Diet, Exercise Habits, and Risk of Alzheimer Disease

To the Editor: In their cohort study, Dr Scarmeas and colleagues[1] found an association of self-reported adherence to a Mediterranean-type diet and high levels of physical activity with a reduced risk of developing Alzheimer disease in a population of elderly residents of New York. However, we have several concerns about the study.

First, self-selection represents a potentially important source of bias, since individuals who adopt healthy lifestyle habits may be different in various ways from those who do not engage in such habits. Second, self-report measures of diet and exercise can be inaccurate. The accuracy of the Food Frequency Questionnaire is controversial,[2] especially in individuals who may already have memory impairment, and objective measures of physical activity, such as accelerometers, are likely more accurate.

Third, the study assessed only one of many possible diets. The DASH (Dietary Approaches to Stop Hypertension) diet is similar but emphasizes greater consumption of low-fat dairy products and carbohydrates and is lower in fat and cholesterol. Moreover, its efficacy in reducing blood pressure has been demonstrated in all segments of the population, including African Americans,[3] a group disproportionately affected by vascular disease and Alzheimer disease.[4]

We agree with the authors that randomized controlled trials (RCTs) are needed to establish a causal relationship between dietary and exercise habits and risk of Alzheimer disease. While numerous observational studies have shown that physically active individuals perform better on neurocognitive tests compared with their less active counterparts, results of RCTs of exercise have been inconsistent.[5] There also have been many observational studies of diet and neurocognition, but most RCTs have focused on dietary supplementation, with generally negative or inconsistent results. Although the observations of Scarmeas et al are encouraging and potentially important, establishing the value of dietary and activity recommendations should await results from future RCTs.

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In Reply: In response to Dr Blumenthal and colleagues, self-selection is a generic problem of all population studies (and clinical trials) in which less healthy participants tend to decline participation. We tried to address the issue of residual confounding by adjusting for multiple factors, including ethnicity, education, smoking, depression, leisure activities, and comorbidities. Additionally, we conducted propensity modeling,[1] which considered the probability of belonging to different physical activity groups conditional on individuals' background characteristics, thus creating participant characteristic balance between different physical activity groups (similar to a matching or a stratification process). With this modeling, the results were unchanged.

Recall bias in recorded responses in the Food Frequency Questionnaire is another valid concern. We addressed it by adjusting for baseline level of cognitive impairment as assessed by the clinical dementia rating in all models. In additional models, we also excluded participants with baseline clinical dementia rating score of 0.5 and those followed up for less than 2 years (indicating possible proximity to dementia diagnosis). Associations remained strong (or even stronger).

We agree that objective measures of physical activity may increase accuracy, but there are practical limitations in their administration on a large scale in such population-based studies. We used a previously validated physical activity questionnaire. In our cohort, we additionally demonstrated the validity of the questionnaire against objective measures of physical performance (chair stands and times to walk 1 m

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and 4 m). We are in the process of investigating the associations of a series of other diets.

There could be many reasons for previous RCTs of either exercise or dietary supplementation being negative or inconsistent, including selection of the intervention (type of supplementation, characteristics of the exercise), timing or duration of intervention (Alzheimer disease pathology may start years before clinical manifestations), or focus on a single nutrient or food. Overall, we agree that caution in the interpretation of our findings is necessary. In the absence of relevant RCTs with positive results, it cannot be considered as sufficient evidence for population recommendations for the prevention of Alzheimer disease. Nevertheless, a healthy diet and physical activity should be health policy targets given their known beneficial effects in other medical conditions such as type 2 diabetes mellitus and cardiovascular disease.[2,3]

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Mediterranean Diet and Cognitive Decline

To the Editor: Dr Féart and colleagues[1] performed a prospective cohort study and concluded that adherence to a Mediterranean diet was associated with slower cognitive decline as assessed by the Mini-Mental State Examination (MMSE). We have a number of concerns about the study.

First, the study participants were not blinded, and using the 24-hour dietary recall introduced potential recall bias because participants might recall differently depending on their disease status.[2] Second, using MMSE as a scale for assessing cognitive function may not have been an optimal choice. A study using the French versions of the Severe Impairment Battery and MMSE in 69 patients with probable Alzheimer disease concluded that the Severe Impairment Battery was better able to discriminate among patients who had scores lower than 11 points on the MMSE.[3] Third, accuracy of the MMSE depends on the educational status of the individual.[4] Fourth, accuracy of the MMSE has also been shown to vary based on age.[5]

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In Reply: In response to Drs Ramaraj and Chellappa, we excluded demented participants at baseline; therefore, all participants were free of dementia when the 24-hour dietary recall was performed. Moreover, at that time we had no specific hypothesis for the potential role of the Mediterranean diet on cognitive decline and dementia onset so that recall should not have been biased with respect to this outcome.

The MMSE was not used as a criterion for dementia but only to ascertain cognitive decline in all participants. In our study, we were interested in change in cognitive performances assessed on the MMSE and on 3 other cognitive tests (Free and Cued Selective Reminding Test, Isaacs Set Test, and Benton Visual Retention Test). In addition, diagnosis of incident dementia was based on a 3-step procedure.[1] All participants whose performance had declined on neuropsychological tests (not on the MMSE) compared with a previous examination, or who were suspected of having dementia by the psychologist, were examined by a neurologist. All potential incident cases of dementia were validated by the independent expert committee of neurologists who analyzed in depth the medical history of each participant and ascertained the cause (Alzheimer disease or other causes of dementia). All of the statistical analyses were adjusted for age (as a time scale in Cox proportional hazards models[2]) and education.

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