

## Healthy lifestyle as potential targets for dementia prevention

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Ageing is accompanied by a decline in several measures of cognitive function, such as memory, reasoning, and psychomotor speed. There are considerable inter-individual differences in the rate of change in cognitive function,<sup>1</sup> highlighting the importance of identifying modifiable factors that are associated with favourable cognitive ageing trajectories. Impaired cognitive status affects the quality of life of individuals, their ability to live independently, but is also a hallmark of Alzheimer's disease and related dementias. Lifestyle factors have attracted a lot of attention as potential targets for prevention, including in the most recent Lancet commission for dementia prevention<sup>2</sup> where three of the 12 modifiable factors are lifestyle factors (alcohol consumption (>21 units/week), smoking, and physical inactivity).

The linked study by Jia and colleagues ([doi: link to study](#)) investigated the association between a healthy lifestyle and decline in memory over 10 years in the China Cognition and Aging Study on over 29,000 participants (49% women, mean age=72.2 years at baseline). The authors calculated a healthy lifestyle score using six factors including healthy diet, physical exercise, social contact, cognitive activity, non-smoking, and never alcohol drinking. The resulting score, ranging from 0 to 6, was categorised as favourable (4 to 6 healthy factors), average (2 to 3 healthy factors), and unfavourable (0 to 1 healthy factors) lifestyle. The authors examined association of healthy behaviours with decline in memory function, measured by the Auditory Verbal Learning test which is a composite measure including tests of immediate, short-delay, long-delay recall, and long-delay recognition. They found each individual healthy behaviour to be associated with a smaller 10-year memory decline. Furthermore, the healthy lifestyle score was associated with a smaller memory decline in a dose-response manner. Compared to the unfavourable lifestyle group the 10-year decline in the favourable lifestyle group was 0.28 standard deviation lower and that in the average lifestyle group

0.16 standard deviation lower. These results do not allow conclusions to be drawn on the optimal “lifestyle posology” (which health behaviours? When in the lifecourse?) to target memory decline at the level of the population. Further insight is also needed to determine whether the differences in memory decline observed in this study are clinically meaningful.

A remarkable finding in this study was that the association between the healthy lifestyle score and 10-year memory decline was evident in both APOE  $\epsilon$ 4 carriers and non-carriers. APOE  $\epsilon$ 4 is the strongest known risk factor for Alzheimer’s disease and related dementias and within the context of ongoing and future targeted prevention trials, this finding is particularly important. These findings support the notion that lifestyle change may counteract the deleterious impact of APOE  $\epsilon$ 4 on cognitive decline and dementia.<sup>3</sup>

The inefficacy of curative solutions for Alzheimer’s disease and related dementias has highlighted the need for prevention. Jia and colleagues used six measures to define a healthy lifestyles but another recent study on Alzheimer’s dementia by Dhana et colleagues used five components (excluding social contact from the list proposed by Jia et al) to define a healthy lifestyle.<sup>4</sup> In terms of threshold that carries risk Jia et al. define never alcohol drinking as healthy but Dhana et colleagues defined drinking 1-15 units per week as healthy. Given emerging evidence on the association of sleep duration with cognitive outcomes,<sup>5</sup> it remains unclear if it should be included in defining a healthy lifestyle. The American Heart Association proposed seven biological and lifestyle factors for brain health<sup>6</sup> that have been shown to be associated with lower risk of dementia.<sup>7</sup> A further area of concern is age when healthy behaviours need to be adopted, recommended in guidelines<sup>2</sup> but missing in definitions of a healthy lifestyle. Identification of the optimal window for intervention requires closer attention to age and duration of exposure. For effective prevention it is necessary to consider a wide range of risk factors to identify specific exposures that carry risk, and examine the salience of threshold and age at exposure for each of these.

Cognitive decline and risk of dementia are likely to be shaped by multiple risk and protective factors. The multi-factorial risk paradigm advocated by the Framingham study has led to a notable reduction in cardiovascular disease.<sup>8</sup> A similar approach, using risk identification with attention to threshold to define risk and age at exposure, for dementia prevention is an urgent public health challenge as highlighted by the recent WHO report.<sup>9</sup>

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