

## **IS THERE A VALUE FOR NON-DRUG INTERVENTIONS FOR DEMENTIA PREVENTION? YES, THIS IS THE WAY TO GO NOW**

**Francesca Mangialasche, Miia Kivipelto**

*Center for Alzheimer Research – Aging Research Center, Karolinska Institutet, Stockholm, Sweden*

As the worldwide population ages, dementia has reached epidemic proportions, with major social, medical and economic burdens. Alzheimer's disease (AD) is the leading cause of dementia and, with no currently available curative treatments, both the World Health Organization (2012) and the G8 Dementia Summit (2013) identified dementia and AD prevention as a major public health priority.

Recent estimates have shown that one in three Alzheimer disease cases worldwide is due to seven modifiable risk factors: diabetes mellitus, midlife hypertension, midlife obesity, physical inactivity, depression, smoking, and low educational attainment. A 10-20% reduction of these risk factors might decrease AD prevalence by 8-15% in 2050 (between 8.8 million and 16.2 million cases). These numbers suggest that we can capitalize on modifiable risk factors for dementia/AD to promote its prevention. In support of these estimates are also recent observational studies, which reported a reduction in the prevalence or incidence of dementia in the last two decades. Such decrease has been attributed to enhanced environmental and behavioural/lifestyle factors, as well as improvements in vascular health.

Sufficient evidence is already available to justify immediate action for dementia prevention, based on the management of vascular and lifestyle-related risk factors. Nevertheless, randomized controlled trials (RCTs) are expected to clarify the extent to which better risk-factor control can reduce dementia/AD rates in subjects with different risk profiles. In view of the multifactorial aetiology of dementia/AD and the co-occurrence of its risk factors, multidomain RCTs targeting multiple risk factors might be needed for an optimal preventive effect. In the past few years, three large RCTs have been initiated in Europe (FINGER, MAPT, PreDIVA) to test the effects of multidomain interventions targeting vascular and lifestyle-related risk factors in nondemented older adults with different risk profiles. One study, the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER), targets a population-based cohort that was selected using a validated risk score. These features will facilitate the applicability of the RCT findings to the general population and generate information that is useful for public health policy. In FINGER, a multidomain intervention consisting of nutritional guidance, exercise, cognitive training, and intensive monitoring of vascular risk factors has been tested in subjects aged 60-77 years. Results have shown that the 2-year intervention was able to promote an improvement in cognitive function, including global cognition, executive functioning, processing speed and memory. A 7-year extended follow-up is ongoing to assess intervention effects on dementia/AD incidence.

Researchers leading the FINGER, MAPT and PreDIVA RCTs launched the European Dementia Prevention Initiative (EDPI), to promote international collaborations and share/harmonize data analyses. EDPI recently launched a collaborative RCT, 'The Healthy Aging Through Internet Counselling in the Elderly' (HATICE) to prevent dementia and cardiovascular diseases among 4 250 at-risk older adults, recruited in three European countries (Finland, France, The Netherlands). In HATICE the preventive intervention is implemented through an easily accessible internet platform, with readily available nurse-support. As a further step towards large international RCTs, the EDPI network together with other European countries recently launched the MIND-AD project (Multimodal preventive trials for Alzheimer's Disease: towards multinational strategies). MIND-AD is based on experiences and data from 5 ongoing European intervention studies on AD/dementia prevention (FINGER, MAPT, PreDIVA, LiPIDI Diet, and HATICE). The novel approach used in MIND-AD consists of multidomain interventions, inclusion of novel models of delivery (e.g. computer-based cognitive training, medical food), critical feedback from trial participants, and synergistic use of data from several European countries with over 10 000 participants. Further, a pilot study will be conducted, in which a multimodal preventive intervention will be tested for the first time in prodromal AD.

In conclusions, although pharmacological approaches are important to treat dementia and AD, current epidemiological evidence illustrates the potential for deriving widespread public health benefits from non-pharmacological interventions, and points at multi-domain interventions as effective strategies to delay or prevent dementia/AD onset.

### **References**

- Kivipelto M, Mangialasche F. Alzheimer disease: To what extent can Alzheimer disease be prevented? Nat Rev Neurol. 10, 552-3 (2014).*
- Kivipelto, M. et al. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER): study design and progress. Alzheimers Dement. 9, 657-665 (2013).*
- Larson EB, et al. New insights into the dementia epidemic. N Engl J Med. 24, 2275-7 (2013).*
- Norton, S., et al. Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. Lancet Neurol. 13, 788-794 (2014).*
- Solomon, A. et al. Advances in the prevention of Alzheimer's disease and dementia. J. Intern. Med. 275, 229-250 (2014).*