



Title: Primary prevention of dementia – review of current trials, methodological issues and perspectives

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Abstract:

Background : Prevention of neurodegenerative disease, such as Alzheimer disease (AD), is a growing public health problem and several potential factors (lifestyle, cognitive stimulation and preventive drugs) have been identified in large observational studies. In order to demonstrate the real effectiveness of these factors randomized controlled trials (RCTs) are needed but few RCTs were developed in the past and first results have so far been generally conflicting with those of epidemiological studies. This lack of effect may have been due to the inefficacy of the interventions tested, but methodological factors probably also played a part (intensity of exposure, critical period of exposure ...). Such trials raise specific methods because they require large numbers of subjects and lengthy follow-up periods.

Methods ; We will present a systematic review of RCTs for the primary prevention of neurodegenerative dementia or cognitive decline. The results of this systematic review and the methodological issues raised (target population, methods of recruitment, clinical relevance of endpoints, follow-up period) will be presented and discussed. Two initiatives will be presented (GuidAge and Mapt trials).

Conclusion : The methodology of primary prevention RCTs for neurodegenerative dementia is of great importance. Dementia prevention trials have so far mainly targeted pharmacological intervention strategies (hormone replacement therapy in women, antioxidants and anti-inflammatory agents) and several of these trials were terminated prematurely due to safety concerns. Some public health initiatives promoting physical exercise and a healthy diet have shown positive results and proved that it is possible to change lifestyle habits, even in elderly persons, so it will be important in future RCT to also evaluate lifestyle interventions which combined different preventive approaches (nutrition and physical exercise). For risk factors that play a role early on in the life course, public health interventions at the population level, rather than RCTs, should be discussed as alternatives methods in order to assess protective effect of these factors.