherol, with conflicting findings. In the European AddNeuroMed Project—a multicenter longitudinal study—we found that diagnoses of AD and diagnoses of MCI were associated with low plasma tocopherol and tocotrienol levels (ref. #103). In the same population, we showed that the combined analysis of tocopherol and tocotrienol plasma levels and automated MRI measures can help differentiate people with AD and MCI from those who are cognitively normal, and to prospectively predict MCI conversion to AD (ref. #104). These studies suggest that different forms of vitamin E can be important for the onset and progression of AD.

17b. Vitamin B12 and folate. Some earlier studies have found that low blood levels of vitamin B12 and folate and high concentrations of homocysteine are related to an increased risk of cognitive impairment and dementia, but evidence has been inconsistent. In the CAIDE population, we found that higher serum levels of homocysteine were associated with poorer cognitive performance during seven years of follow-up, even in older adults without dementia. In the same population, increased levels of serum folate and holotranscobalamin—the biologically active

fraction of vitamin B12—were associated with better cognitive performance, even in people without dementia (ref. #77). In a Finnish neuropathological study (Vantaa) in very old individuals (85+), preliminary results show that higher plasma homocysteine is associated with increased brain burden of β-amyloid and neurofibrillary tangles.

Intervention studies

18. Possible short- and long-term effects of cognitive training

Previous intervention research on cognitive training reveals that memory functioning is flexible and plastic across the lifespan. We investigated the effects of behavioral training, structural and functional brain correlates of behavioral plasticity, and the impact of genetics on training gains in several cognitive domains, such as working memory and episodic memory. In a working memory training study, we observed larger performance gains after adaptive training (training in which task difficulty is adjusted individually) than after low-level practice in younger and older adults. These gains transferred to a test of sustained attention for which participants did not train, and training and transfer effects were maintained across a three-month timespan (ref. #56). We also observed decreases in neocortical activity and increases in subcortical activity, which were both related to the behavioral performance gains (ref. #55). Finally, we found that variations in a gene linked to the LMX1 transcription factor, which is implicated in the development of dopamine-producing neurons in the midbrain, affect the magnitude of gains from working memory training (ref. #53).

In addition, we investigated whether individuals with higher levels of task-relevant cognitive resources gain more or less from instruction and training in imagery-based memory strategies than individuals with lower levels of cognitive resources. Initial instruction reduced between-person differences in memory performance, compensating for inefficient processing among the initially less able. However, further practice after instruction magnified between-person differences, uncovering individual differences in memory plasticity (ref. #97). We are currently examining the neural correlates of patterns of intervention-related behavioral changes in children, younger adults, and older adults after training in binding together two pieces of information. This work is being done in collaboration with colleagues from the Max Planck Institute for Human Development in Berlin, Germany.

Finally, we found that spatial navigation training is associated with fewer declines in regional brain volumes in adulthood and old age (ref. #98, 146). Our research also shows that younger adults learning a new language at a rapid pace display improvements in memory performance (ref. #111) and increases in cortical thickness of brain regions classically involved in language processing (ref. #112).

19. Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) is the first carefully designed and monitored population-based randomized controlled trial that aims to prevent cognitive decline. The intervention consists of four components: nutritional guidance, physical activity, cognitive and social activity, and intensive monitoring and treatment of metabolic and vascular risk factors (**Figure 14**). Participants in the reference group receive general public health advice on lifestyle and vascular risk factors.

The primary outcome is cognitive impairment, and an extended follow-up of seven years after the end of the intervention is planned to investigate the impact on dementia incidence. Preliminary analyses on differences between the intervention and control groups in various vascular, metabolic, and dietary factors support the hypothesis of beneficial effects from the multi-domain intervention. The intervention group has better glucose metabolism (fasting glucose and oral glucose tolerance test); lower total cholesterol and LDL values; lower weight, waist circumference, and body mass index; and lower systolic BP than the control group. After one year of intervention, participants in the intervention arm have also improved their diet in comparison with participants in the control arm: they have a significantly lower intake of saturated fats and higher intake of omega-3 fatty acids, fibers, and vitamins.
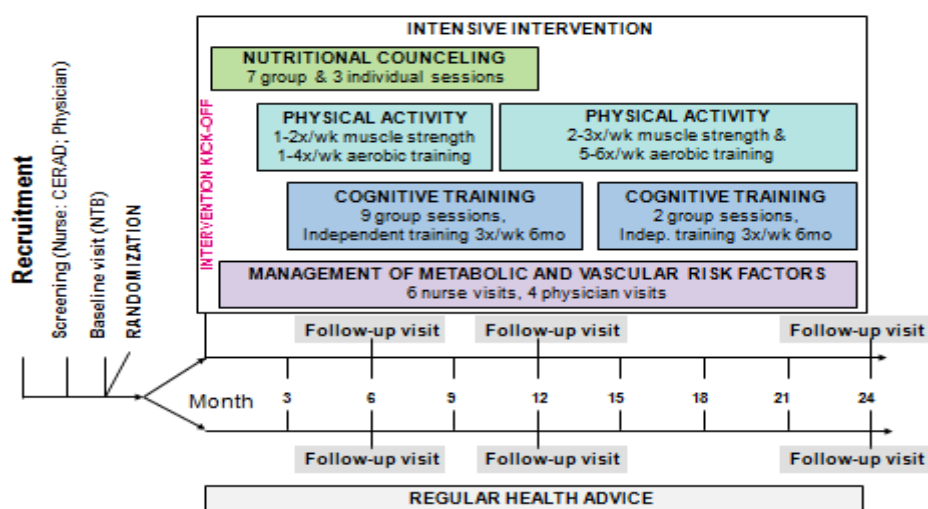

Figure 14. Design of the FINGER Study: illustration of the intervention procedure and assessments (ref. #162).

Neuroimaging

20. Population-based structural imaging of grey- and white-matter integrity in aging

Effects of aging on brain integrity have been extensively studied for many years. One important drawback of previous studies is that most studies included individuals spanning all of adulthood with a bias towards younger individuals, which has led to limited knowledge about age-related effects in late adulthood. Another important issue is the health status of the individuals enrolled in brain imaging studies. Because the aim is often to describe successful aging, massive exclusion of older participants with age-related diseases is common. The findings of such studies do not reflect loss of brain integrity in the general aging population, which is more likely characterized by chronic multimorbidity. Conversely, since most studies have been cross-sectional, there is a risk that people with preclinical dementia were included, which may affect the results. A way to overcome these issues is to investigate brain integrity via longitudinal population-based studies. A total of 555 participants in the SNAC-K study underwent structural MRI at baseline and three and/or six years later. Our most relevant findings in 2011 and 2012 were:

20a. Individual differences in white matter microstructure as measured using DTI are structured according to tracts, and aging is not a process with homogenous effects on white matter microstructure across the brain (ref. #100).

20b. Ongoing work using T1-weighted MR images shows that the hippocampus undergoes the strongest age-related volume reduction, even after exclusion of people with preclinical dementia. This result contrasts with the results of previous studies, which show preservation of the structure when comparing younger to healthy young-older adults.

Forthcoming studies concern i) the effects of health status and environmental factors, such as physical activity and genetics, on brain integrity and cognition and ii) assessment of longitudinal effects on grey and white matter macro- and micro-structural changes.

21. Functional brain activation during cognitive and emotional processing in young and old adults

Ongoing work includes analyses of two previously collected large functional magnetic resonance imaging (fMRI) datasets. The neural correlates of age-related differences in cognition and emotion are investigated in these analyses. In both projects, genotyping has also been performed, which makes it possible to link genetic information to brain function and structure and to behavioral data. Our four main projects are:

21a. In a first study we aimed to examine age-differences in encoding and retrieval of emotional and non-emotional information across different retention intervals (after five minutes, one week and three weeks). Key findings include observations of an increasing rate of false recognition of negative pictures after one and three weeks, and this effect was more pronounced in older adults. Moreover, after three weeks of retention, activity in the amygdala was seen in the older adults, suggesting a reactivation of automatic processes related to emotional information. Another important result found only in the young adults is a reduction of medial temporal lobe

engagement (and especially the hippocampus) over time for neutral items, but an increase in or stable activity for emotional items over time (ref. #81).

21b. Thirty young and thirty older adults have been scanned using cognitive and emotional fMRI-protocols, and analyses are currently underway. We found that activity in select regions of the prefrontal cortex may reflect greater affective processing when viewing happy than neutral or angry faces (ref. #69). Greater activity in yet other regions may reflect more cognitive control involved in decoding and/or regulating negative emotions associated with neutral or angry (rather than happy), and older (rather than young) faces.

21c. This study uses a cognitive interference task to investigate functional differences in activity patterns associated with interference resolution and their behavioral implications in young and older adults. Findings suggest that age-related structural brain changes contribute to reductions in efficient recruitment of key brain regions involved in interference control, which triggers a unique neural network facilitating conflict resolution in elderly people (work in progress). In addition to activation tasks using fMRI, resting state fMRI and DTI data were collected.

21d. Another ongoing project includes the study of the structural connectivity of functional networks (such as the default mode network, activated in the absence of any goal-directed external task, or the fronto-parietal attention network). Resting-state fMRI data will be used to identify the exact location of the networks' nodes, marking the starting points of the white matter tracts whose structural properties will be calculated using tractography on the DTI data. The effects of age on networks' structural properties will be studied, as well the relationships between the structural properties and cognitive data collected outside the scanner (offline tasks).

AF JOCHNICK CENTER FOR THE COGNITIVE NEUROSCIENCE OF AGING

The af Jochnick Center for the Cognitive Neuroscience of Aging is made possible through a donation from the af Jochnick Foundation over a 10-year period (2011–2020). Research within the center seeks to delineate the neural underpinnings of aging-related changes in cognitive functions, with special focus on how losses of various dopamine (DA) markers relate to cognitive deficits in old age. Of particular interest is how DA changes across the adult life span relate to other age-related brain changes, such as losses of grey- and white-matter integrity as well as alterations in functional connectivity with regard to cognitive problems in late life.

22. Dopamine functions and cognitive aging

In multimodal imaging work with young and old adults, we use both PET and fMRI to determine relationships between DA activity and functional brain activity during working memory performance. Results show that age-related losses of D1 receptors in caudate and frontal cortex contribute to under-recruitment of task-relevant fronto-parietal regions and working-memory deficits in old age (ref. #61). Further, D1 receptor losses in aging are related to reduced fronto-parietal connectivity and increased fronto-frontal connectivity (ref. #127). In another study, young adults were given a dopaminergic antagonist that blocks approximately 50% of D1 receptors in caudate and frontal cortex. Under the influence of the antagonist, the young showed reduced fronto-parietal connectivity and increased fronto-frontal connectivity along with impaired working-memory performance, thereby mimicking the patterns seen among old adults under normal conditions (ref. #129).

Other research indicates that the brain DA systems may be segregated in aging. Whereas young adults showed high intercorrelations in D1 binding within and between regions in the nigrostriatal, mesolimbic, and mesocortical pathways, old adults exhibited strong within-pathway links, but markedly reduced relationships in D1 binding of nigrostriatal to mesolimbic and mesocortical pathways. Importantly, weak between-pathway correlations in old adults were found only for the slower half of the sample, as measured with a cognitive interference task. These results suggest that D1 receptor densities in different pathways are not regulated independently in younger adults, but segregate in old age, and that this segregation of D1 receptor systems may be related to age-related cognitive slowing (ref. #128).

Moreover, intra-individual variability (IIV) in speed of responding in reaction-time tasks has been associated with various conditions characterized by altered DA neurotransmission (e.g., Parkinson's disease, schizophrenia, and ADHD). In one study, we obtained direct evidence of a DA-IIV link (ref. #102). Here, old adults exhibited reduced D1 binding in various cortical regions (**Figure 15**) that was linked to increased IIV during an interference resolution task. The DA-cognition relationship may also be observed irrespective of age. In an age-homogenous sample of young adults, we observed strong associations between D1 markers in striatum and hippocampus and performance on tasks assessing knowledge, speed, and executive functioning (ref. #83).

Finally, we have documented novel evidence for DA release after training in updating information in working memory (ref. #62). This research, along with other intervention work on working memory, was summarized in a recent review (ref. #157).

23. Cognition, Brain, and Aging

The Cognition, Brain, and Aging (COBRA) project is a longitudinal study that involves scientists from ARC, Umeå University, and the Max Planck Institute for Human Development in Berlin. COBRA follows around 180 persons who were between 63 and 67 years at baseline across nine years, with three measurement occasions. Multiple brain measures are assessed at each interval using PET and MRI (i.e., dopamine D2 receptors, markers of grey- and white-matter integrity, and functional networks). Cognition is assessed using measures of working memory, episodic memory, and speed, and information on lifestyle factors is collected through administered questionnaires (**Figure 16**).

The degree of average age-related change in DA availability, grey matter, and white matter remains unclear because of the paucity of longitudinal data. The shared and unique contributions of changes in DA, grey matter, and white matter to changes in cognitive performance in old age are unknown. It is also unknown which of the candidate neural correlates (DA, grey matter, or white matter) of cognitive decline first displays signs of change in old age. Our main hypothesis is that age-related DA changes precede changes in the other brain indices assessed and serve as the most powerful antecedent of age-related cognitive changes. Finally, the lifestyle factors associated with changes in the brain parameters assessed are largely unknown. New knowledge in these areas is critical because identifying key lifestyle factors that modify brain and cognition in old age will inform the focus of prevention strategies.
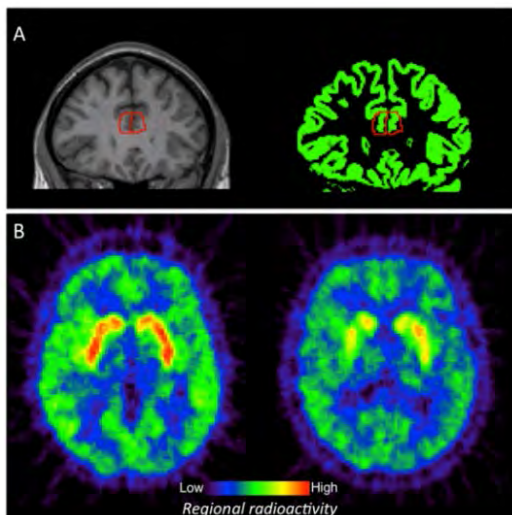

Figure 15. Dopamine D1 binding in the striatum in young (left) and old (right) adults, indicating receptor losses in aging (ref. #102).
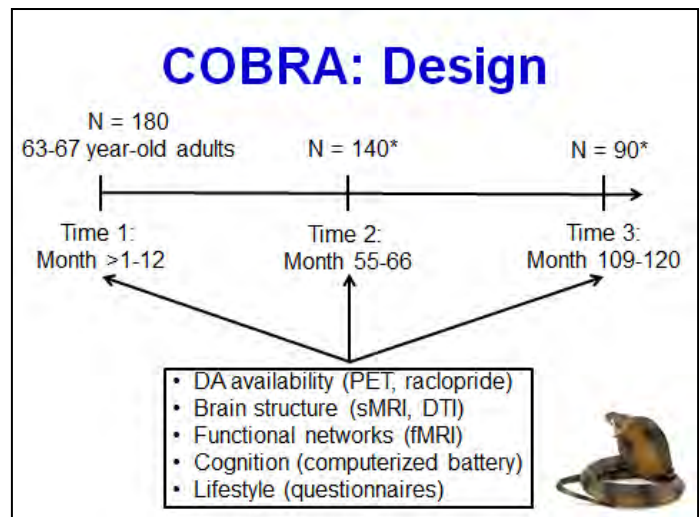

Figure 16. A schematic representation of the design of the COBRA project.

Other achievements

- All FAS centers were evaluated in 2011; ARC received a grade of excellent, and the evaluators recommended a funding increase.
- In an external review of all research conducted at KI in 2010, ARC was evaluated in two different research areas: Epidemiology/Public Health and Neuroscience. ARC received an "outstanding" in both fields and was described as "one of the worldwide leading groups in dementia research."
- In the KI review process, Miia Kivipelto's group was evaluated separately from ARC because of her double affiliation: ARC and the KI Alzheimer Disease Research Center (KI-ADRC). Her group was rated "excellent" in both Epidemiology/Public Health and Neuroscience research areas.
- Three ARC researchers became professors: Miia Kivipelto, professor of clinical geriatric epidemiology; Johan Fastbom, professor of geriatric pharmacology; and Marti Parker, professor of geriatric epidemiology.
- Other career advancements included the appointment of Kristina Johnell as lecturer and the advancement of Chengxuan Qiu to associate professor.
- The staff grew with the recruitment of younger researchers, including Martin Lövdén and Jonas Persson in the psychology sector.
- Six students completed their PhDs and nine new doctoral students were accepted.
- We held three ARC meetings at which the three sectors summarized their recent research findings.

Figure 17. ARC's new professors. From left to right: Marti Parker, Johan Fastbom, and Miia Kivipelto.

- An open house was held at the House of Aging Research on 6 April 2011. Together with the Stockholm Gerontology Research Center and Swedish Dementia Centre, ARC organizes such an open house every two to three years, inviting the general public, students, politicians, and interest groups to listen to researchers present their findings and demonstrate how data are collected. Approximately 400 visitors attended the 2011 open house.

Open house at the House of Aging Research, April 2011

Figure 18. Open house at the House of Aging Research.

- Chengxuan Qiu organized the 2012 China-Sweden Conference on Health in Aging together with Jining Medical University and Jining First People's Hospital, Shandong, China. The conference was held 23–25 May 2012 in Qufu/Jining, Shandong, China, with the financial support of FAS.

China-Sweden Conference on Health in Aging, May 2012

Picture: Jian Ye

Figure 19. Participants in the China-Sweden Conference on Health in Aging.

- SNAC-K Day in October 2012: all participants in the SNAC-K project were re-invited to a meeting, which is organized every three years by the SNAC-K researchers to report major findings from the project. Four ARC researchers spoke to SNAC-K study participants about findings and ongoing work using SNAC-K data.
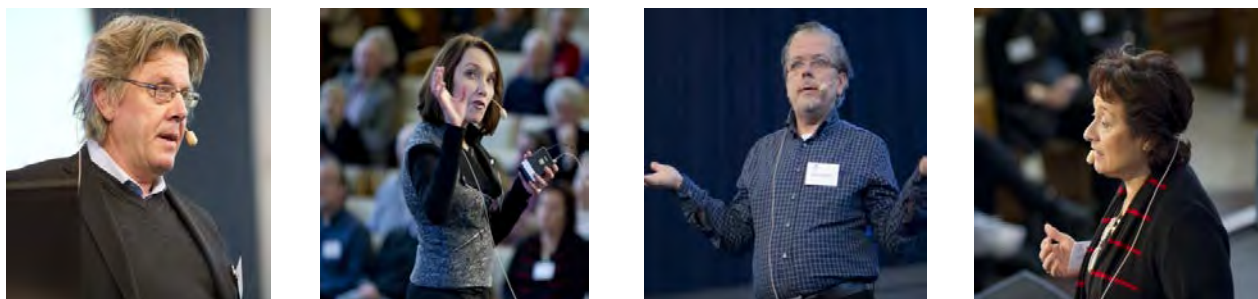
Pictures: Stefan Zimmerman

Figure 20. SNAC-K day 2012. From left to right: Lars Bäckman, Miia Kivipelto, Johan Fastbom, and Laura Fratiglioni.

- Mats Thorslund and Lennarth Johansson organized a symposium at the Nordic Congress of Gerontology on "Policy research and practice in the care of elderly people with complex health problems and severe needs. Experiences in the Nordic countries" in June 2012.
- Miia Kivipelto, Laura Fratiglioni, and Bengt Winblad organized a Key symposium sponsored by the Journal of Internal Medicine and the Royal Swedish Academy of Science: "Updating Alzheimer's disease diagnosis—Implications for prevention and treatment." The two-day long symposium, held in Stockholm in December 2012, was attended by the most prominent researchers in field.

Pictures: Ulf Sirborn (left), Stefan Zimmerman (right)

Figure 21. Key symposium: Updating Alzheimer's disease diagnosis—implications for prevention and treatment.

Clinical and societal impact

CLINICAL IMPACT

1. 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:

   - At the Swedish National Board of Health and Welfare, we have been involved in the development and updating of the national indicators for quality of drug use in elderly people, published first in 2004 and updated in 2010 by the National Board of Health and Welfare. Similarly, we have recently taken part in the development of national guidelines for drug utilization reviews.

   - Using the computer program that 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 and other indicator-based measurements.

   - 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* for pharmacological experts providing support at a distance. MiniQ is now implemented in more than 650 health care units in 16 counties.

2. We have been able to reinforce the relevance of the clinical diagnosis of "mixed dementia" through research findings that show the prominent role of vascular factors and vascular lesions in the development of dementia.

3. We have indicated clear preventive strategies against cognitive decline that are now being tested using randomized controlled trials.

SOCIETAL IMPACT

ARC's impact in society is both direct and indirect.

1. **Indirect impact** is essentially based on our growing presence in the debates at different levels and in different forums in society. Positive indicators of our increased presence in society are:

   - During 2011 and 2012, 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. Indeed, there has been an increasing interest in questions surrounding aging and eldercare, and in both the media and the public debate, there has been an increasing demand for expertise on eldercare. This contrasts with earlier debates that were grounded in political ideology and/or wishful thinking as regards developments in the health status of elderly people.

   - On several occasions, ARC researchers have tried to give an objective and where possible evidence-based view of developments in eldercare as a complement to the statements

made by social care service providers and the responsible politicians. This was especially true in connection with the media reporting in recent years that highlighted startling abuses found within eldercare in Sweden.

- We have noticed an increase in the demand for teaching and participating in conferences, including outside academia. As well as speaking to local and county councils and pensioners' organizations, we have also given lectures to various political parties at national and local levels, to the parliamentary social committee, to associations of disabled persons, and at seminars organized by trade unions and the National Board of Health and Welfare at Almedalen (an important week-long Swedish political forum).

2. **Direct impact** is based on the implementation of scientific methods when planning care for elderly people, for example:

- *Care of persons affected by dementia.* The debate on the question of how many staff members are required within Swedish dementia care has, in our opinion, been largely based on results from our research.

- *Free choice of different care alternatives.* Our research has also shown that elderly people with such complex needs for care that they fulfill the criteria for being granted a place in an institution have, in practical terms, great difficulty deciding for themselves between the available care alternatives.

- *Care of persons with multiple health problems/multimorbidity.* Our longstanding research in this area and participation in several projects initiated by the government concerning elderly people with complex health problems and severe needs have probably resulted in a continued and increased awareness of how the different parts of the care system should work together to provide integrated care. This has also resulted in several national initiatives in which ARC and others have been commissioned by the government to evaluate 19 local trial projects. These projects, running for several years, received national funds to provide integrated care for elderly people with complex health problems.

Guest researchers

From	Researcher	Topic
Sector Medicine		
Unit of Geriatric Medicine, University of Florence, Italy, Aug–Oct 2011	Enrico Mossello, MD	Personality and lifestyle in old age
Specialist in Neurology, University Hospital, Florence, Italy, Sept–Dec 2012	Camilla Ferrari, MD	Studying APOE in non-demented subjects
University of South Florida, United States, April 2011	Elizabeth Hahn, PhD student	Change in sleep pattern and AD
Maastricht University, The Netherlands, May–June 2012	Ron Handels, PhD student	Natural history of AD
CNR Aging Section, Institute of Neuroscience, Padua, Italy, Sept 2011–Feb 2012	Anna Marseglia, psychologist	Diabetes and cognitive functioning
University of Western Ontario, Canada Feb 2010, April 2011, Feb 2012	Shahram Oveisgharan, MD	Blood pressure changes from midlife to late-life
University of Brescia, Italy, Sept 2012–March 2013	Caterina Pirali, MD, resident in geriatrics	Age-related changes, biological tests in SNAC-K
Sector Psychology		
University of Texas, Dallas, United States, Summer 2011	Bart Rypma, assoc prof	Neural bases of working memory in aging
Max Planck Institute, Center for Lifespan Psychology, Germany, Nov 2012	Elisabeth Wenger, PhD student	Differences in adult structural brain plasticity
Department of Psychology, Stockholm University, Dec 2012–Oct 2013	Åke Wahlin, professor	Biological age
Sector Social Gerontology		
School of Aging Studies, University of Southern Florida, United States, June 2011	Ross Andel, assoc prof	Work situation and late-life cognition
State University of New York at Albany, United States, Jan–June 2011, May 2012	Benjamin Shaw, assoc prof	Health behaviors and lifestyle
Davis School of Gerontology University of Southern California, United States, May–June 2011, May-June 2012	Merril Silverstein, prof, editor of J Gerontology: Soc-Sci	Family sociology and sense of coherence
University of Southern California, United States, May 2011	Margaret Gatz, prof	Midlife predictors of late-life cognition

Collaboration

In-house collaboration

Organization	Contact person	Topic	ARC researcher
Stockholm Gerontology Research Center	Mårten Lagergren, assoc prof	SNAC-K project, information, health trends	L Fratiglioni et al.
	Sven Erik Wånell, director	Care of elderly people	M Thorslund
		Public health issues	L Fratiglioni
Äldre i Centrum magazine	Inger Raune, editor-in-chief and publisher	Dissemination of research findings	All
Swedish Dementia Centre	Wilhelmina Hoffman, MD, director	Implementation of research findings	L Fratiglioni et al.

Collaboration with KI and Karolinska University Hospital

Organization	Contact person	Topic	ARC researcher
Department of Clinical Neuroscience	K Orth-Gomér, prof emerita	Vital exhaustion & CV disease progression	H-X Wang
	Marianne Kristiansson, adjunct prof	Personality traits and risk behavior	H-X Wang
Department of Dental Medicine, KI	Inger Wårdh, DDS, PhD; Mats Trulsson, DDS, PhD	Dental health and cognitive impairment	M Parker
Department of Med Epidemiol & Biostatistics	Nancy Pedersen, prof	HARMONY Project: dementia in twins	L Fratiglioni W Xu B Caracciolo
Department of Medical Physics	Tie-Qiang Li, MD, assoc prof	Magnetic resonance imaging	L Bäckman M Lövdén
Department of NVS	Anders Wimo, adjunct prof	SNAC project: health economics	L Fratiglioni M Kivipelto K Johnell
	Caroline Graff, PhD, prof	Genetic studies	L Bäckman L Fratiglioni
Department of Public Health Sciences	Kozma Ahacic, PhD	Alcohol-related care	I Kåreholt
Division of Clinical Geriatrics, NVS	Lars-Olof Wahlund, prof	SNAC-K MRI project	L Bäckman L Fratiglioni
	Niels Andreasen, prof	Memory clinic studies	M Kivipelto
Institute of Environmental Medicine	Anders Ahlbom, prof; Karin Modig, PhD	Time trends in morbidity	L Fratiglioni
	Göran Pershagen, prof; Tom Bellander, prof	CEANS: Air pollution & health of the elderly	L Fratiglioni

Collaboration with Stockholm University

Organization	Contact person	Topic	ARC researcher
Centre for Health Equity Studies	Ilona Koupil, prof	Early cognitive ability and later risk of dementia	H-X Wang
	Johan Fritzell, prof	Intergenerational solidarity and exchange	C Lennartsson
	Olle Lundberg, prof	SWEOLD	M Thorslund
Department of Psychology	Åke Wahlin, prof	Health and cognition	L Bäckman
	Håkan Fischer, prof	Functional neuroimaging and cognitive aging	L Bäckman G Kalpouzos
		Personality traits and risk behavior	H-X Wang
	Lars-Göran Nilsson, Olof Eneroth prof	Cognition in healthy aging within the Betula project	L Bäckman M Lövdén
	Maria Larsson, prof	Olfactory functions— SNAC-K	L Bäckman
Department of Social Work	Marta Szebehely, prof	Transformations of care: consequences of changing public policies	C Lennartsson
	Sven Trygged, PhD	Social consequences of stroke	I Kåreholt
Department of Sociology	Elisabeth Thomson, prof	Swedish generation & gender survey	C Lennartsson
Stress Research Institute	Martin Hyde, researcher and deputy division manager	Comparison of living conditions of older people in England and Sweden	C Lennartsson L Dahlberg
Swedish Institute for Social Research (SOFI)	Michael Gähler, assoc prof	Swedish level-of-living survey	C Lennartsson

Collaboration in Sweden

Organization	Contact person	Topic	ARC researcher
Dalarna University	Kevin McKee, prof	Living conditions of older people in the United Kingdom and Sweden	C Lennartsson
	Lena Dahlberg, lecturer	Formal and informal care	C Lennartsson
Jönköping University Institute of Gerontology	Marie Ernsth Bravell, sr lecturer	Patterns of care and support in old age	I Kåreholt
Karlstad University, Dept of Health Sciences	Duangjai Lexomboon, DDS, PhD, lecturer	Dental health and cognitive impairment	M Parker
Lund University, Dept of Health Sciences	Sölve Elmståhl, prof	SNAC project	C Qiu et al.
Mälardalen University, Västerås	Lene Martin, prof	Nurses' role in drug monitoring among older people	J Fastbom
Municipality of Jönköping	Dan Lundgren	Leadership styles & care of old persons	I Kåreholt
Nestor Research and Development Center, Stockholm	Britt Almberg, PhD, director	Computerized Internet-based model for drug use	J Fastbom
Swedish Bain Power Network	Bengt Winblad, prof	Neurodegeneration	L Bäckman L Fratiglioni
The Swedish Institute of Assistive Technology	Raymond Dahlberg, PhD	Aging research network	M Parker
Department of Psychology, Umeå University	Anna Stigsdotter-Neely, assoc prof	Beneficial effects of cognitive training	L Bäckman
Dept of Medical Neuroscience, Umeå University	Lars Nyberg, prof	COBRA project	L Bäckman M Lövdén
Umeå Center for Functional Brain Imaging	Katrine Åhlström Riklund, prof	COBRA project	L Bäckman M Lövdén
Sahlgrenska Academy, Gothenburg University	Ingmar Skoog, prof; Deborah Gustafson, prof	Swedish Brain Power: risk factors for dementia	C Qiu H-X Wang
	S Wallerstedt, assoc prof	Multi-dose drug dispensing	J Fastbom
Dept of Psychology, Gothenburg University	Boo Johansson, prof; Valgeir Thorvaldsson, PhD	Early detection of dementia—Swedish Brain Power	L Bäckman E J. Laukka
Dept of Public Health, Uppsala University	Tommy Cederholm	Diet and health in the elderly within SNAC-K	L Fratiglioni, W Xu, B Shakersain

Collaboration in Europe

Organization	Contact person	Topic	ARC researcher
European Brain Council	Anders Gustavsson, i3 Innovus Stockholm	Cost of disorders of the brain in Europe 2010	W Xu L Fratiglioni
Finland			
National Institute for Health and Welfare, Helsinki	Jaakko Tuomilehto, MD, PhD, prof	FINRISK study on risk factors for Parkinson's, Nordic Brain Network	M Kivipelto A Solomon C Qiu
	Tiia Ngandu, MD, PhD	FINGER study design and progress	M Kivipelto A Solomon F Mangialasche
Dept of Neurology, University Eastern Finland	Hilkka Soininen, Prof; Minna Rusanen, MD	CAIDE project	M Kivipelto A Solomon
University of Helsinki and Eastern Finland	R Sulkava, Prof; Liisa Myllykangas, MD, PhD; Maarit Tanskanen, MD, PhD	The Vantaa 85+ study	M Kivipelto A Solomon
Kuopio Research Centre of Geriatric Care	Sirpa Hartikainen, Prof	Drug use in AD	M Kivipelto
Åbo Akademi University, University of Turku	Matti Laine, Prof; Juha Rinne, Prof	Dopamine release and working-memory training	L Bäckman
University of Tampere	Marja Jylhä, Prof, School of Health Sciences and the Gerontology Research Center (GEREC) (University of Tampere)	Health among the oldest old	C Lennartsson
France			
INSERM, Paris	Jean-Marie Robine, director, National Institute of Health and Medical Research	5-COOP study of centenarians in five countries	M Parker
Germany			
Max Planck Institute for Human Development, Berlin	Ulman Lindenberger, director; Shu-Chen Li, research scientist; Simone Kühn, sr researcher; Yee Lee Shing and Markus Werkle-Bergner, researchers; Douglas Garrett, postdoc	Genetics & cognitive aging, functional brain activation, neural basis for cognitive plasticity	L Bäckman M Lövdén
German Institute for Intern Educ Research, Frankfurt	Florian Schmiedek, prof	Statistical modeling of longitudinal data, cognitive plasticity, intelligence	M Lövdén L Bäckman

Collaboration in Europe (cont'd.)

Organization	Contact person	Topic	ARC researcher
Neurocognition of Decision Making Research Group, Free University Berlin	Hauke Heekeren, prof; Irene Nagel, researcher; Claudia Preuschhof, postdoc	Genetics & cognitive aging, functional brain activation	L Bäckman

Iceland

School of Social Sciences, University of Iceland	Sigurveig H Sigurðardóttir, assoc prof	Formal and informal care in Iceland	I Kåreholt

Italy

Dept of Psychiatry, University of Bologna	Diana de Ronchi, prof; Anna Rita Atti, MD, PhD	Psychogeriatric aspects in the elderly	L Fratiglioni
Department of Genetics University of Bologna	Claudio Franceschi, prof, and collaborators from 13 European countries	NUAGE: diet and the prevention of functional decline of the elderly, an EU-supported project	L Fratiglioni W Xu B Caracciolo
Department of Geriatrics, University of Perugia	Patrizia Mecocci, prof	The role of oxidative stress in AD, shared responsibility for a PhD student	L Fratiglioni
Department of Neurology, University of Palermo	Roberto Monastero, assoc prof	Migraine project within SNAC-K	L Fratiglioni
Geriatric Unit, University of Brescia	Alessandra Marengoni, MD, PhD	Chronic diseases & multimorbdity	L Fratiglioni

Slovenia

Department of Neurology, University Medical Centre, Ljubljana	Milica Kramberger, PhD	EEG and cognitive impairment	I Kåreholt

Spain

Dept of Psychiatry, Hospital Universitario de Álava, Vitoria	Ariadna Besga, PhD	Cholesterol and biomarkers for dementia	I Kåreholt
Dept of Neurology, Hospital Clinico San Carlos, Madrid	Sara García-Ptacek, PhD	Subjective cognitive impairment	I Kåreholt

Collaboration outside Europe

Organization	Contact person	Topic	ARC researcher
Australia			
Ageing Research Unit, Australian National University	Prof Karin Anstey, director	Collaboration to validate an evidence-based dementia risk assessment tool	C Qiu
Canada			
Department of Psychology, University of Alberta, Edmonton	Roger A Dixon, prof	Cognitive compensation in aging	L Bäckman
University of Victoria	Stuart WS MacDonald, assoc prof	The transition from normal aging to dementia	L Bäckman, E Jonsson Laukka
China			
Department of Neurology, First Teaching Hospital of Jining Medical College	Zhongrui Yan, chief physician and prof	To develop a project among Chinese communities focusing on aging, atherosclerosis, and health	C Qiu
Institute of Psychology, Chinese Academy of Sciences, Beijing	Juan Li, prof	Cognitive aging	C Qiu
Public Health School of Tianjin Medical University	Xiuying Qi, prof Guowei Huang	Diabetes and obesity Epigenetics and AD	W Xu
Japan			
Nihon Fukushi University	Noriko Kurube	Comparisons of Swedish and Japanese care recipients	M Parker H Long
United States			
Division of Research, Kaiser Permanente, California	Rachel Whitmer, PhD	The Kaiser Permanente Medical Care Program of Northern California on predictors of cognitive decline and dementia	M Kivipelto A Solomon
Laboratory of Epidemiology, Demography, and Biometry, NIA-NIH	Lenore J Launer, prof and chief, neuroepidemiology section	The Age, Gene/Environment Susceptibility (AGES)-Reykjavik Study	C Qiu

Collaboration outside Europe (cont'd.)

Organization	Contact person	Topic	ARC researcher
School of Aging Studies, University of South Florida, Tampa	Ross Andel, assoc prof	Socioeconomic position and later health and cognition	I Kåreholt
		Sleep and dementia	L Fratiglioni H-X Wang
University of Southern California	Brent J Small, prof and director of undergraduate studies	Memory, genes, and aging	L Bäckman
	Margaret Gatz, prof	Risk factors for dementia, activity participation and later cognition	L Fratiglioni M Parker
Syracuse University, New York	Merril Silverstein, prof	Intergenerational solidarity	C Lennartsson
University at Albany, State University of New York	Ben Shaw, assoc prof	Health and health behaviors in a life-course perspective	N Agahi
School of Psychology, Wayne State University, Detroit	Naftali Raz, prof	Measurement and analysis of longitudinal magnetic resonance images	L Bäckman
Department of Psychology, University of Alabama at Birmingham	Michael Crowe, PhD	Personality and cognitive function	H-X Wang
Division of Biostatistics, Indiana University School of Medicine	Sujuan Gao, prof	Leisure activities and cognitive functioning	H-X Wang

Awards

Laura Fratiglioni
Waijlit and Eric Forsgren Prize
to a prominent Alzheimer's
researcher, 2011

Miia Kivipelto
Junior Chamber International Finland:
The Young Outstanding Person 2011
Prize and Junior Chamber International: one of
the top 10 outstanding young
people in the world 2011

Mats Thorslund
Stora Gerontologipriset 2011
(2011 Gerontology Prize from the
Swedish Gerontological Society)

Martin Lövdén

Royal Swedish Academy of Sciences' Lennart
"Aktiestinsen" Israelsson Foundation Individual
and Society Award, 2012

Miia Kivipelto

Number 27 on Expressen's list
of the top 50 women in Sweden, 2011

Johan Fastbom

Rune Lönngren's Prize for his work on
drug use among elderly people from the
Swedish Academy of Pharmaceutical Sciences,
2012

Education

UNDERGRADUATE COURSES

The psychology group at ARC was engaged in two different undergraduate courses as part of the Psychology Program at KI in 2011–2012. ARC had overall responsibility for the course Cognitive Processes and responsibility for a smaller section of another course, Developmental Psychology—Aging.

Cognitive Processes is a ten-week course (15 credits) covering basic cognitive psychology (e.g., memory, language, problem solving, intelligence, and cognitive plasticity) and the neural basis of these processes. The course includes lectures, seminars, and demonstrations related to the different cognitive domains covered. The course also includes a section on statistics. Finally, students perform a small research project in which they analyze their own data and write a report. Sari Karlsson (PhD) headed this course in 2011, and Agneta Herlitz (professor), in 2012. It was the fourth and fifth occasion this course has been given at ARC, and approximately 60 students attended the course each year. The course was appreciated by the students, who on a 5-point scale (1=not good, 5=very good) gave it the grade 4.0 (2011) and 4.1 (2012).

MASTER'S COURSES

Carin Lennartsson and Neda Agahi of the social gerontology group at ARC are 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 higher ages. The course includes lectures

Developmental Psychology—Aging is a two-week course (1.5 credits) that includes lectures on the effects of healthy and pathological aging on a selection of psychological, medical, and social domains. Yvonne Brehmer (PhD) was responsible for this course, which received good overall ratings, 4.0 (2011) and 3.9 (2012) on a 5-point scale.

Since 2011 the social gerontology group at ARC has been responsible for the undergraduate course Society and Health (6 credits), which is also part of the psychology program at KI. This course takes an epidemiological and a sociological perspective, giving the students an opportunity to learn about health inequalities in different contexts. The four-week course is headed by Neda Agahi and Carin Lennartsson and runs in the fall term. The course includes lectures and seminars. Five out of the eight lectures are given by researchers from the social gerontology group. The students reported that they particularly appreciated the population-level perspective provided by the course.

and seminars. The examination consists of a group assignment and an individual open-book home exam. Course evaluations show that the students appreciated the multidisciplinary approach of the course.

Since 2011, ARC has been responsible for Geriatric Epidemiology, a course for the Master Program in Public Health Epidemiology at KI. In 2011, the week-long

course was organized at Norrbacka, Karolinska University Hospital, with 18 participants (Lecturer: Chengxuan Qiu). In 2012, the course was organized at ARC with 20 participants (Responsible: Chengxuan Qiu and Anna-Karin Welmer). The intention of the course is to provide the overall picture of worldwide population aging and the opportunities and challenges it poses, to illustrate the application of common modern epidemiological approaches to aging research, and to teach critical evaluation of the literature. The course includes lectures and interactive discussion with lecturers, group work, and discussion of epidemiological literature. Students were satisfied with the course.

NATIONAL GRADUATE SCHOOL FOR AGING RESEARCH

During 2011, the National Graduate School for Aging Research was run by ARC in collaboration with the Centre for Aging and Supportive Environments (CASE) in Lund, the Department of Sociology at Umeå University, and the Division of Occupational Therapy and the Alzheimer Disease Research Center at KI in Stockholm. In 2012, ARC and CASE both successfully reapplied to FAS for continued funding for 2013 through 2015.

The idea behind the graduate school is to use the partners' respective competencies as the basis of a graduate school for aging research at a national level with substantial multidisciplinary interaction. The goal is to cover the different scientific disciplines related to elderly 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 was led by Laura Fratiglioni and a steering group that included all of ARC's senior researchers and a director of studies.

The Director of Studies, Carin Lennartsson, had operative responsibility for course development and the planning of teaching. Administrative tasks specific to the school were carried out by Hélène von Strauss and Kimberly Kane.

Together with CASE, ARC continued to work toward developing a national platform for graduate studies on aging. This work included the development of the SWEDUCAGING website, www.sweducaging.se, where all higher education institutions that organize postgraduate courses on aging across Sweden will post information on their course offerings. The aim of the website is to assist students in selecting high-quality courses and to provide a tool for supervisors, teachers, and course organizers to facilitate the coordination and development of future educational programs. Led by CASE and ARC, representatives of higher educational institutions met in Lund in 2012 to discuss the work that will take place over the next three years on the national platform. This work includes identifying courses with similar content, identifying overlap in course subject matter, identifying desirable courses missing from current offerings, and collaborating to implement new courses.

Figure 22. PhD students at ARC.

In 2011, Carin Lennartsson presented information about ARC and the activities of the research school at SWEDAGE day, organized by FAS. Information about the graduate school's activities was presented on ARC's homepage, www.ki-su-arc.se and in the school's biannual newsletter. News about upcoming events was also distributed via e-mail to ARC's collaborators and their students.

Admission to all educational activities is free. Graduate school participants from the collaborating universities can apply for financial support to assist with the cost of advanced-level courses at universities other than their own. The total number of graduate students at all partner universities in the school throughout 2011 and 2012 was approximately 100, although the number varied because of ongoing recruitment of new doctoral students and graduation of current students. ARC had a total of 16 doctoral students in 2011 and 17 in 2012. Specific activities of the school during 2011 and 2012 are summarized in the following tables.

Weekly seminars	Organizers	Function
Spring 2011 Eleven seminars	Neda Agahi, Anna Rieckmann, Weili Xu	Seminar coordination group
Fall 2011 Thirteen seminars	Neda Agahi, Anna Rieckmann, Weili Xu	Seminar coordination group
Spring 2012 Eleven seminars	Neda Agahi, Anna Rieckmann, Weili Xu	Seminar coordination group
Fall 2012 Eleven seminars	Beata Ferencz, Pär Schön, Anna-Karin Welmer	Seminar coordination group

Journal Club	Leaders	Affiliation
Spring 2011 Structural equation modeling and SNAC-K (DTI data)	Martin Lövdén and Erika Jonsson Laukka	ARC
Socioeconomic position— what does it really mean?	Magnus Nermo and Erik Bihagen	Swedish Institute for Social Research (SOFI), Stockholm University
Spring 2012 Research and publication ethics—a discussion	Agneta Herlitz	ARC

International Forums	Speaker	Affiliation
Spring 2011 Health behaviors and lifestyles during later life	Benjamin Shaw	University at Albany, New York, United States
Neuroepidemiology of brain aging	Lenore J Launer	National Institute on Aging, NIH, Maryland, United States
Resisting frailty in later life	Kevin McKee	Dalarna University, Sweden
Fall 2011 Risk factors for dementia in a life-course perspective	Rachel Whitmer	Kaiser Permanente Division of Research, San Francisco, United States
Compensatory activity and connectivity in aging brains	Roberto Cabeza	Center for Cognitive Neuroscience, Duke University, United States
Spring 2012 Genes, gender, and longevity	Kaare Christensen	University of Southern Denmark, Odense, Denmark
Considering the oldest old in different contexts	Gunhild O. Hagestad	Agder University College, Kristiansand, Norway

How to modify disease progression in AD through lowering homocysteine	David Smith	Department of Pharmacology, University of Oxford, United Kingdom
Contributions from 25 years of longitudinal studies of older people in the United Kingdom	Carol Brayne	University of Cambridge, United Kingdom
Fall 2012 The plasticity of face recognition processes	James Tanaka	University of Victoria, Canada
Depression, stress, and brain volumes	Mirjam Geerlings	University Medical Center Utrecht, the Netherlands

Doctoral seminars and workshops	Leaders	Affiliations
Spring 2011 and Fall 2012 Statistical Workshop	Matteo Bottai	Head of the Unit of Biostatistics at Institute of Environmental Medicine, KI
Spring 2011 Danish-Swedish PhD Fellows Workshop, Copenhagen, Denmark	Ingelise Andersen, Bitte Modin, Carin Lennartsson	Dept. of Population Health, University of Copenhagen; Centre for Health Equity Studies, Stockholm University; ARC
Fall 2011 Second Statistical Workshop	Matteo Bottai	Head of the Unit of Biostatistics, Institute of Environmental Medicine, KI
Spring 2012 Breakfast meeting: Cover letters, responses to reviewers	Kimberly Kane	ARC
Finnish-Swedish PhD Symposium on Aging Research: Studying the oldest old—challenges and experiences	Carin Lennartsson, Marja Jylhä, Kirsi Lumme-Sandt	ARC; Tampere School of Public Health
Fall 2012 Danish-Swedish PhD Fellows Workshop, Stockholm	Bitte Modin, Ingelise Andersen, Carin Lennartsson	Centre for Health Equity Studies, Stockholm University; Dept of Population Health, Copenhagen University; ARC

Doctoral courses	Leaders	Affiliation
2011 Health and health behavior in a life course perspective (3 credits)	ARC's Social Gerontology Sector, Benjamin Shaw	ARC; State University of New York at Albany, United States
Sixth international course of Neuroepidemiology: methods and clinical applications, organized by in Erice, Italy (1.5 credits)	Giovanni Savettieri, Walter Rocca	University of Palermo, Italy; Mayo Clinic, United States; and ARC
Analysis of data from longitudinal designs (7.5 credits)	Boo Johansson, Valgeir Thorvaldsson	Department of Psychology, Gothenburg University and ARC
Summer school of modern methods in biostatistics and epidemiology, Treviso, Italy (3–9 credits)	Marcello Pagano, Rino Bellocco, Marco Bonetti, Debora Rizzuto	Harvard School of Public Health, United States; Department of Medical Epidemiology and Biostatistics, KI; Bocconi University, Italy; and ARC
2012 Application of epidemiological methods in aging research (1.5 credits)	Laura Fratiglioni, Anna-Karin Welmer, Weili Xu	ARC
Summer school of modern methods in biostatistics and epidemiology, Treviso, Italy (3–6 credits)	Marcello Pagano, Rino Bellocco, Marco Bonetti, Debora Rizzuto	Harvard School of Public Health, United States; Department of Medical Epidemiology and Biostatistics, KI; Bocconi University, Italy; and ARC

Commitments

LAURA FRATIGLIONI

- Member, International Oversight Committee for the Canadian Longitudinal Study on Aging
- Member, Scientific Advisory Board, Joint Program for Neurodegenerative Disease in the EU
- Member, Advisory Committee of the Alzheimer's Association International Society to Advance Alzheimer Research and Treatment (ISTAART)
- Member, Advisory Boards of two European projects (COURAGE, NeuroEPI)
- Member, Scientific Advisory Board, Swedish National Institute of Public Health
- Expert reviewer, Loo and Hans Osterman Foundation for Medical Research at KI
- Expert member, Söderström-Königska Sjukhemmet at The Swedish Society of Medicine
- Board Member, Strategic Research Program in Epidemiology at KI
- Member, Board of Research at KI
- Member, Research Strategic Committee of KI and Karolinska University Hospital
- Chair, Swedish Research Council board for EES/SHARE infrastructure
- Co-organizer, Journal of Internal Medicine Key Symposium: Updating Alzheimer's disease diagnosis–Implications for prevention and treatment

LARS BÄCKMAN

- Chair, Class IX (Social Sciences), Royal Swedish Academy of Sciences
- Chair, Selection Committee for Post-doctoral Applications, Swedish Research Council

MATS THORSLUND

- Member, Scientific Advisory Board, Swedish National Board of Health and Welfare
- Member, Editorial Board, European Journal of Ageing
- Member, Scientific Advisory Board, EU's Joint Program "More Years, Better Lives"

JOHAN FASTBOM

- Member, Regional Drug and Therapeutics Committee in Stockholm

AGNETA HERLITZ

- Deputy Head of Department of NVS, KI
- Expert reviewer, Research Council of Norway
- Expert reviewer, KID funding, KI
- Expert reviewer, Travel and Research Grants, KI
- Expert reviewer, university positions at Stockholm University, Gothenburg University, Umeå University, and Uppsala University
- Member, Royal Swedish Academy of Sciences, National Committee for Psychology

- Chair, National Evaluation of Norwegian Research in Psychology and Psychiatry—the Evaluation of Research in Biology, Medicine, and Health

MARTI PARKER

- Fellow, Gerontological Society of America since 2003, a peer-reviewed distinction
- Member, International Network on Health Expectancy and the Disability Process (REVES), membership by invitation only
- Member, Handicap Institute's Network for Researchers in Aging
- Board member, Swedish National Association for Aging Research (*Riksföreningen för Åldrandeforskning* or RÅF)
- PI for Sweden, 5-Country Oldest Old Project based in Archamps, France, chaired by Jean-Marie Robine, Démographie & Santé and Francois Herrmann, University of Geneva, Switzerland
- Editorial board member, International Journal of Ageing and Later Life

MIIA KIVIPELTO

- Responsible for clinical database GEDOC at the Memory Clinic, Karolinska University Hospital
- Member, steering committees and advisory boards for drug companies concerning AD
- Member, Research and Education Council at Department of NVS, KI
- Member, priority group of National Board of Health and Welfare (*Socialstyrelsen*) concerning preventive measures for chronic disorders
- Member, Regional Ethical Review Board in Stockholm
- Member, Public Health Steering Committee of Alzheimer's Society, England
- Co-organizer, Journal of Internal Medicine Key Symposium: Updating Alzheimer's disease diagnosis–Implications for prevention and treatment

KRISTINA JOHNELL

- Expert reviewer, NHS Research Scotland (NRS), United Kingdom
- Expert reviewer, university position at the University of Gothenburg
- Member, Strategic Research Program in Epidemiology Junior Steering Committee, KI
- Equal Treatment Representative at Department of NVS, KI

MARTIN LÖVDÉN

- Member, Swedish National Committee for Psychological Sciences, appointed by the Royal Swedish Academy of Sciences, 2011–present
- Member, Selection Committee for International Postdoc Grants, section Humanities and Social Sciences of the Swedish Research Council, 2012–present

CARIN LENNARTSSON

- Member, Swedish Gender and Generation Study, 2010–present

Communication/dissemination of research findings

TO THE SCIENTIFIC COMMUNITY

During 2011 and 2012 ARC's research findings were published in a wide range of peer-reviewed journals, including specialist journals in gerontology, medicine, epidemiology, psychology, neuroscience, sociology, and social work. ARC researchers also edited a book; contributed to numerous book chapters in international handbooks, reviews, and textbooks; and wrote several reports for a wide variety of public organizations, including the National Board of Health and Welfare, Stockholm County Council, and the Stockholm Gerontology Research Center.

Both senior and junior ARC researchers presented their findings at numerous national and international conferences, including the Nordic Congress of Gerontology, Cognitive Aging Conference, Alzheimer's Association International Conference (AAIC, previously ICAD), International Society of Research on Emotion, International Congress of Psychology, Gerontological Society of America Scientific Meeting, Annual Meeting for the Organization for Human Brain Mapping (HBM), Annual Meeting of the Society for Neuroscience (SfN) and the International Conference on Evidence-based Policy in Long-Term Care.

As reported in the section "Other achievements," ARC was involved in organizing several symposia. ARC researchers participated in numerous research networks and have an expansive network of collaborators both nationally and internationally (see "Collaboration"). The extensive teaching activities (seminars, international forums, journal club meetings) also can be seen as a part of ARC's communication strategy (see "National Graduate School for Aging Research").

During 2012, ARC's website, http://ki-su-arc.se/, was completely reorganized and redesigned. The new site will be launched in spring of 2013. A new brochure about ARC was begun in 2012; anticipated date of publication is spring 2013.

OUTSIDE THE SCIENTIFIC COMMUNITY

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 and heads of sectors from the Stockholm Gerontology Research Center 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 (http://www.aldrecentrum.se/).

In April 2011, the House of Aging Research held a very successful open house, which was attended by approximately 400 visitors, including members of the general public, students, politicians, and interest groups.

Researchers from ARC presented their findings and demonstrated data collection. An expert panel discussion was held that included researchers from ARC (see "Other achievements" for more details/photographs). Finally, we organized a meeting for all participants in the SNAC-K project (SNAC-K Day, October 2012; see page 36).

Several ARC researchers took part in *Almedalsveckan* in 2011 and 2012; *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 China, Japan, and France. Contacts with the media are summarized below.

ARC in the media

Media	Number of appearances
Newspapers	17 articles in newspapers such as *Dagens Nyheter*, *Svenska Dagbladet*, *Göteborgsposten*, and the *New York Times*.
Magazines	15 articles in magazines such as *Focus*; *Medicinsk Vetenskap*; *SPRF, Medlemstidning för Sveriges Pensionärers Riksförbund*; *Icon*; *Dagens Samhälle*; and *Der Spiegel*.
Television	7 TV appearances on program such as *Aktuellt* and *Nyhetsmorgon*.
Radio	15 interviews on Swedish radio.
Internet	Three research results received a great deal of attention on the Internet: Debora Rizzuto's study on lifestyle, social factors, and survival after age 75; Martin Lövdén's study on the effects of intensive language training on interpreters' brains; and Marti Parker's study on chewing and dementia risk.

Income and costs

Summary of major financial resources and costs in 2011 and 2012 are reported in **Figures 23** and **24**.
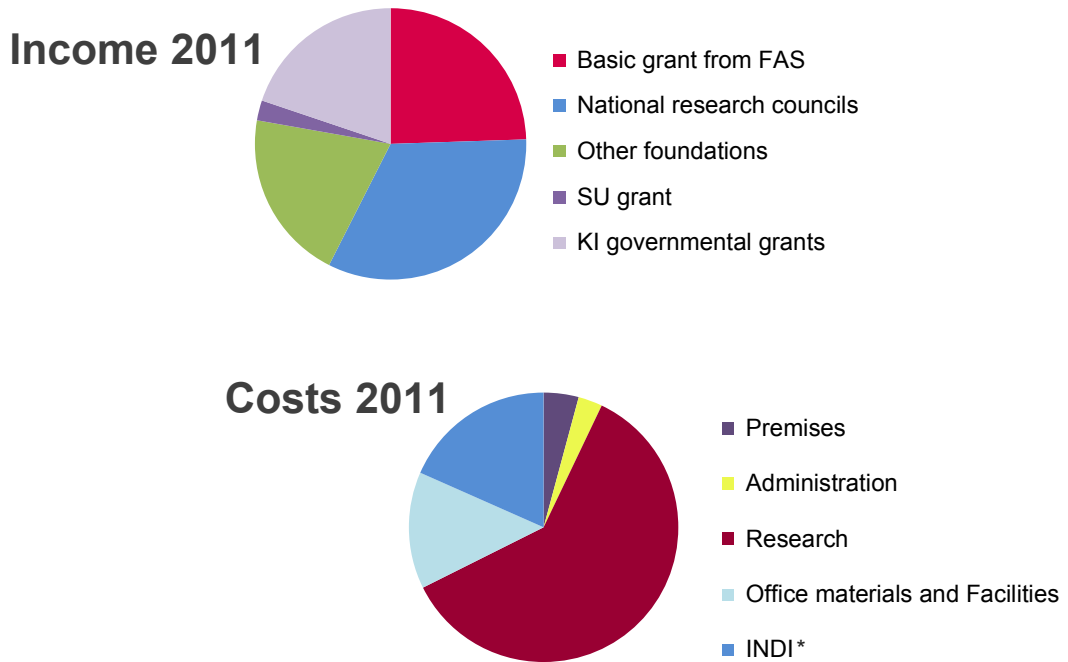
Income 2011

- Basic grant from FAS
- National research councils
- Other foundations
- SU grant
- KI governmental grants

Costs 2011

- Premises
- Administration
- Research
- Office materials and Facilities
- INDI*

Figure 23. Income and costs, 2011.

Income 2012

- Basic grant from FAS
- National research councils
- Other foundations
- SU grant
- KI governmental grants

Costs 2012

- Premises
- Administration
- Research
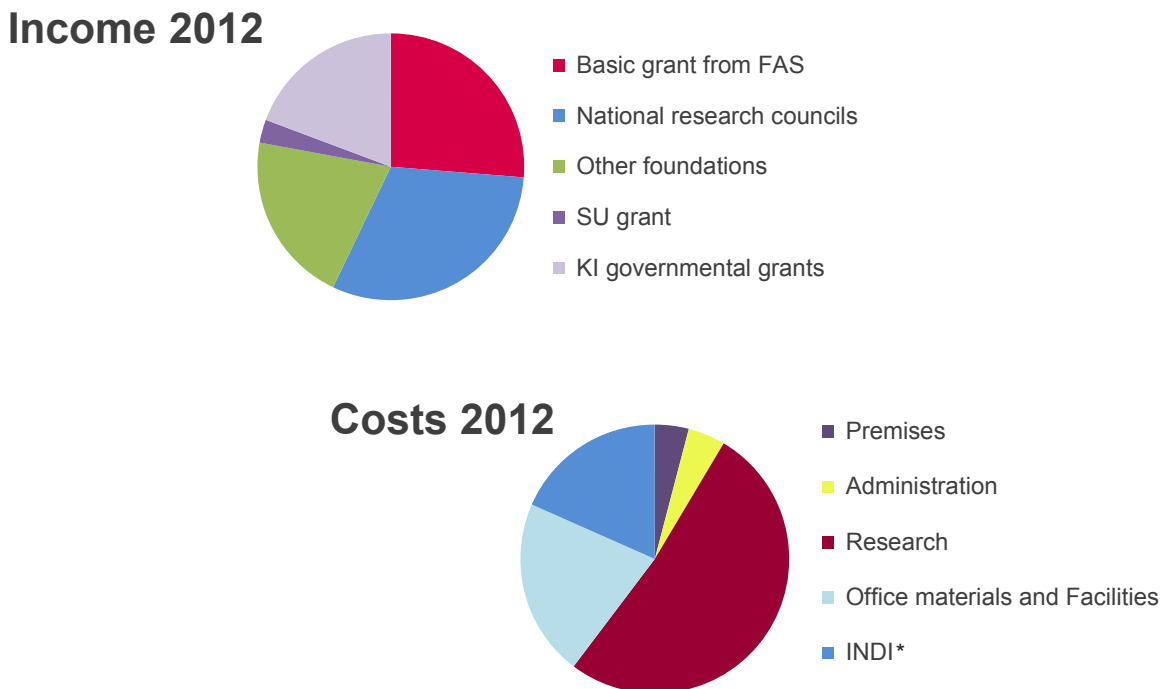- Office materials and Facilities
- INDI*

Figure 24. Income and costs, 2012.

*Indirect costs paid to Karolinska Institutet.

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List of Funders

Major funders (in alphabetical order)

European Union

Jochnick Foundation

Swedish Council for Working Life and Social Research (FAS)

Swedish Research Council for the Humanities (VR)

Swedish Research Council for Large Databases (VR)

Swedish Research Council for Medicine (VR)

The Wallenberg Foundations

The National Board of Health and Welfare (*Socialstyrelsen*)

Other funders (in alphabetical order)

Alzheimer Foundation, Sweden (*Alzheimerfonden*)

Apoteksbolagets forskningsfond

Emil and Wera Cornell Foundation

Dementia Fund (*Demensfonden*)

Sigurd and Elsa Golje Memorial Foundation

KI Foundations

King Gustaf V and Queen Victoria's Foundation

Sweden's Central Bank's Jubilee Fund (*Riksbankens jubileumsfond*)

Gamla tjänarinnor Foundation

Söderström/Königska Foundation

Foundation for Knowledge and Development of Competence (*Stiftelsen för kunskap och kompetensutveckling*)

Ragnhild and Einar Lundström Memorial Foundation

Hierta-Retzius Scholarship Fund

Stockholm County Council/ALF

Gun and Bertil Stohne Foundation

The Swedish Society of Medicine

Future plans

SCIENTIFIC OBJECTIVES

Our major objective is to ensure sustainable growth of research at ARC. We strive to maintain high-quality research in a challenging, multidisciplinary, and creative research environment. Maintaining sustainable growth of high-quality research is essential for attracting talented doctoral students and postdocs, initiating new collaboration in Sweden and abroad, and continuing to attract guest researchers. This effort also represents the source of new energy, ideas, and methods that are indispensable to maintaining an internationally competitive edge. Finally, we place special focus on our younger researchers who are forming their own research groups, as they represent the future of aging research in Sweden.

More specifically, over the next two years our research will focus on six major themes:

1. **Health in aging from a functional and medical perspective.** Good health is a requirement for quality of life and individuals' involvement in society, both of which support system sustainability that is otherwise threatened by the demographic explosion of the aging population. Using data already collected in four cohort studies of middle-aged and elderly people, we will implement four interrelated projects: i) integrating different health dimensions in a single index to better describe health and health trajectories among older adults and to relate health to work capability and societal engagement; ii) quantifying the effects of the major social, environmental, psychological, and biological determinants and their life-long interaction on health and survival in older adults; iii) assessing geographical variation in mental and physical health and health determinants in Sweden; and iv) exploring time trends in mortality and morbidity in the older population.

2. **Inequalities in health and care.** We will analyze diversity and investigate inequalities (e.g., gender-based, socioeconomic) using a wide spectrum of indicators of health and well-being.

Inequalities must be studied over time, as results from 20 years ago may no longer hold true. The demographic and socioeconomic composition of the population changes; for example, more recent cohorts have more education and include more women active in the labor market and more non-manual workers than earlier cohorts. Working conditions and gender roles have also changed. How do these changes influence late-life health? Can these changes explain health trends? Which health indicators best estimate complex care needs? What are the living conditions of very old adults (85+ years)?

3. **Normal brain aging and dementia.** We intend to identify factors that determine why some older individuals remain cognitively healthy well into their 80s, whereas others show decline much earlier. The research will be organized into four main areas: i) individual differences in the rate of cognitive decline in normal aging, ii) postponing dementia onset: risk and protective factors, iii) the mind-body connection, and iv) cognitive interventions. Research in the first three areas will draw empirically on data from

the SNAC-K project, whereas research in the last area will be comprised of various intervention studies. The general focus is on establishing which factors determine the full spectrum of outcomes, from well-preserved cognitive functioning through impairment to dementia.

4. **Preserving cognitive functioning in old age.** The results of pharmaceutical approaches to prevention and treatment of cognitive impairment and dementia have been disappointing. Promoting behavioral factors that protect against age-associated cognitive impairment (e.g., education) may be a more promising route. We intend to: i) utilize the Swedish comprehensive school reform, initiated in 1949 and rolled out across the country over more than 10 years, in a way similar to a quasi-experiment, to test whether education has causal effects on intelligence, late-life disease, dementia, and mortality; ii) investigate whether education in the form of foreign language acquisition affects cognitive performance in old age and whether it can ameliorate the negative effects of retirement on cognition; and iii) identify means to enhance the effects of training on cognitive performance in old age.

5. **Aging-related conditions beyond health.** We seek to expand the frame of our research to include social and economic deprivation that can occur in old age, such as financial strain, inadequate housing, social isolation, and exclusion from civic and social activities. We plan to investigate: i) the emergence and

accumulation of health problems in combination with social and economic deprivation over the life course and ii) the impact of different welfare models by comparing data from Sweden and United Kingdom. This broader perspective will improve our understanding of poor health and other disadvantages in old age, with the ultimate goal of contributing to an evidence base for social policy.

6. **Large interventions.** Three intervention studies are ongoing, and some preliminary analyses will be available over the next two years. The first intervention, FINGER, focuses on whether engagement in social, physical, and cognitive activities along with alterations in nutrition may delay progression from cognitive impairment to clinically verified dementia. The main outcomes are dementia (after extended follow-up), disability, quality of life, and use of health care. The second intervention is a collaborative EU project, Healthy Aging Through Internet Counseling in the Elderly (HATICE, http://www.hatice.eu), aimed at preventing dementia, multimorbidity, and cardiovascular disease. The intervention consists of management of vascular and lifestyle-related risk factors through an easily accessible Internet platform. Finally, New Dietary Strategies Addressing the Specific Needs of the Elderly Population for a Healthy Ageing in Europe (NU-AGE, http://www.nu-age.eu) is a clinical trial to verify the effect of specific dietary intakes on physical and cognitive functions in elderly people. The project involves 15 European sites, including ARC.

EDUCATIONAL OBJECTIVES

Over the next two years, we intend to:

1. Continue our work with the Graduate School in Aging Research, in collaboration with the Centre for Ageing and Supportive Environments, by organizing the same educational activities that were successfully carried out during the first five years of the Graduate School at ARC. The collaboration with the Centre for Ageing and Supportive Environments enables use of our respective competencies and educational activities as a platform for aging research at the national level on a multidisciplinary basis.

2. Enlarge the ARC-related school to include other research groups. Current research fields that have been well-covered at the school from its conception are cognitive aging, social gerontology, geriatric epidemiology, and occupational therapy. Two fields of research, epidemiology and prevention of cardiovascular and neurological disorders, have now been added thanks to the direct participation of the EpiLife Center in Gothenburg and the national Swedish Brain Power network. Neurological and cardiovascular pathologies are the major public health challenges in people over 75 years of age that pose a heavy burden at both the individual and societal level.

3. Reinforce the focus on methodological issues such as design and statistical analysis within the educational program. A new collaboration has already been established with the statistical unit at the Institute of Environmental Medicine, KI, and with international experts recruited by ARC and EpiLife.

4. Expand our international collaboration for educational purposes, especially within the Nordic and European countries.

5. Continue our engagement in various master programs.

ORGANIZATIONAL OBJECTIVES

ARC has grown in recent years, not only in terms of the number of people working at our center (**Figure 25**), but also financially and in terms of productivity (**Figure 26**). This means that we intend to rethink our organization, which is currently based on six senior researchers. Involvement of more junior researchers at all levels of leadership has already begun, with three younger researchers being appointed as members of the Steering Group in 2012. Furthermore, we are planning to organize a junior faculty and to promote more group activities for the PhD students and postdocs. Finally, two professors and three lecturers will be recruited in the near future, as will four to five new PhD students.
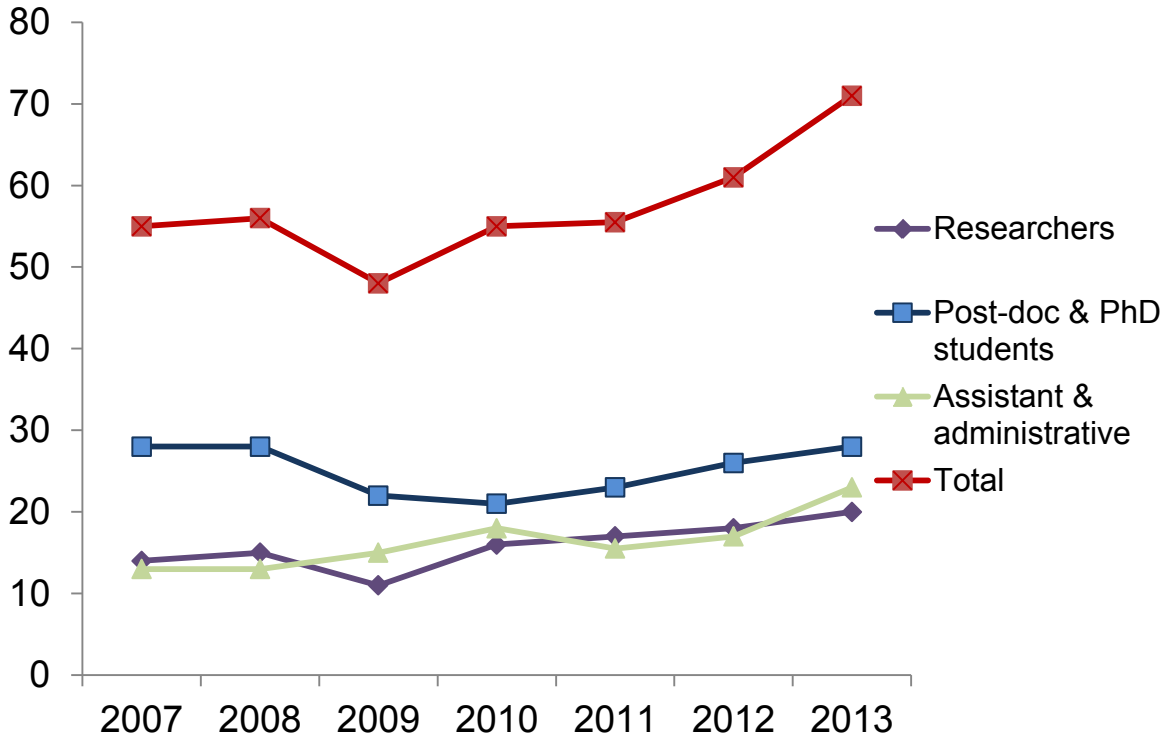
Figure 25. Number of staff at ARC from 2007 through 2012 and expected number in 2013.
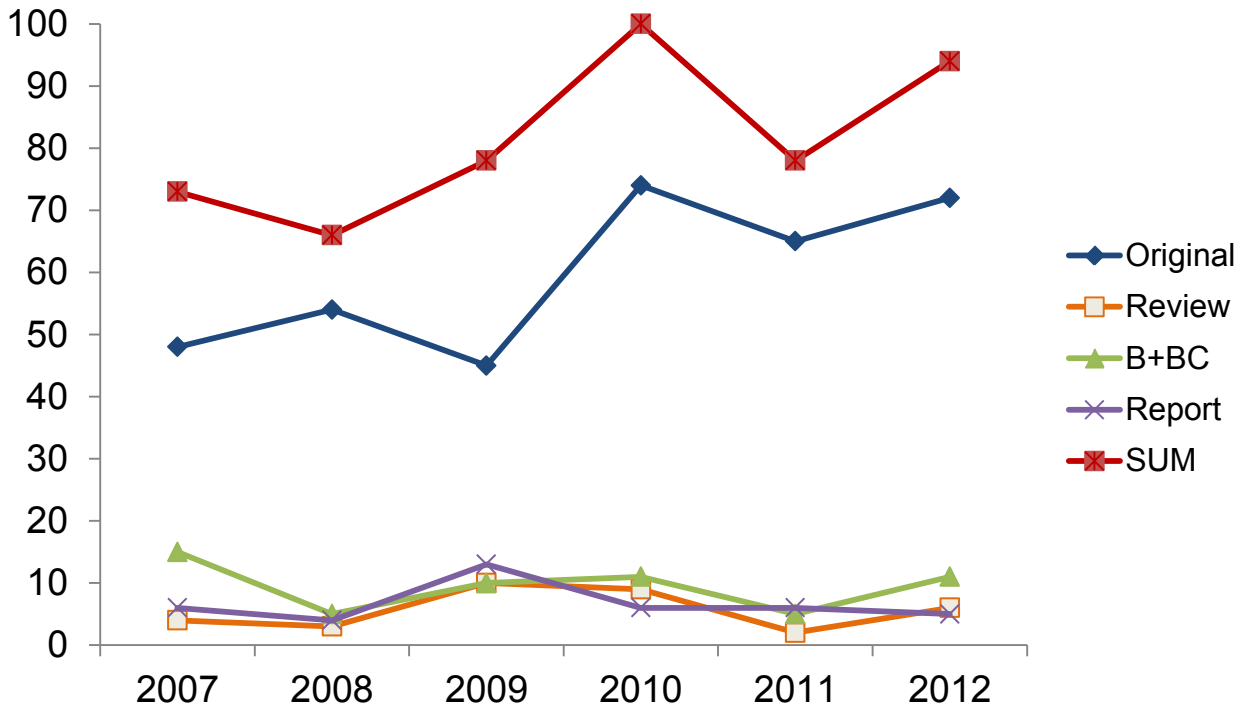

Figure 26. Number of publications at ARC by type and year of publication from 2007 through 2012 (B=books; BC=book chapters).

APPENDIX: Publications 2011–2012

ORIGINAL ARTICLES

A.   Longevity, morbidity, and functioning

1.   Agahi N, Silverstein M, Parker MG. Late-life and earlier participation in leisure activities: their importance for survival among older persons. Act Adapt Aging 2011; 35(3):210-222.

2.   Almborg AH, Welmer AK. Use of the International Classification of Functioning, Disability and Health (ICF) in social services for elderly in Sweden. Disabil Rehabil 2012; 34(11):959-964.

3.   Khanam MA, Qiu C, Lindeboom W, Streatfield PK, Kabir ZN, Wahlin Å. The metabolic syndrome: prevalence, associated factors, and impact on survival among the elderly in rural Bangladesh. PLoS One 2011; 6(6):e20259.

4.   Khanam MA, Streatfield PK, Kabir Z, Qiu C, Cornelius C, Wahlin Å. Prevalence and patterns of multimorbidity among elderly people in rural Bangladesh: a cross-sectional study. J Health Popul Nutr 2011; 29(4): 406-414.

5.   Kåreholt I. Age and sex differences in the relation between education and physical and cognitive functioning among men and women aged 76 years and older. Int J Behav Med 2012; 19(S1):224.

6.   Marengoni A, Angleman S, Fratiglioni L. Prevalence of disability according to multimorbidity and disease clustering: a population-based study. J Comorbidity 2011; 1:11–18.

7.   Marengoni A, Fratiglioni L. Disease clusters in older adults: rationale and need for investigation. J Am Geriatr Soc (Letter) 2011; 59(12):2395-2396.

8.   Rizzuto D, Orsini N, Qiu C, Wang HX, Fratiglioni L. Lifestyle, social factors, and survival after age 75: population based study. BMJ 2012; 345:e5568.

9.   Rydwik E, Welmer AK, Kåreholt I, Angleman S, Fratiglioni L, Wang HX. Adherence to physical exercise recommendations in people over 65 – The SNAC-Kungsholmen study. Eur J Public Health [In press: online] 2012. Available from: doi: 10.1093/eurpub/cks150.

10.   Shaw BA, Agahi N, Krause N. Are changes in financial strain associated with changes in alcohol use and smoking among older adults? J Stud Alcohol Drugs 2011; 72(6):917-925.

11.   Shaw BA, Agahi N. A prospective cohort study of health behavior profiles after age 50 and mortality risk. BMC Public Health 2012; 12:803.

12.   Sommerfeld DK, Welmer AK, Widén Holmqvist L, von Arbin M. Changes in functioning between days 5 and 10 after stroke in elderly. Phys Occup Ther Geriatr 2011; 29(2):77-89.

13.   Sommerfeld DK, Welmer AK. Pain following stroke - initially and at 3 and 18 months after stroke, and its association with other disabilities. Eur J Neurol 2012; 19(10):1325-1330.

14.   Wang HX, Jin Y, Hendrie HC, Liang C, Yang L, Cheng Y, et al. Late life leisure activities and risk of cognitive decline. J Gerontol A Biol Sci Med Sci 2012; 68(2):205-213.

15.   Wang HX, Xu W, Pei JJ. Leisure activities, cognition and dementia. Biochim Biophys Acta 2012; 1822(3):482-491.

16.   Welmer AK, Kåreholt I, Angleman S, Rydwik E, Fratiglioni L. Can chronic multimorbidity explain the age-related differences in strength, speed and balance in older adults? Aging Clin Exp Res 2012; 24(5):480-489.

17.   Welmer AK, Mörck A, Dahlin-Ivanoff S. Physical activity in people 80 years and older as a means of counteracting disability, balanced in relation to frailty. J Aging Phys Act 2012; 20:317-331.

18.   Yang ZY, Yang Z, Zhu L, Qiu C. Human behaviors determine health: strategic thoughts on the prevention of chronic non-communicable diseases in China. Int J Behav Med 2011; 18(4):295-301.

B.   Treatment and care of elderly persons

19.   Borg M, Johansson B, Lundborg M, Fastbom J. [Model Halland. Structured working method for reviewing elderly's medications]. *Lakartidningen* 2011; 108(11):606-608.

20.   Haasum Y, Fastbom J, Fratiglioni L, Kåreholt I, Johnell K. Pain treatment in elderly persons with and without dementia: a population-based study of institutionalized and home-dwelling elderly. *Drugs Aging* 2011; 28(4):283-293.

21.   Haasum Y, Fastbom J, Fratiglioni L, Johnell K. Undertreatment of osteoporosis in persons with dementia? A population-based study. *Osteoporos Int* 2012; 23(3):1061-1068.

22.   Haasum Y, Fastbom J, Johnell K. Institutionalization as a risk factor for inappropriate drug use in the elderly: a Swedish nationwide register-based study. *Ann Pharmacother* 2012; 46(3):339-346.

23.   Jedenius E, Johnell K, Fastbom J, Strömqvist J, Winblad B, Andreasen N. Dementia management programme in a community setting and the use of psychotropic drugs in the elderly population. *Scand J Prim Health Care* 2011; 29(3):181-186.

24.   Johansson L, Long H, Parker MG. Informal caregiving for elders in Sweden: an analysis of current policy developments. *J Aging Soc Policy* 2011; 23(4):335-353.

25.   Johnell K, Fastbom J. Gender and use of hypnotics or sedatives in old age: a nationwide register-based study. *Int J Clin Pharm* 2011; 33(5):788-793.

26.   Johnell K, Fastbom J. Antiepileptic drug use in community-dwelling and institutionalized elderly: a nationwide study of over 1 300 000 older people. *Eur J Clin Pharmacol* 2011; 67(10):1069-1075.

27.   Johnell K, Fastbom J. Comparison of prescription drug use between community-dwelling and institutionalized elderly: a nationwide study. *Drugs Aging* 2012; 29(9):751-758.

28.   Johnell K, Fischer H. Dopaminergic and serotonergic drug use: a nationwide register-based study of over 1 300 000 older people. *PLoS One* 2011; 6(8):e23750.

29.   Meinow B, Parker MG, Thorslund M. Consumers of eldercare in Sweden: the semblance of choice. *Soc Sci Med* 2011; 73(9):1285-1289.

30.   Sjöberg C, Edward C, Fastbom J, Johnell K, Landahl S, Narbro K, et al. Association between multi-dose drug dispensing and quality of drug treatment - a register-based study. *PLoS One* 2011; 6(10):e26574.

31.   Sköldunger A, Wimo A, Johnell K. Net costs of dementia in Sweden - an incidence based 10 year simulation study. *Int J Geriatr Psychiatry* 2012; 27(11):1112-1117.

32.   Sköldunger A, Johnell K, Winblad B, Wimo A. Mortality and treatment costs have a great impact on the cost-effectiveness of disease modifying drugs in Alzheimer's disease. *Curr Alzheimer Res* 2013; 10(2):207-216.

33.   Sundström G, Herlofson K, Daatland SO, Boll Hansen E, Johansson L, Malmberg B, et al. Diversification of old-age care services for older people: trade-offs between coverage, diversification and targeting in European countries. *J Care Serv Manag* 2011; 5(1):35-42.

34.   Wastesson JW, Parker MG, Fastbom J, Thorslund M, Johnell K. Drug use in centenarians compared to nonagenarians and octogenarians in Sweden: a nationwide register-based study. *Age Ageing* 2012; 41:218-224.

35.   Wastesson JW, Ringbäck Weitoft G, Parker MG, Johnell K. Educational level and use of osteoporosis drugs in elderly men and women: a Swedish nationwide register-based study. *Osteoporos Int* 2013; 24(2):433-442.

36.   Weitoft GR, Ericsson O, Fastbom J. Prescription drugs: Health in Sweden: The National Public Health Report 2012. Chapter 18. *Scand J Public Health* 2012; 40(9 Suppl):293-304.

37.   Wimo A, Sjölund BM, Sköldunger A, Johansson L, Nordberg G, von Strauss E. Incremental patterns in the amount of informal and formal care among non-demented and demented elderly persons: results from a 3-year follow-up population-based study. *Int J Geriatr Psychiatry* 2011; 26(1):56-64.

C.   Health trends and inequality

38.   Ahacic K, Damström K, Kåreholt I. Recurring alcohol-related care between 1998 and 2007 among people treated for an alcohol-related disorder in 1997: a register study in Stockholm County. *BMC Public Health* 2011; 11:574.

39.   Ahacic K, Kennis R, Kåreholt I. Changes in sobriety in the Swedish population over three decades: age, period, or cohort effects? *Addiction* 2012; 107(4):748-755.

40.   Ahacic K, Trygged S, Kåreholt I. Income and education as predictors of stroke mortality after the survival of a first stroke. *StrokeTreat* 2012; 2012:983145.

41.   Fors S, Lennartsson C, Lundberg O. Live long and prosper? Childhood living conditions, marital status, social class in adulthood and mortality during mid-life: a cohort study. *Scand J Public Health* 2011; 39(2):179-186.

42.   Fors S, Modin B, Koupil I, Vågerö D. Socioeconomic inequalities in circulatory and all-cause mortality after retirement - the impact of mid-life income and old age pension: evidence from the Uppsala Birth Cohort Study. *J Epidemiol Community Health* 2011; 66(7):e16.

43.   Fors S, Agahi N, Shaw BA. Paying the price? The impact of smoking and obesity on health inequalities in later life. *Scand J Public Healt* 2013; 41(2):134-141.

44.   Lennartsson C. Need and support: determinants of intra-familial financial transfers in Sweden. *Int J Soc Welf* 2011; 20(1):66-74.

45.   Lovén J, Herlitz A, Rehnman J. Women's own-gender bias in face recognition memory: the role of attention at encoding. *Exp Psychol* 2011; 58(4):333-340.

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47.   Schön P, Parker MG, Kåreholt I, Thorslund M. Gender differences in associations between ADL and other health indicators in 1992 and 2002. *Aging Clin Exp Res* 2011; 23(2):91-98.

48.   Thorslund M, Wastesson J, Agahi N, Lagergren M, Parker MG. The rise and fall of women's advantage: a comparison of national trends in life expectancy at age 65 years. *Eur J Ageing* [In press: online] 2013. Available from: doi: 10.1007/s10433-013-0274-8

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50.   Trygged S, Hedlund E, Kåreholt I. Education and post-stroke separation among couples with mutual children. *J Divorce Remarriage* 2011; 52(6):401–414.

D.   Brain aging

51.   Andel R, Crowe M, Kåreholt I, Wastesson J, Parker MG. Indicators of job strain at midlife and cognitive functioning in advanced old age. *J Gerontol B Psychol Sci Soc Sci* 2011; 66B(3):287-291.

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57. Brose A, Schmiedek F, Lövdén M, Lindenberger U. Normal aging dampens the link between intrusive thoughts and negative affect in reaction to daily stressors. *Psychol Aging* 2011; 26(2):488-502.

58. Brose A, Schmiedek F, Lövdén M, Lindenberger U. Daily variability in working memory is coupled with negative affect: the role of attention and motivation. *Emotion* 2012; 12(3):605-617.

59. Burzynska A, Nagel IE, Preuschhoff C, Li S-C, Lindenberger U, Bäckman L, et al. Microstructure of frontoparietal connections predicts cortical responsivity and working memory performance. *Cereb Cortex* 2011; 21(10):2261-2271.

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61. Bäckman L, Karlsson S, Fischer H, Karlsson P, Brehmer Y, Rieckmann A, MacDonald SW, Farde L, Nyberg, L. Dopamine D_1 receptors and age differences in brain activation during working memory. *Neurobiol Aging* 2011; 32(10):1849-1856.

62. Bäckman L, Nyberg L, Soveri A, Johansson J, Andersson M, Dahlin E, et al. Effects of working-memory training on striatal dopamine release. *Science* 2011; 333(6043):718.

63. Caracciolo B, Bäckman L, Monastero R, Winblad B, Fratiglioni L. The symptom of low mood in the prodromal stage of mild cognitive impairment and dementia: a cohort study of community-dwelling elderly. *J Neurol Neurosurg Psychiatry* 2011; 82(7):788-793.

64. Caracciolo B, Gatz M, Xu W, Pedersen NL, Fratiglioni L. Differential distribution of subjective and objective cognitive impairment in the population: a nation-wide twin-study. *J Alzheimers Dis* 2012; 29(2):393-403.

65. Caracciolo B, Gatz M, Xu W, Marengoni A, Pedersen NL, Fratiglioni L. Relationship of subjective cognitive impairment and cognitive impairment no dementia to chronic disease and multimorbidity in a nation-wide twin study. *J Alzheimers Dis* [In press: online] 2013. Available from: doi 10.3233/JAD-122050

66. Cavallin L, Bronge L, Zhang Y, Oksengård AR, Wahlund LO, Fratiglioni L, et al. Comparison between visual assessment of MTA and hippocampal volumes in an elderly, non-demented population. *Acta Radiol* 2012; 53(5):573-579.

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