Promoting brain and cardiovascular health and preventing cognitive impairment in Finland – Lessons from the FINGER study

Miia Kivipelto, MD, PhD
Professor
Karolinska Institutet (KI-ADRC and ARC) and Karolinska University Hospital
Outline

- CVD and diabetes prevention in Finland
- Dementia prevention
  - CAIDE
  - FINGER
- Practical implications
Dementia and AD: importance of life-long exposure to multiple factors

Birth | Childhood-2nd decade | Adult life-Middle age | Transition | Old age

0 | 20 | 60 | 75

Healthy brain | ? | Alzheimer brain

Genetic | Environment

Mangialasche, Kivipelto et al., 2012
The pre-FINGER framework

- Long tradition in risk factor monitoring: The FINRISK Study
- Intervention studies: North Karelia Project, Diabetes Prevention Study, Dose-Responses to Exercise Training
- Integrating multidomain intervention to prevent cognitive impairment into the existing framework
The National FINRISK Study

- Risk factor surveys since 1972
- Every five years in five regions in Finland
- Independent cross-sectional samples, n≈10000
- Same methodology for 40 years
- Age range 25-74 years (30-59 years in 1972 and 1977)
- Participation rates over 90 % in 1970’s, and 65% in 2012

(eg. Vartiainen et al., Int J Epidemiol 2010)
North Karelia Project & FINMONICA study
Midlife surveys (mean age 50.4±6 years)
1972,1977
1982,1987
1st FOLLOW-UP: Random sample
n=2000 (mean age 71.3±4 years)
1998
Participants (n=1449)
Non Participants (n=551)
Cognitively Normal (n=1306)
MCI (n= 82)
Demented (n=61) *
2nd FOLLOW-UP
2005-2007
Participants (n=893)
Not evaluated (n = 57)
Non Participants (n=543)
Cognitively Normal (n=613)
MCI (n=165)
Demented (n=62)
Diagnostic evaluation: 840 subjects
## Modifiable risk factors for dementia and AD

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Protective factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrovascular disorders</td>
<td>High education</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Physical activity</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>Active lifestyle</td>
</tr>
<tr>
<td>Obesity</td>
<td>Moderate alcohol intake</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Antioxidants</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>Fish oils</td>
</tr>
<tr>
<td>Smoking</td>
<td>Coffee</td>
</tr>
<tr>
<td>Depression</td>
<td>Antihypertensives</td>
</tr>
<tr>
<td>Stress</td>
<td>Statins</td>
</tr>
<tr>
<td>Head trauma</td>
<td>NSAIDs?</td>
</tr>
<tr>
<td></td>
<td>Estrogen?</td>
</tr>
<tr>
<td></td>
<td>.......</td>
</tr>
</tbody>
</table>
Midlife risk profile, 20 years prediction

<table>
<thead>
<tr>
<th>CAIDE Dementia Risk Score</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
</tr>
<tr>
<td>&lt; 47</td>
<td>0</td>
</tr>
<tr>
<td>47-53</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 53</td>
<td>4</td>
</tr>
<tr>
<td>Education, years</td>
<td></td>
</tr>
<tr>
<td>≥ 10</td>
<td>0</td>
</tr>
<tr>
<td>7-9</td>
<td>2</td>
</tr>
<tr>
<td>0-6</td>
<td>3</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>0</td>
</tr>
<tr>
<td>Men</td>
<td>1</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td></td>
</tr>
<tr>
<td>≤ 140</td>
<td>0</td>
</tr>
<tr>
<td>&gt; 140</td>
<td>2</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td></td>
</tr>
<tr>
<td>≤ 30</td>
<td>0</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>2</td>
</tr>
<tr>
<td>Cholesterol, mmol/l</td>
<td></td>
</tr>
<tr>
<td>≤ 6.5</td>
<td>0</td>
</tr>
<tr>
<td>&gt; 6.5</td>
<td>2</td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
</tr>
<tr>
<td>Active</td>
<td>0</td>
</tr>
<tr>
<td>Inactive</td>
<td>1</td>
</tr>
</tbody>
</table>

Kivipelto et al., Lancet Neurology 2006
# Midlife risk profile, 20 years prediction

## CAIDE Dementia Risk Score

<table>
<thead>
<tr>
<th>Factor</th>
<th>Category</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>&lt; 47</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>47-53</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>&gt; 53</td>
<td>4</td>
</tr>
<tr>
<td><strong>Education, years</strong></td>
<td>≥ 10</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>7-9</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>0-6</td>
<td>3</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>Women</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Men</td>
<td>1</td>
</tr>
<tr>
<td><strong>Systolic BP, mmHg</strong></td>
<td>≤ 140</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt; 140</td>
<td>2</td>
</tr>
<tr>
<td><strong>BMI, kg/m²</strong></td>
<td>≤ 30</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt; 30</td>
<td>2</td>
</tr>
<tr>
<td><strong>Cholesterol, mmol/l</strong></td>
<td>≤ 6.5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt; 6.5</td>
<td>2</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td>Active</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Inactive</td>
<td>1</td>
</tr>
</tbody>
</table>

Kivipelto et al., Lancet Neurology 2006
Randomized controlled trials for dementia prevention
Reduction in coronary heart disease mortality in Finland - a success story!

The North Karelia Project

Risk factor changes explained 60% reduction in mortality

The Finnish Diabetes Prevention Study (DPS): Diabetes incidence was decreased by 58%

Goals:
- Weight reduction $\geq 5\%$
- Moderate fat $<30$ E%
- Low saturated fat $<10$ E%
- High fibre $\geq 15$g/1000kcal
- Physical activity $\geq 30$ min / day

*Tuomilehto et al. N Engl J Med 2001*
FINGER

- Was initiated within the Academy of Finland Public Health Challenges Program 2009
- Aims to reduce cognitive impairment in an at risk population through a 2-year multi-domain life-style intervention
- Is based on the population of the FINRISK study

Clinicaltrials.gov NCT01041989

Kivipelto et al., Alzheimer & Dementia 2013
Participants:
- N=1260
- Age 60-77y
- Randomized into 2 groups

Time schedule:
- Intervention completed 2014
- Extended 7-year follow-up starts 2015

Clinicaltrials.gov NCT01041989
Kivipelto et al., Alzheimer & Dementia 2013
INCLUSION CRITERIA: persons at risk of dementia/cognitive decline

- Dementia Risk score $\geq 6$
  
  Based on risk factors assessed in earlier population surveys: Age, Education, Sex, SBP, Cholesterol, BMI, Physical Activity (Kivipelto et al., Lancet Neurology 2006)

AND

- Cognitive performance at mean level or slightly lower than expected for age
  (based on CERAD test battery)

Kivipelto et al., Alzheimer & Dementia 2013
INTENSIVE INTERVENTION

NUTRITION:
7 group sessions, 3 individual sessions

EXERCISE:
- 1-2x/wk muscle
- 2-4x/wk aerobic

EXERCISE:
- 2x/wk muscle
- 4-5x/wk aerobic

EXERCISE:
- 2x/wk muscle strength training
- 5-6x/wk aerobic training

COGNITIVE TRAINING:
- 9 group sessions
Independent training

COGNITIVE TRAINING:
- 2 group sessions
Independent training

MONITORING AND MANAGEMENT OF METABOLIC AND VASCULAR RISK FACTORS
Nurse: Visit every 3 months, Physician: 3 additional visits

REGULAR HEALTH ADVICE

Kivipelto et al., Alzheimer & Dementia 2013
FINGER intervention
OUTCOMES

- **Primary:**
  - Cognitive impairment (Neuropsychological Test Battery, Trail Making & Stroop tests)

- **Secondary:**
  - Dementia (after 7 years)
  - Depressive symptoms (Zung scale)
  - Vascular risk factors, morbidity and mortality
  - Disability (questionnaire, ADL + IADL)
  - Quality of life (RAND-36, 15D)
  - Utilization of health resources
  - Blood markers (i.e. inflammation, redox status, lipid and glucose metabolism, telomere length)
  - Brain MRI measures (n=150) and PET (n=60)

*Kivipelto et al., Alzheimer & Dementia 2013*
FINLAND

Oulu cohort T. Strandberg

Kuopio cohort H. Soininen

Seinäjoki cohort J. Tuomilehto

Turku cohort A. Jula

Helsinki cohort M. Kivipelto

Vantaa cohort T. Laatikainen

Safety Committee Monitoring Committee

FINGER Study
PI: M. Kivipelto

Coordination Group/THL:
Heads: T. Laatikainen, J. Lindström
Coordinators: T. Ngandu, S. Ahtiluoto
Field coordinator: J. Lehtisalo
Data manager, Statistician, Administrator

Supervision:
Nutrition: J. Lindström
Exercise: R. Rauramaa, S. Pajala
Cognitive & social activation: T. Hänninen, T. Ngandu
Vascular factors: J. Tuomilehto, T. Strandberg, R. Antikainen

Volunteer organizations Practices in the community
RELEVANCE OF THE FINGER STUDY

- Will test to what extent a multi-domain intervention may delay cognitive impairment and dementia onset in people at increased risk.

- The broad range of secondary outcomes enables estimation of total benefit and mediating pathways.

- Will provide data urgently needed for health education and community planning.
Practical implications in Finland
Finnish recommendations for best practices in the treatment of progressive memory diseases 2008

- **Statement 1:** Risk factors for memory diseases should be recognised and treated. Everyone should participate in the treatment of such risk factors.

- **Statement 2:** Memory symptoms and related warning signs should be recognised. When a memory symptom is detected, further examination should be performed according to the Current Care Guidelines.

- …. (Totally 13 statements)
Finland’s National Memory Programme – Creating a Memory Friendly Finland 2012-2020 (Ministry of Health)

1. Promotion of brain health and prevention
2. Right attitudes for treatment and care of memory disorders
3. Guarantee high quality of life for patients and caregivers with right support, treatment, care and rehabilitation
4. Support research and knowledge
Summary - Some key issues

- Finland has long and successful tradition for CVD and diabetes prevention
- Infrastructure for studying NCD (e.g. FINRISK surveys, base for CAIDE and FINGER)
- Close collaboration between the National Institute for Health and Welfare (THL) and universities
- Multi-disciplinary researcher networks
- Pragmatic implementation programs (e.g. Diabetes Prevention Study → Diabetes Prevention Program)
ACKNOWLEDGEMENTS

Grant support: Academy of Finland, Novo Nordisk Foundation, Alzheimer’s Research and Prevention Foundation, Alzheimer Association, VR, La Carita säätiö, The Social Insurance Institution of Finland and Juho Vainio Foundation

Hilkka Soininen
Tuula Pirttilä †
Rainer Rauramaa
Raimo Sulkava
Merja Hallikainen
Tuomo Hänninen
Teemu Paajanen
Alina Solomon
Anna-Maija Tolppanen
Minna Rusanen
Marjo Eskelinen
Miika Vuorinen

Miia Kivipelto (FINGER PI)
Tiina Laatikainen
Antti Jula
Jaana Lindström
Markku Peltonen
Satu Pajala
Tiia Ngandu
Satu Ahtiluoto
Jenni Lehtisalo
Esko Levälähti
Aulikki Nissinen

Bengt Winblad
Laura Fratiglioni
Lars Bäckman
Ingemar Kåreholt
Francesca Mangialasche
Gabriela Spulber
Babak Hooshmand
Krister Håkansson

Göran Hagman
Ulrika Akenine
Karin Wallin

Sandrine Andrieu
Carol Brayne
Edo Richard
Willem A. van Gool

Turku PET Centre
Juha Rinne
Life matters!