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Reference Materials

Title: **Advances in the prevention of Alzheimer's Disease**

Author(s): Shireen Sindi, Francesca Mangialasche, Miia Kivipelto

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Abstract:

Alzheimer's disease (AD), the leading cause of dementia, has reached epidemic proportions, with major social, medical and economical burdens. With no currently available curative treatments, both the World Health Organization and the G8 Dementia Summit recently identified dementia and AD prevention as a major public health priority. Dementia and AD have a wide range of risk factors (genetic, vascular/metabolic and lifestyle-related), which often co-occur and thus interact with each other. Previous intervention efforts aimed at preventing dementia and AD focused on the management of single risk factors, with relatively modest findings. Also, the effect of risk factors depends on age at exposure, indicating that the timing of preventive interventions needs to be carefully considered. In view of the complex multifactorial nature of AD, as well as its long pre-clinical (asymptomatic) phase, interventions simultaneously targeting multiple risk factors and disease mechanisms at an early stage of the disease are most likely to be effective. Three large European multidomain prevention trials have been launched with the goal of preventing cognitive decline, dementia and AD in older adults with different risk profiles. Pharmacological trials are also shifting towards prevention of Alzheimer dementia, by targeting at-risk individuals prior to the onset of cognitive symptoms. The current review will summarize and discuss the evidence on risk and protective factors from observational studies, ongoing lifestyle-related and pharmacological randomized controlled trials (RCTs), as well as future directions for dementia and AD prevention.

Risk and protective factors for late-onset dementia and Alzheimer's disease

Risk Factors

Age

Genetic

Familial aggregation, APOE ε4, Different genes (e.g., CR1, PICALM, CLU, TREM2, TOMM40) have been proposed (www.alzgene.org)

Vascular and metabolic

Cerebrovascular lesions, Cardiovascular diseases, Diabetes mellitus and pre-diabetes

Midlife positive association but late-life negative association

Hypertension, High BMI (overweight and obesity), High serum cholesterol

Lifestyle

Smoking, High alcohol intake

Diet

Saturated fats, Homocysteine

Others

Depression, Traumatic brain injury, Occupational exposure (extremely low-frequency electromagnetic field, heavy metals), Infective agents (Herpes Simplex Virus Type I, Chlamydomydia pneumonia, Spirochetes)

Protective Factors

Genetic

Different genes (e.g. APP, APOE ε2) have been proposed (www.alzgene.org)

Psychosocial factors

High education and socioeconomic status, High work complexity, Rich social network and social engagement, Mentally stimulating activity

Lifestyle

Physical activity, Moderate alcohol intake

Diet

Mediterranean diet, Polyunsaturated fatty acids and fish-related fats, Vitamin B6, B12, folate, Antioxidant vitamins (A, C, E), Vitamin D

Drugs

Antihypertensive drugs, Statins, HRT, NSAIDs

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