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NATIONAL INSTITUTE FOR HEALTH AND WELFARE

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Lifestyle Intervention to Prevent Cognitive Impairment

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Are there ways to prevent cognitive impairment and dementia/AD?

- **State of the art**

- **Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability**

FINGER

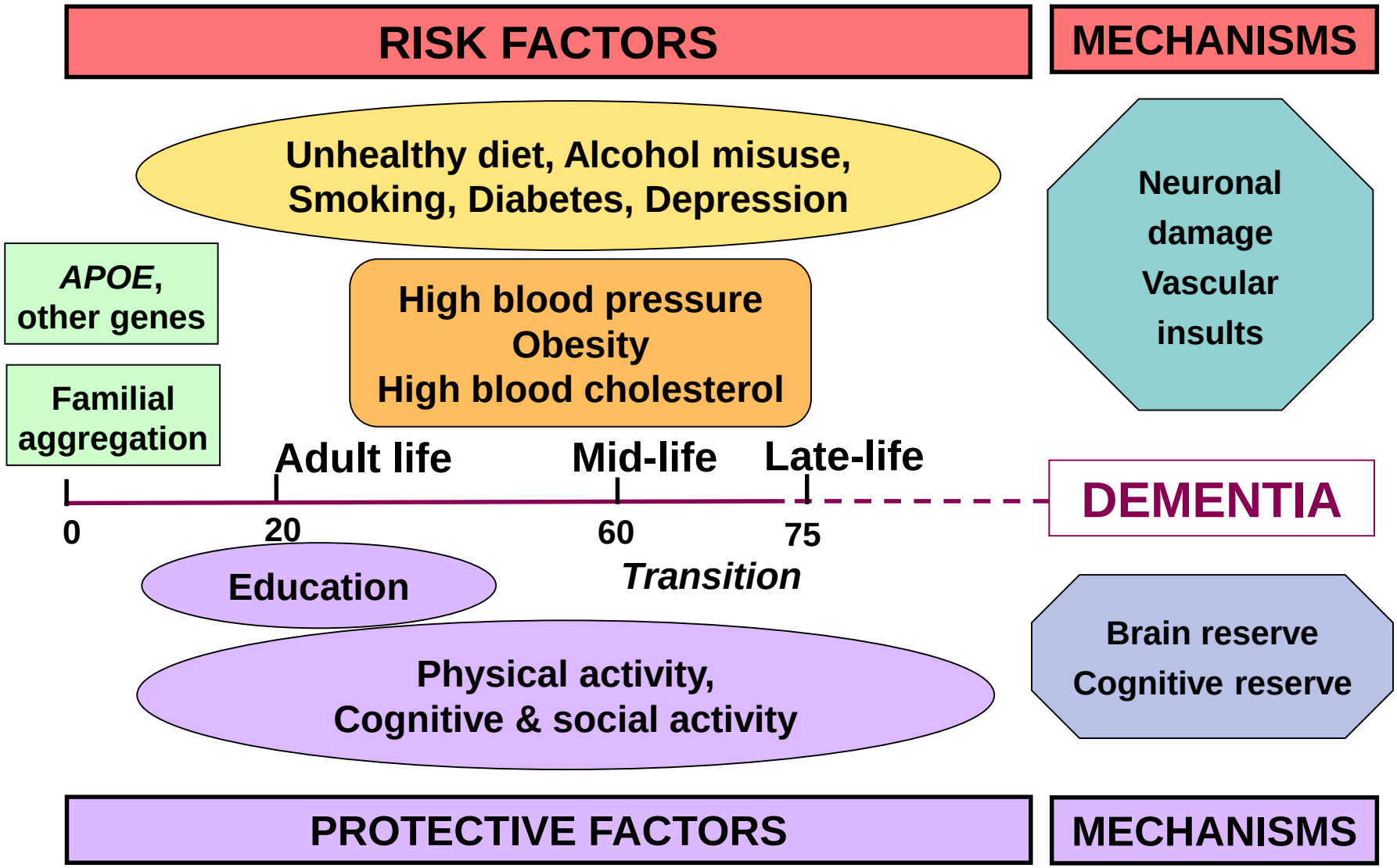
- **Future directions: Multi-domain, multinational studies and pragmatic prevention programs**

EDPI
European Dementia Prevention Initiative

HATICE

MIND-AD

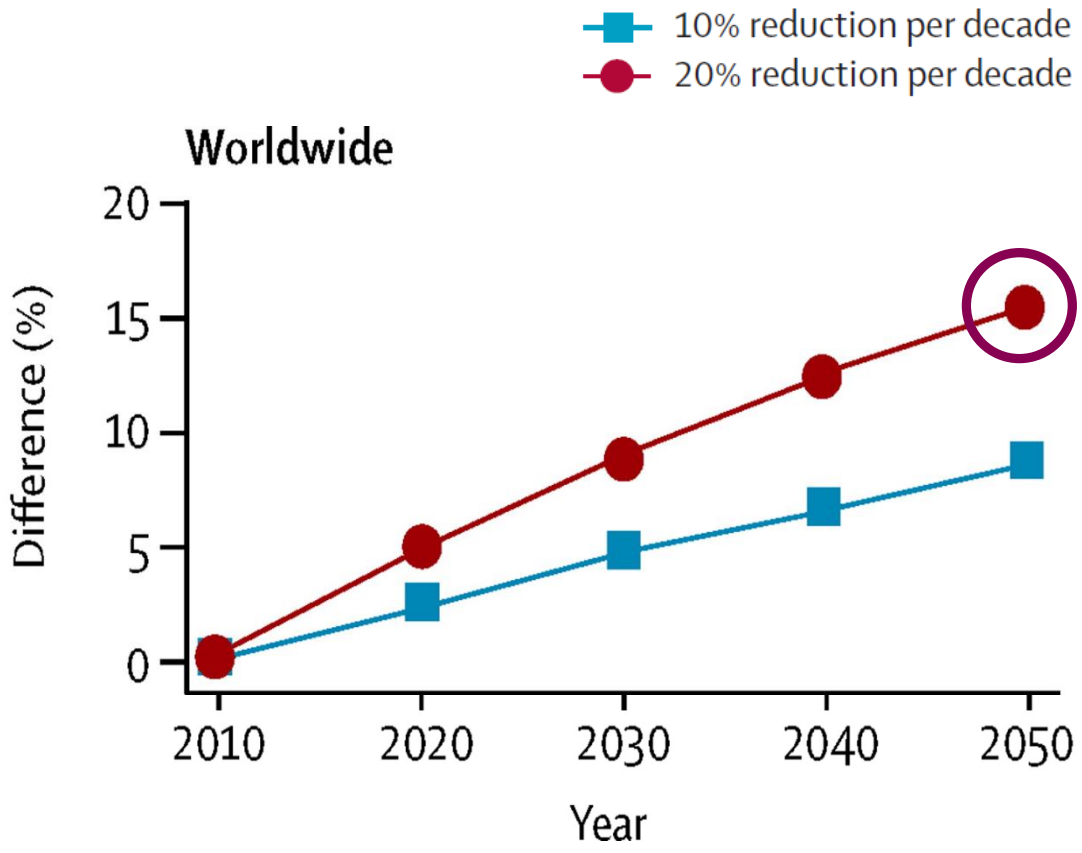
Dementia and Alzheimer disease: importance of life-long exposure to multiple factors



Kivipelto, Mangialasche et al., Oxford Ger Text Medicine 2015, in press

To what extent can Alzheimer dementia be prevented?

Risk factor	PAR
Diabetes mellitus	2.9%
Midlife hypertension	5.1%
Midlife obesity	2.0%
Physical inactivity	12.7%
Depression	7.9%
Smoking	13.9%
Low education	19.1%
Combined PAR*	28.2%



PAR=population-attributable risk.
*Adjusting for non-independence of the risk factors.

Norton et al., Lancet Neurol, 2014; Kivipelto and Mangialasche, Nature Neurol Rev, 2014

Randomize  **led trials**

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Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability

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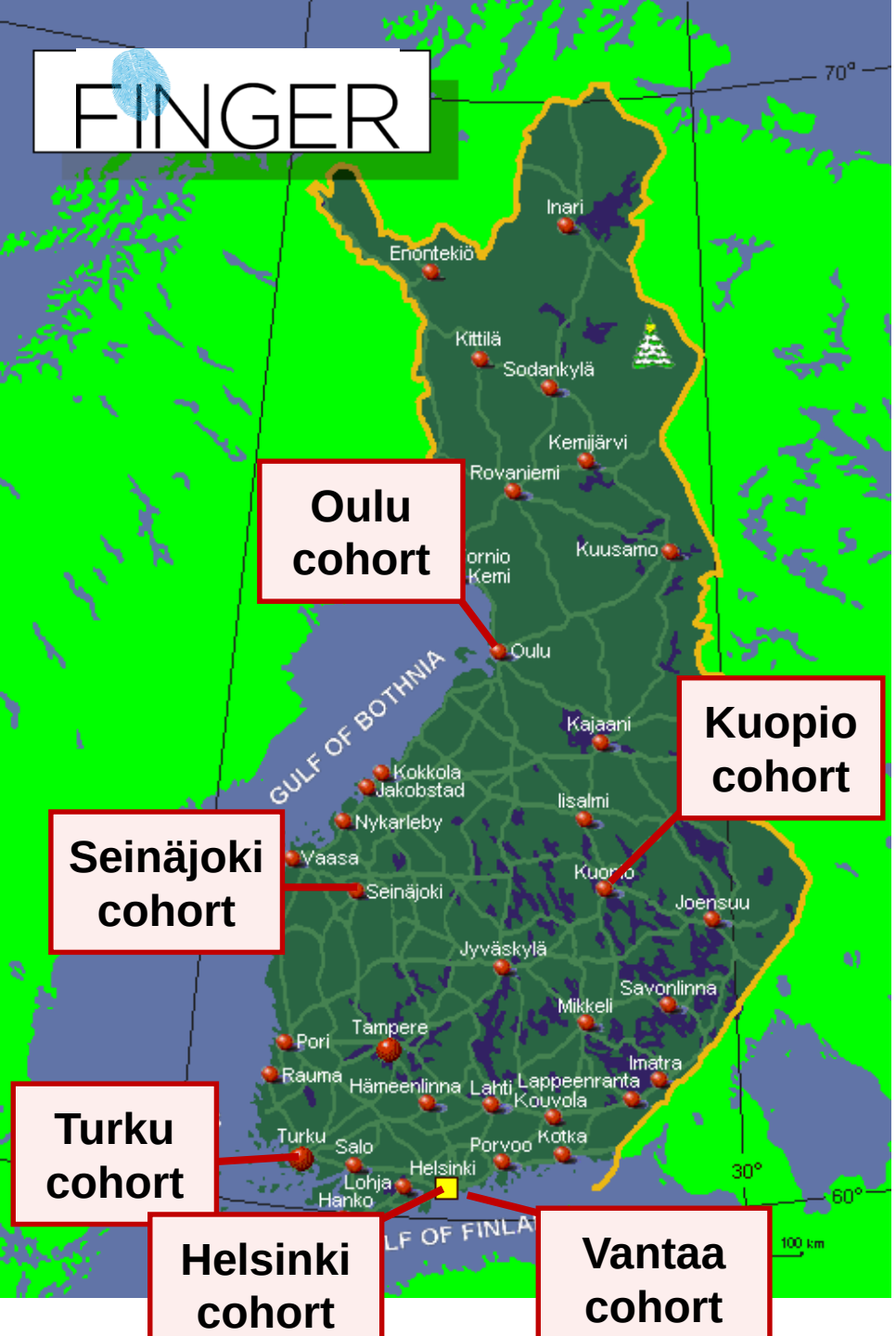
- **Proof-of-concept trial - multidomain approach to cognitive decline prevention**
- **At-risk segment of the general elderly population (not patients)**

- **2-year multi-domain lifestyle intervention:**
  → Nutritional guidance
  → Physical activity
  → Cognitive training and social activities
  → Monitoring of metabolic and vascular risk factors: hypertension, dyslipidemia, obesity, impaired glucose tolerance

Clinicaltrials.gov NCT01041989

Protocol in *Kivipelto, Solomon et al., Alzheimer & Dementia 2013*



Principal Investigator:
Prof. Miia Kivipelto

Participants:

- **Previous national surveys (FINRISK)**
- **N=1260**
- **Age 60-77y**
- **Randomized into 2 groups (1:1)**

Time schedule:

- **Intervention completed February 2014**
- **Extended 5-year follow-up starts April 2015**
- **Extended 7-year follow-up planned**

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INCLUSION CRITERIA: persons at risk of dementia/cognitive decline

- **Dementia Risk score ≥ 6 points**

  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)

Protocol in Kivipelto et al., Alzheimer & Dementia 2013

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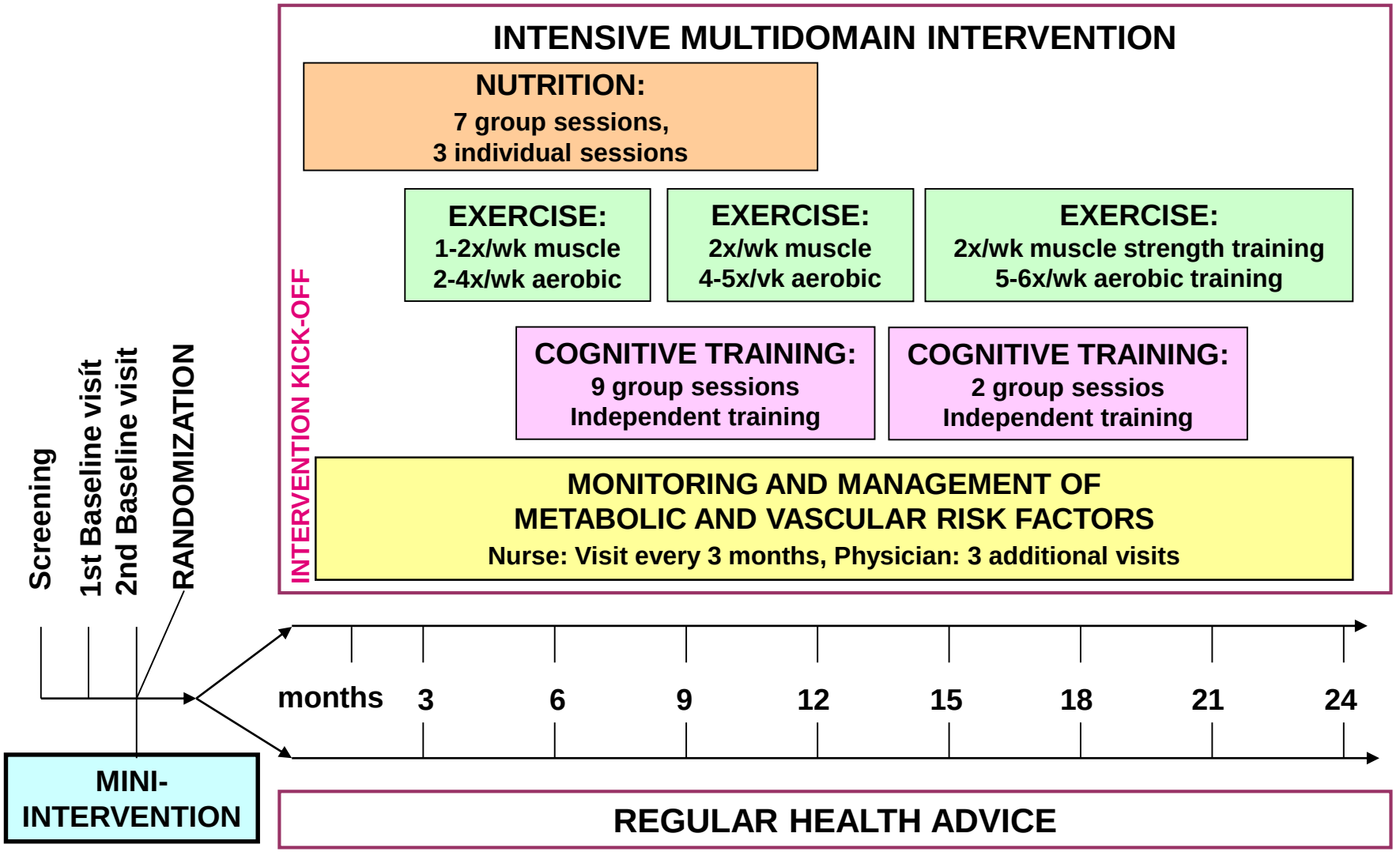
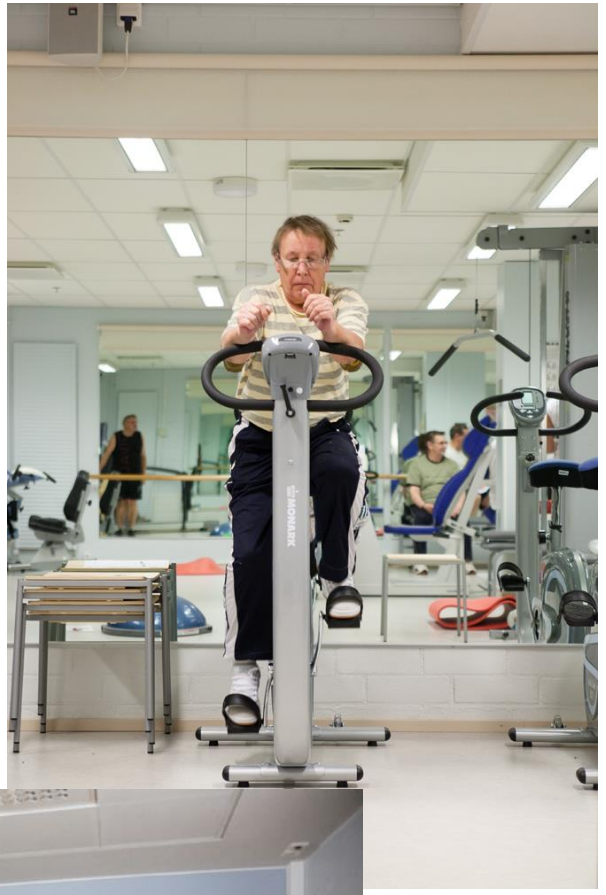
INTERVENTION SCHEDULE



Kivipelto et al., Alzheimer & Dementia 2013

FINGER intervention



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OUTCOMES

- **Primary:**
  - →**Neuropsychological Test Battery (NTB) total z score (cognitive change)**
- **Secondary:**
  - **Dementia/AD (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=200) and PET (n=60)**

Kivipelto et al., Alzheimer & Dementia 2013

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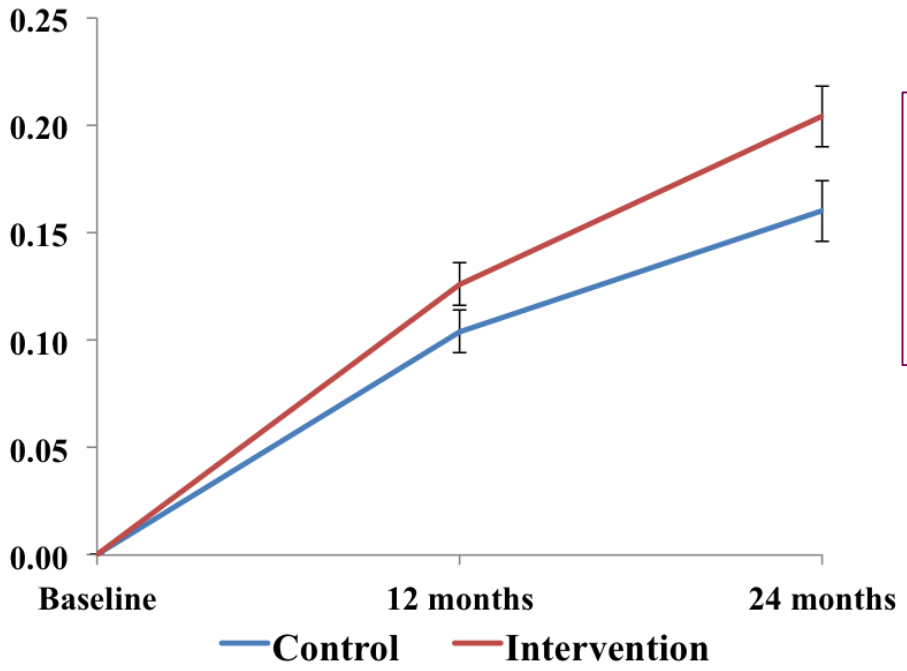
Results

Primary efficacy outcome: global cognition

(NTB composite Z score)



Intervention group: 25% higher improvement

Difference between intervention and control groups per year:

Estimate (95% CI) = 0.022 (0.002-0.042)

p=0.03

Lines = estimates for cognitive change from baseline to 12 and 24 months
Higher scores = better performance
Error bars = standard errors
P-values = difference in trajectories over time between groups

Kivipelto, Ngandu, Mangialasche et al., Lancet 2015

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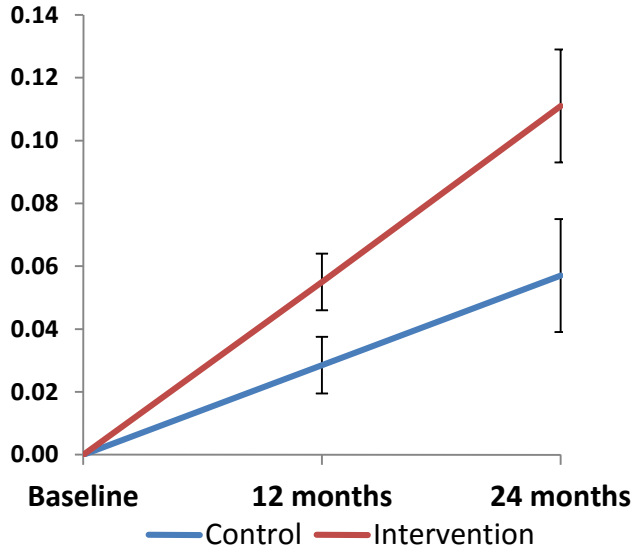
Results

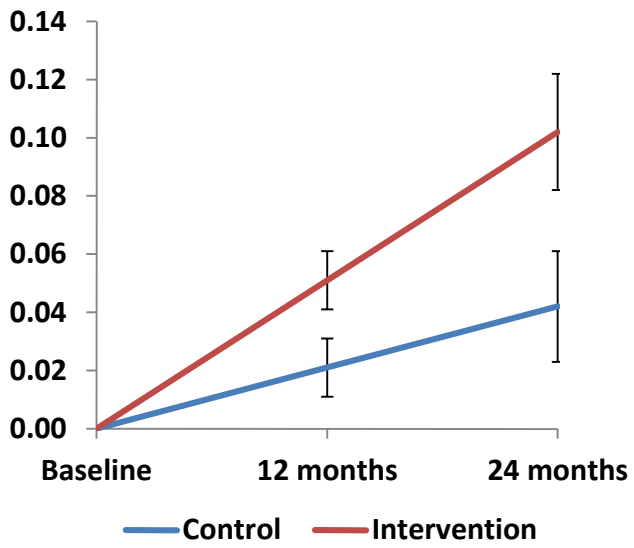
Intervention effects on various cognitive domains (secondary outcomes)

Executive functioning



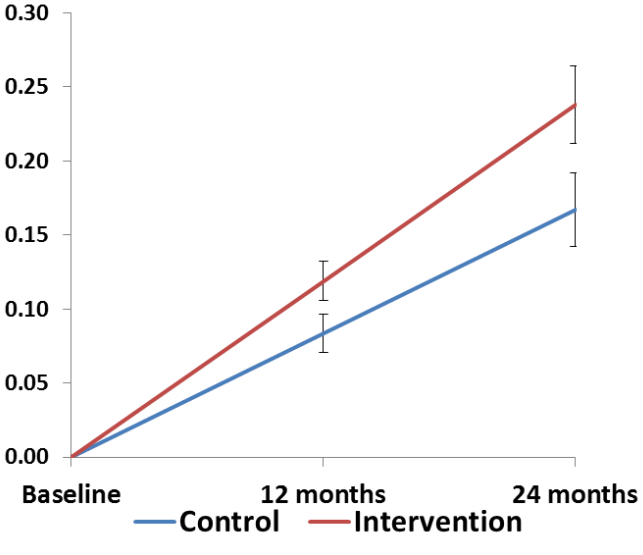
83% higher improvement

Processing speed



150% higher improvement

Memory (abbreviated score)



40% higher improvement

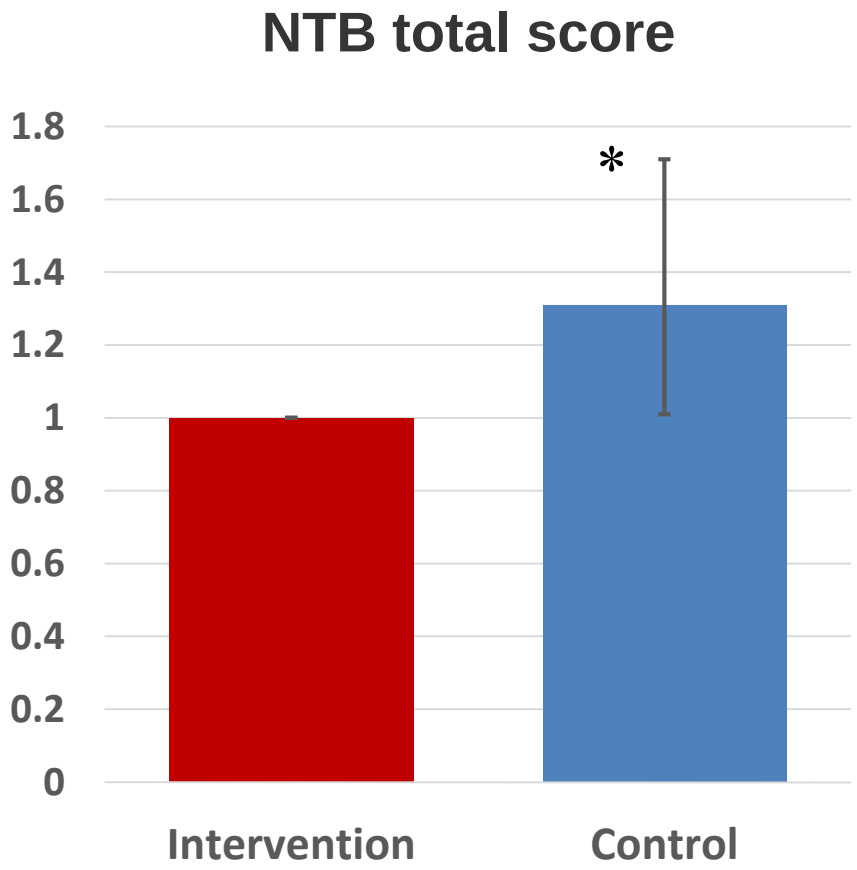
Difference between intervention and control groups per year:

Estimate (95% CI), p-value

0.027 (0.001-0.052)	0.030 (0.003-0.057)	0.038 (0.002-0.073)
p=0.04	**p=0.03**	**p=0.04**

Kivipelto et al., Lancet 2015

Risk for cognitive decline



Control group:
30% increased risk
Cognitive decline

* p<0.05

Kivipelto, Ngandu, Mangialasche et al., Lancet 2015

Intervention effects on secondary outcomes

	Control	Intervention	Difference between intervention and control groups per year	
	Mean change (SE)	Mean change (SE)	Estimate (95% CI)	P value
Vascular factors				
Body mass index (kg/m2)	-0·33 (0·05)	-0·49 (0·05)	-0·077 (-0·149 - -0·006)	0·02
Lifestyle factors **				
Fish intake at least twice/week (%)	+0·8	+11·0	10·2	<0·001
Daily intake of vegetables (%)	-1·0	+2·9	3·9	0·023
Physical activity ≥2 times/week (%)	-2·1	+7·0	9·1	<0·001

Mixed-model repeated-measures analyses

*** Multinominal logistic regression (change in % units between baseline and 24 months)*

Kivipelto et al, Lancet 2015

Prevention of dementia: Future?

Necessary of multi-national studies and pragmatic prevention programs

European Dementia Prevention Initiative

www.edpi.org

- **FINGER** Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability
- **Pre-DIVA** Prevention of Dementia by Intensive Vascular Care
- **MAPT** Multidomain Alzheimer Preventive Trial

Data pooling and joint analyses
> 6000 participants

JPND research
EU Joint Programme – Neurodegenerative Disease Research

- Pilot Studies on Preventive Strategies related to Neurodegenerative Diseases

Multimodal preventive trials for Alzheimer's Disease: towards multinational strategies (MIND-AD)

Alzheimer's Disease International

LIPIDIDIET

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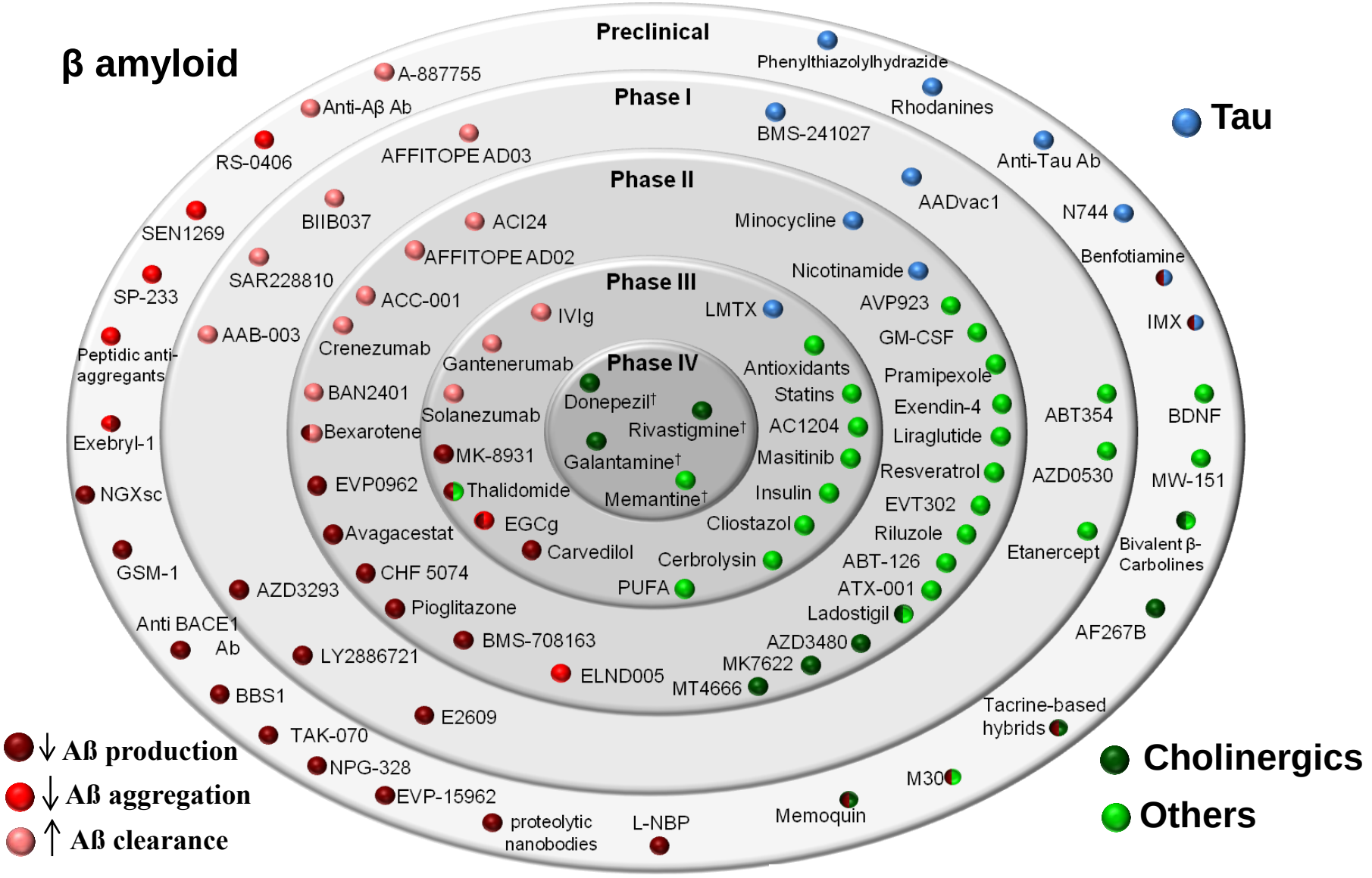
HATICE

Ongoing clinical trials in Alzheimer disease (AD)



† *Currently approved for AD treatment*

Mangialasche , Kivipelto et al, modified 2013 from Lancet Neurology, 2010

Take home points: how to prevent dementia

1. Timing: starting early, at-risk persons

2. Multi-factorial aetiology – multi-domain interventions effective for several cognitive domains

3. FINGER: a pragmatic model that can be tested and adapted in various settings and populations

4. Future: Multi-national prevention RCTs & Pragmatic prevention programs, integrated interventions

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Life matters!