# Kivipelto NBN Projects

Prof. Miia Kivipelto has broad national, Nordic, and international collaborations, she is PI and/or co-investigator in several international collaborative projects: (role in projects as Principal Investigator (PI) or Co-investigator marked).

• Nordic Brain Network (NBN): (PI: Miia Kivipelto) Professor Kivipelto and her team have recently established the 'Nordic Brain Network', which has increased the resources available to the field of cognitive impairment, dementia/Alzheimer's disease and aging research and promoted collaboration among Nordic countries, with its members primarily working in Sweden and Finland. NBN is affiliated with two centers of Excellence at KI, Dept of NVS (Aging Research center and Center of Alzheimer Research), and University of Finland and National Institute for Health and Welfare in Helsinki, Finland. Memory clinics from Stockholm (Karolinska University Hospital) and from Kuopio are also involved. The NBN also collaborates with several other universities in Nordic countries and numerous international researchers from various regions in the world. <a href="http://www.nordicbrainnetwork.com/?page\_id=205">http://www.nordicbrainnetwork.com/?page\_id=205</a>.

## **Epidemiological Research**

- Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study (PI: Miia
  Kivipelto, main collaborators: Prof. Hilkka Soininen (Dept. Neurology, Univ. of Kuopio),
  Prof. Jaakko Tuomilehto and Prof. Tiina Laatikainen (National Institute of Health and
  Welfare, Helsinki) and The Aging Research Center (ARC), KI, Stockholm. The CAIDE
  study investigates lifestyle and cardiovascular risk factors for dementia, Alzheimer's
  disease (AD) and structural brain changes using the follow-up period extending up to
  almost 30 years.
- Kungsholmen Project (KP) and SNACK (two large population based studies) (Co-investigator: Miia Kivipelto). Close collaboration with the researchers in charge of the database: Professors Laura Fratiglioni and Bengt Winblad. M. Kivipelto has responsibility for the laboratory database and biomarker for KP. Established collaborations with several PhD and post doc researcher working with these databases and connected to ARC. Close collaboration with research scientist Chengxuan Qiu within FLARE Project (collaborative project between ARC and National Institute for Health and Welfare in Helsinki). http://www.snac-k.se/.
- FINRISK: The Finnish risk factor monitoring system originates from the North Karelia Project (started 1972) (Co-investigator: Miia Kivipelto), collaboration with Professors Erkki Vartiainen, and Veikko Salomaa, FINRISK is one of the first community-based projects in the world for preventing cardiovascular disease. Population surveys are conducted every 5th year, using independent, random and representative samples from several areas in Finland. The database currently includes over 50 000 individuals. It is regularly updated by computerized record linkage to the Hospital Discharge, Causes of Death, and Drug Reimbursement Registers. Work is ongoing to integrate dementia research into FINRISK (i.e. linkage to CAIDE, dementia diagnoses validation in registers), and to study the role of drugs (cardiovascular-related, anti-inflammatory, etc) in dementia prevention. The goal is to utilize in the same way existing databases and linkage possibilities in Sweden.
- Vantaa 85+: (Co-investigator): Miia Kivipelto, collaboration with Prof. Anders Paetau, Prof. Liisa Mykkynkags, Dr. Tuomo Polvikoski, and Maarit Tanskanen). Vantaa 85+ is a population-based study that enrolled residents of the city of Vantaa

aged at least 85 years in 1991. The final cohort included 553 (92%) individuals. Follow-up examinations were conducted in 1994, 1996, 1999 and 2001. Autopsies including neuropathological examinations have been dome for 306 participants and post-mortem brain MRI for 145. Work is currently ongoing to study the relations between diabetes and dementia (both Alzheimer and vascular), and their mechanisms (brain amyloid deposition, tau pathology, infarcts, microinfarcts, cerebral amyloid angiopathy, post-mortem MRI measurements).

- The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), (Miia Kivipelto is co-author and Core Analytic Team member. GBD is led by Professor Christopher Murray, University of Washington, Institute of Health Metrics and Evaluation (IHME) is the largest and most comprehensive effort to date to measure epidemiological levels and trends worldwide.
- Socioeconomic and other risk and protective factors for Dementia: An
  epidemiological study of the population in Oppland County. (Co-investigator:
  Miia Kivipelto). Project led by Professor Kristian Tambs, National Institute of Public
  Health and the GENIDEM group.
- International Network of Public Health and Aging (INOPA) project, 2005ongoing (Co-investigator: Miia Kivipelto), collaboration with Professor Åke Wahlin.
  The goal is to promote cooperation and exchange of knowledge in aging research,
  and to establish coordinated research on age-related diseases, health and health
  behaviors, and cognition across populations.
- EU 7<sup>th</sup> Framework program Innovative Midlife Intervention for Dementia deterrence (In-MINDD) project. (Miia Kivipelto is Scientific Advisory Board Member and coauthor of several output articles). Project led by Dr. Kate Iriving, Dublin City University. The project goal was to creat a multi-factorial model for dementia risk and establish an online knowledge base.
- EU project "Social Innovation in Active and Healthy Ageing" (Co-investigator: Miia Kivipelto) funded by King Baudoin Foundation in Brussels.
- The Stroke Riskometer<sup>™</sup> App: validation of a data collection tool and stroke risk predictor (Co-investigator: Miia Kivipelto, also member and co-author of the Strok Riskometer Writing Group). Collaboration with Professor Valery Feigin, AUT University, New Zealand.

#### Clinical Research

- Clinical database (GEDOC) at the Memory Clinic, Karolinska University Hospital, Huddinge (PI: Miia Kivipelto, collaboration with Professor Lars-Olof Wahlund, Professor Niels Andreasen, Professor Agneta Nordberg, Dr. Vesna Jelic and Dr. Pia Andersen). GEDOC Clinical-based database including patients at the Memory Clinict, Karolinska University Hospital, Huddinge. GEDOC is used for clinical-based studies aiming to identify biomarkers for early diagnosis of AD. Since the 1990s, the Memory Clinic has used the GEDOC electronic database and biobank for clinical dementia. The database includes over 7000 patients and comprehensive longitudinal data for a duration of over 10 years.
- Cortisol and Stress in Alzheimer's Disease (Co-STAR) project (PI: Miia Kivipelto).

This project is a collaboration with Associate Professor Alina Solomon (University of Eastern Finland), Dr. Shireen Sindi (Karolinska Institute) Prof. Lars-Olof Wahlund (Karolinska Institute), Dr. Vesna Jelic, Dr. Pia Andersen and Psychologist Göran Hagman (Karolinska University Hospital). The aim of this project is to investigate stress-related factors, biomarkers and their associations with cognitive and daily life functioning in memory clinic patients. <a href="http://www.nordicbrainnetwork.com/?page\_id=1077">http://www.nordicbrainnetwork.com/?page\_id=1077</a>

- Collaborations with other centers within the Swedish Brain Power. http://swedishbrainpower.se/
- Early detection of dementia: Finding the best combination of cognitive and non-cognitive markers of preclinical dementia. (Co-investigator: Miia Kivipelto), collaboration with Dr. Erika Laukka, Aging Research Center, Karolinska Institute.
- Aging cognitively in-shape: the crossroads of the immune system at the brain barrier. (Co-investigator: Miia Kivipelto). Collaboration with Professor Joana Palha, University of Minho, Portugal, within the collaboration on finding predictors of cognitive decline in well clinically-characterized cohorts of elders.

### **Intervention studies**

- Clinical Trials Unit, Memory Clinic, Karolinska University Hospital (Miia Kivipelto is Head and Coordinator). Collaborations with Professors and clinicians at KI and Karolinska University Hospital: E.g. Professor Lars-Olof Wahlund, Professor Niels Andreasen, Professor Agneta Nordberg, Dr. Vesna Jelic and Dr. Pia Andersen. Phase I-III randomized controlled trials in subjects with prodromal AD or dementia, testing efficacy of potential disease-modifying treatment, including anti-amyloid drugs and nutraceuticals.
- Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) (PI: Miia Kivipelto) is a consortium with seven experienced sub-group leaders in Finland (e.g. Prof. Hilkka Soininen, Prof. Tiina Laatikainen, Prof. Jaakko Tuomilehto, among others) and one in Canada (Prof. Vladimir Hachinski) and several sub-study leaders (e.g. Prof. Juha Rinne for PET analyses and Mikko Hiltunen for genetics). The study is coordinated at National Institute of Health and Welfare and conducted in collaboration with several universities in Finland and Sweden. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (NCT01041989, Clinicaltrials.gov): a multi-center randomized controlled trial (intervention study) carried out in Finland, testing the effect of a 2-year multi-domain intervention in delaying cognitive impairment and disability in elderly at risk. <a href="https://www.thl.fi/fi/web/thlfi-en/research-and-expertwork/projects-and-programmes/finger-research-project.">https://www.thl.fi/fi/web/thlfi-en/research-and-expertwork/projects-and-programmes/finger-research-project.</a> Extended follow-ups and several substudies (e.g. MRI, PET, biomarkers) are currently ongoing.
- EDPI: The European Dementia Prevention Initiative: (PI and Founders: Miia Kivipelto and collaborators: Sandrine Andrieu and Edo Richard). EDPI is an international collaboration within Europe, aiming to improve preventive strategies against dementia. It is an investigator-initiated initiative of several groups involved in ongoing dementia prevention trials in Europe. In addition to three ongoing randomised controlled dementia prevention trials in Europe, EDPI-collaborators recently managed to obtain funding from the European Union under the 7th Framework Program for a new dementia prevention study using an innovative internet-based intervention strategy, called HATICE (Healthy Ageing Through Internet

Counselling in the Elderly). <a href="http://www.edpi.org/">http://www.edpi.org/</a>. Main collaborators: Edo Richard, Amsterdam, Sandrine Andrieu, Toulouse, France.

- MIND-AD project: Multimodal preventive trials for Alzheimer's Disease: towards multinational strategies. (PI: Miia Kivipelto. International collaborators: Prof. Hilkka Soininen (Finland); Prof. Sandrine Andrieu (France); Prof. Tobias Hartmann, (Germany); Dr. Edo Richard (The Netherlands); Prof. Patrizia Mecocci (Italy); Prof. Carol Brayne (UK); Alzheimer Europe; Alzheimer's Disease International (ADI)); National collaborators (Sweden): Prof. Anders Wallin and psychologist Arto Nordlund (Gothenburg University and Sahlgrenska Academy), Prof. Katarina Nägga and Prof. Maria Nilsson (Lund University), Prof. Lars-Olof Wahlund, Nutritionist and researcher Gerd Faxen Irving, Prof. Anders Wimo, Geriatrician and researcher Vesna Jelic, psychologist Göran Hagman (Karolinska University Hospital and Karolinska Institutet). The goal is to identify effective prevention strategies for AD/dementia tailored to different risk groups. The project is based on experiences and data from 5 ongoing European intervention studies on AD/dementia prevention, including FINGER (Finland), MAPT (France), PreDIVA (The Netherlands), LiPiDiDiet (Germany, Finland, The Netherlands, Sweden) and HATICE (Finland, France, The Netherlands, Sweden) studies. www.mind-ad.eu/. MIND-AD sub-project using magnetoencephalography MEG project (PI: Miia Kivipelto), project will carried out in collaboration with Professor Maartin Ingvar and Dr. Daniel Lundqvist athe the NatMEG lab, Clinical Neuroscience Dept, Karolinska Institute within the MIND-AD project.
- LipiDiDiet project, a large collaborative project financed by EU 7<sup>th</sup> framework (2007-2012) (Co-investigator: Miia Kivipelto, attending epidemiological and clinical WPs). The European LipiDiDiet RCT tests a complex nutrient combination (medical food: Souvenaid -Fortasyn Connect) in patients with prodromal AD, implementing the new diagnostic criteria for the first time in a multinational trial (www.lipididiet.eu), including Sweden, Finland, Germany and the Netherlands <a href="http://www.lipididiet.eu/index.php?id=6640#c38947">http://www.lipididiet.eu/index.php?id=6640#c38947</a>.
- HATICE: Healthy Ageing Through Internet Counselling in the Elderly. (PI: Miia Kivipelto and collaborators: Sandrine Andrieu and Edo Richard). HATICE is the first major research project following the launch of the EDPI in 2011. Cardiovascular risk factors including hypertension, diabetes, obesity, smoking and lack of physical exercise are common in the elderly and increase the risk of myocardial infarction, stroke and dementia. The main aims of HATICE are: 1) Develop an innovative, interactive internet intervention platform to optimise treatment of cardiovascular disease in the elderly, 2) Test this new intervention in a randomised controlled trial to investigate whether new cardiovascular disease and cognitive decline can be prevented. <a href="http://www.hatice.eu/">http://www.hatice.eu/</a>
- IMI-EPAD: The European Prevention of Alzheimer's Dementia. (Co-investigator: Miia Kivipelto is National Lead for Scandinavia). EPAD is an initiative launched by The Innovative Medicines Initiative (IMI), which is the largest public-private initiative in Europe. Its main goal is to accelerate the development of better and safer medications. EPAD aims to develop an infrastructure that efficiently enables the undertaking of adaptive, multi-arm Proof of Concept studies for early and accurate decisions on the ongoing development of drug candidates or drug combinations. http://www.imi.europa.eu/content/epad.

- Multimodal strategies to promote a healthy brain in aging: Innovative evidence-based tools (MULTI-MODE) project, funded by EIT-Health, a body of the EU. (PI: Miia Kivipelto). Collaborators: Prof. Lefkos Middleton (Imperial College, UK); Professor Arfan Ikram (Rotterdam University, the Netherlands); Professor Laura Fratiglioni (Karolinska Institute, Sweden), Professor Magnus Boman (Research Institutes of SWEDEN); Professors Josep Maria Haro and Carla Obradors (Parc Sanitari Sant Joan de Déu, Spain), Jean Kramarz (AXA, France). The goal of MULTI-MODE is to produce and commercialise 2 evidence-based, e-health tools to predict dementia risk and prevent cognitive decline and dementia for use by citizens/health care staff. Its dissemination/education will reduce health costs/societal burden.
- "Successful aging after 65: Effects of environmental stimulation on cognitive health and neural plasticity". (Co-investigator: Miia Kivipelto). This is a joint project between the Linnaeus University, Harvard Medical School, KI and Medical University of South Carolina.
- WW-FINGERS:Professor Kivipelto recently launched the launched WW-FINGERS, which is an interdisciplinary network to share experiences, harmonise data, and plan joint international initiatives for dementia/cognitive impairment prevention in various countries / regions. This platform creates a unique opportunity for rapid knowledge dissemination and implementation.
   http://alz.org/wwfingers/overview.asp Main current partners: Wake Forest University (US), Kaiser Permanente, Division of Research, Northern California (US), Shandon University (China), National University of Singapore, UNSW, Sydney (Australia), Imperial College, London (UK).

Main other collaborators: Prof. Ingemar Björkhem, Clinical chemistry Karolinska Univ Hospital, Stockholm (cholesterol metabolism), Prof. Angel Cedazo-Minguez, Karolinska Institutet (experimental studies), Prof. Anders Wimo, NVS, KI (pharmacoeconomy), Associate professor liris Hovatta, University of Helsinki (telomere measurements), Prof. Ingmar Skoog, Gothenburg University (Epidemiology of dementia), Associate prof. Rachel Whitmer, Div of Research, Kaiser Permanente, Oakland, USA (sharing databases, pooled analyses)

## Innovation and collaboration with the private sector:

- Consultant for companies within the private sector (e.g. Swedish Care International, Nestle, Nutricia) about preventive interventions for cognitive impairment/dementia.
- Collaborations with: (1) with Merz (CAIDE dementia risk score app and dissemination) (Ref. Sindi, Kivipelto et al., 2015), (2) Nutricia (LipiDiDiet & MIND-AD project), (3) pharma industry (IMI-EPAD project), (4) Neurotrack (USA) (FINGER intervention education models (E-health)).
- PI EIT-Health MULTI-MODE project, collaboration Research Institutes of SWEDEN (RISE)
   AXA (among others) to develop & commercialize of evidence-based eHealth products to predict dementia risk and prevent cognitive decline for use by citizens/health care staff.
- Co-PI of the EU-supported HATICE project that targets vascular risk factors through internet-based counselling for the elderly (www.hatice.eu).
- Co-investigator Stroke Riskometer App for Stroke prevention. (Ref: Parmar, Kivipelto, et al. 2014).

Awards for social impact: 2011 - Junior Chamber International Award for 10 Outstanding Young Persons of the World; 2009 - Academy of Finland Award for Social Impact Numerous lectures and activities for the general public / larger community, e.g. seminars/theme days — Dissemination of FINGER findings; 1st lecture Sept 2015- South Osthrobotnia Hospital District in collaboration with the Finnish Alzheimer Association & Red

Cross for (500+ participants); Finnish Sibelius Academy (Dementia prevention), Stockholm's city & Stiftelsen Äldrecentrum; Dementia and Alzheimer Associations (Sweden, Finland, Europa); International Brain Awareness week seminar series, Lectures for Diabetes Foundation, Brain foundation, Alzheimer Association, Approx. 10 times/year during 2003-2017.