The identification of effective prevention and treatment strategies in Alzheimer’s dementia remains challenging in the face of the ever-growing public health and financial burden imposed by this condition on the older population and health care systems worldwide [1, 2]. A number of recent intervention studies targeting the main neuropathological alterations characteristic of Alzheimer’s dementia have failed to demonstrate tangible effects on the progression of cognitive decline and/or other relevant end points [3–6]. This has not only prompted the search for new druggable targets and/or the repurposing of existing drugs for the management of other disease states, but also renewed the interest in the investigation of the effects of prevention measures [7]. In the context of dementia prevention, a number of epidemiological studies have reported associations between the presence of cardiovascular risk factors in young and middle age, e.g., hypertension and diabetes, cognitive trajectories, and risk of Alzheimer’s disease and other types of dementia later in life [8–12]. Therefore, specific pharmacological treatments for the management of these risk factors might theoretically provide a protective effect towards the onset and progression of Alzheimer’s disease. The angiotensin receptor blockers are a class of antihypertensive drugs that have been extensively used in clinical practice over the last 30 years for the management of various clinical manifestations associated with high cardiovascular risk, e.g., the post-myocardial infarction phase, heart failure, and diabetic nephropathy [13–15]. In this issue of the Journal, Oscanoa et al. report the results of a systematic review and meta-analysis on the association between the use of these medications and the incidence of Alzheimer’s disease [16]. Ten studies, one randomized controlled, two case-control, and seven cohort, of 2,271,262 participants (mean age, 71.6 years, and follow-up, 7 years), were selected for the final analysis. When the case-control and cohort studies were analysed together, the use of angiotensin receptor blockers was associated with a significantly lower incidence of Alzheimer’s disease (hazard ratio, HR, 0.69, 95% CI 0.56 to 0.85, p=0.001). The only identified randomized controlled study reported a similar trend (HR 0.31, 95% CI 0.14 to 0.68, p=0.003) [16, 17]. In subgroup analysis, the magnitude of the effect size appeared to be greater in studies of participants with a mean age of ≥75 years (HR 0.64, 95% CI 0.47 to 0.88, p=0.006) when compared to those in younger cohorts (HR 0.73, 95% CI 0.50 to 1.08, p=0.11). While promising, the results of the study by Oscanoa et al. need to be interpreted with some caution for a number of reasons. First, as also acknowledged by the authors, virtually all selected studies were observational, which limited the robustness of the captured evidence. Second, the reduced effects observed in participants younger than 75 years cast some doubts on the potential preventative role of these agents in young and middle age adults. Third, the available data did not allow the investigation, in sub-group analysis, of other patient characteristics, for e.g., specific cardiovascular risk factors, depression, education, socioeconomic status, genetic and hormonal factors, diet, and physical activity, potentially associated with different risks of Alzheimer’s disease during treatment with angiotensin converting enzyme inhibitors [18]. In the light of the contrasting results of other meta-analyses on the impact of the overall use of antihypertensive medications vs. that of individual classes on the risk of Alzheimer’s disease [19–21], additional, appropriately designed studies are required to investigate the protective effects of different blood pressure lowering strategies on cognitive decline and dementia and the role of specific patient characteristics in modulating such effects.

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