IS THERE VALUE IN NON-PHARMACOLOGICAL INTERVENTIONS FOR DEMENTIA PREVENTION?
NOT YET, NEED TO INVEST ON TOOLS: IMAGING AND FLUID BIOMARKERS

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The hope for disease modification as well as technological advances in biomarker discovery fuel the search for biological indicators of the Alzheimer's disease pathophysiological process, which can be used to identify neurodegeneration independently of its clinical manifestations. Ideally, such a biomarker, alone or in combination with other markers, would distinguish between individuals with and without Alzheimer's disease pathology independently of the clinical symptomatology. Individuals with asymptomatic early Alzheimer's disease would probably benefit most from interventions aiming to prevent further neural damage to maintain their independence, ability to work and fulfilment of social roles. Furthermore, pathophysiological markers may also offer the added benefit of directly assessing response to treatment options that target core processes of AD pathogenesis. The application of novel therapeutics with potentially significant side effects could thereby be restricted to patients with biological evidence of treatment response in line with the notion of personalised medicine. However, biomarker evidence of treatment efficacy should currently not replace clinical evidence of patient benefit. This is both true for pharmacological and non-pharmacological interventions.

In future, we will hopefully be in a position to reliably identify the Alzheimer's disease pathophysiological process before it causes irreversible cerebral damage. We expect that by the same time, treatment options will be available which slow down the neurodegenerative process. In the meantime, we need to live with the imperfections of available biomarkers. To start with, they can only be used as an aid to the clinical diagnosis in individuals showing cognitive symptoms, not in cognitively normal subjects. Even in specialized centres, the biomarker-assisted early diagnosis of Alzheimer's disease is still far from being perfectly accurate; therefore, a diagnosis of Alzheimer's disease should never be solely based on laboratory or imaging findings. In case of a positive biomarker, the clinical course of the disease should be carefully monitored in order to initiate treatment with antidementia drugs if symptoms progress to dementia. Even if the biomarker results are negative, some follow up of the clinical course should be performed since Alzheimer's disease could still be the cause of the symptoms. Importantly, if prodromal Alzheimer's disease is diagnosed on the basis of biomarkers findings, affected individuals must not be left alone with their worries and fears. So far, no appropriate programs exist for these individuals. There is also limited knowledge about the psychosocial reactions to biomarker information and about the individual benefits that accompany the use of biological indicators of Alzheimer's disease pathology. Research on these ethical considerations has to be conducted in addition to studies aiming to develop improved biomarkers in order to provide patient oriented and individualized diagnostic services. The outcomes of these research strategies will determine the success of any new therapeutic interventions, be it pharmacological or non-pharmacological.