MIND diet associated with reduced incidence of Alzheimer’s disease

Martha Clare Morris, Christy C. Tangney, Yamin Wang, Frank M. Sacks, David A. Bennett, Neelum T. Aggarwal

Department of Internal Medicine and the Rush Alzheimer’s Disease Center at Rush University Medical Center, Chicago, IL, USA
Department of Clinical Nutrition and the Rush Alzheimer’s Disease Center at Rush University Medical Center, Chicago, IL, USA
Department of Nutrition, Harvard School of Public Health, Boston, MA, USA
Department of Behavioral Sciences and the Rush Alzheimer’s Disease Center at Rush University Medical Center, Chicago, IL, USA
Department of Neurology and the Rush Alzheimer’s Disease Center at Rush University Medical Center, Chicago, IL, USA

Abstract

Introduction: In a previous study, higher concordance to the MIND diet, a hybrid Mediterranean-Dietary Approaches to Stop Hypertension diet, was associated with slower cognitive decline. In this study we related these three dietary patterns to incident Alzheimer’s disease (AD).

Methods: We investigated the diet-AD relations in a prospective study of 923 participants, ages 58 to 98 years, followed on average 4.5 years. Diet was assessed by a semiquantitative food frequency questionnaire.

Results: In adjusted proportional hazards models, the second (hazards ratio or HR = 0.65, 95% confidence interval or CI 0.44, 0.98) and highest tertiles (HR = 0.47, 95% CI 0.26, 0.76) of MIND diet scores had lower rates of AD versus tertile 1, whereas only the third tertiles of the DASH (HR = 0.61, 95% CI 0.38, 0.97) and Mediterranean (HR = 0.46, 95% CI 0.26, 0.79) diets were associated with lower AD rates.

Discussion: High adherence to all three diets may reduce AD risk. Moderate adherence to the MIND diet may also decrease AD risk.

Keywords: Cognition; Alzheimer’s disease; Nutrition; diet; Epidemiological study; Aging

1. Introduction

Dietary patterns have been associated with protective relations to cognitive decline and incident dementia in epidemiological studies [1,2]. Encouraging support for these findings was recently provided by reports of secondary analyses of two dietary intervention trials. In the Prevención con Dieta Mediterránea (PREDIMED) trial [3], participants at high vascular risk were randomized to dietary counseling of either the Mediterranean diet (supplemented with either extra-virgin olive or mixed nuts) or a low-fat control diet. After 6.5 years of nutritional intervention, those randomized to the Mediterranean diet had significantly higher scores on the Mini-Mental State Examination (MMSE) and Clock Drawing Test compared with the control diet participants. In the second trial [4], 124 overweight participants with elevated blood pressure were randomized to the DASH diet (Dietary Approaches to Stop Hypertension) alone or in combination with exercise and caloric restriction, or to a usual diet control group. After 4 months of the intervention, the participants on the DASH diet exhibited greater improvements in psychomotor speed compared with the usual diet control.

The results of these dietary intervention trials provide evidence that dietary patterns may reduce the risk of dementia. However, whereas both the cultural-based Mediterranean diet and the blood pressure-lowering DASH diet have demonstrated protective effects on cardiovascular conditions that can adversely affect brain health, their dietary components may not specifically capture the levels and types of foods shown to optimize brain health. In a previous study,
we described a hybrid of the Mediterranean-DASH diets, called MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) that emphasizes the dietary components and servings linked to neuroprotection and dementia prevention. Similar to the Mediterranean and DASH diets, the MIND diet score emphasizes natural plant-based foods and limited intakes of animal and high saturated fat foods but uniquely specifies the consumption of berries and green leafy vegetables, and does not specify high fruit consumption (three to four servings per day in the DASH and Mediterranean diets), high dairy (2+ servings per day in DASH), high potato consumption (2 servings per day in the Mediterranean), or greater than one fish meal per week (>6 meals/week in the Mediterranean). The MIND diet score was associated with a slower rate of cognitive decline equivalent to 7.5 years of younger age among the participants in the top third of MIND diet scores compared with the lowest third [5]. In this study, we examined the relative associations of the MIND, DASH, and Mediterranean diets to the risk of developing incident Alzheimer’s disease (AD).

2. Methods

2.1. Study population

The study was conducted among participants of the Rush Memory and Aging Project (MAP), a study of volunteers living in retirement communities and senior public housing units in the Chicago area. The ongoing open cohort study began in 1997 and includes annual clinical neurological examinations as previously described [6]. From 2004 to February 2013, the MAP study participants were invited to complete food frequency questionnaires. Over the course of the diet study, 1545 older persons enrolled in the MAP study, 80 died and 159 withdrew before the diet study began, leaving 1306 participants eligible for the analyses of diet and incident AD. Of these, 1068 completed the dietary questionnaires of which 923 had at least two neuropsychological assessments and maximum scores for each diet.

2.2. Alzheimer disease

The clinical diagnosis of probable AD was determined at each annual evaluation as previously described [7]. Briefly, the AD diagnosis was made by an experienced clinician using data from a structured neurological examination and medical history, cognitive performance testing, and with the assistance of an algorithmically based rating of cognitive impairment. The AD diagnosis was based on criteria of the joint working group of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association [8] which require a history of cognitive decline with impairment in memory and at least one other cognitive domain. According to these diagnostic criteria, there were 144 incident cases of AD and 14 incident cases of non-Alzheimer’s type dementia which were analyzed as noncases.

2.3. Diet scores

The diet scores were computed from responses to a semi-quantitative food frequency questionnaire (FFQ), a modified version of the Harvard FFQ that was validated for use in older Chicago community residents [9]. Participants were asked to report usual frequency of intake over the previous 12 months of 144 food items. Nutrient levels and total energy for each food item were based on the US Department of Agriculture food composition table [10]. Olive oil consumption was scored 1 if identified by the participant as the primary oil usually used at home and 0 otherwise. For all other diet score components we summed the frequency of consumption of each food item portion associated with that component and then assigned a concordance score of 0, 0.5, or 1. (Table 1) The total MIND diet score was computed by summing over all 15 of the component scores.

The MIND diet score has 15 dietary components including 10 brain healthy food groups (green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine) and five unhealthy food groups (red meats, butter and stick margarine, cheese, pastries and sweets, and fried/fast food). Olive oil consumption was scored 1 if identified by the participant as the primary oil usually used at home and 0 otherwise. For all other diet score components we summed the frequency of consumption of each food item portion associated with that component and then assigned a concordance score of 0, 0.5, or 1. (Table 1) The total MIND diet score was computed by summing over all 15 of the component scores.

The MIND diet score has 15 dietary components including 10 brain healthy food groups (green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine) and five unhealthy food groups (red meats, butter and stick margarine, cheese, pastries and sweets, and fried/fast food). Olive oil consumption was scored 1 if identified by the participant as the primary oil usually used at home and 0 otherwise. For all other diet score components we summed the frequency of consumption of each food item portion associated with that component and then assigned a concordance score of 0, 0.5, or 1. (Table 1) The total MIND diet score was computed by summing over all 15 of the component scores.

The MIND diet score has 15 dietary components including 10 brain healthy food groups (green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, and wine) and five unhealthy food groups (red meats, butter and stick margarine, cheese, pastries and sweets, and fried/fast food). Olive oil consumption was scored 1 if identified by the participant as the primary oil usually used at home and 0 otherwise. For all other diet score components we summed the frequency of consumption of each food item portion associated with that component and then assigned a concordance score of 0, 0.5, or 1. (Table 1) The total MIND diet score was computed by summing over all 15 of the component scores.

2.4. Covariates

Non-dietary variables in the analyses were obtained from structured interview questions and measurements at the participants’ baseline clinical evaluations. Age (in years) was computed from self-reported birth date and date of the baseline cognitive assessment. Education (years) is self-reported years of regular schooling. APOE-genotyping was performed using high throughput sequencing as previously described. Participation in cognitively stimulating activities was computed as the average frequency rating, based on a 5-point scale, of different activities (e.g. reading, playing games, writing letters, visiting the library) [13].
Table 1
Dietary component servings and maximum scores for the DASH, Mediterranean, and MIND diet scores

<table>
<thead>
<tr>
<th>DASH components</th>
<th>Max score</th>
<th>Mediterranean diet components</th>
<th>Max score</th>
<th>MIND components</th>
<th>Max score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total grains ≥7/d</td>
<td>1</td>
<td>Nonrefined Grains &gt;4/d</td>
<td>5</td>
<td>Whole Grains ≥3/d</td>
<td>1</td>
</tr>
<tr>
<td>Vegetables ≥4/d</td>
<td>1</td>
<td>Vegetables &gt;4/d</td>
<td>5</td>
<td>Green Leafy ≥6/wk</td>
<td>1</td>
</tr>
<tr>
<td>Fruits ≥4/d</td>
<td>1</td>
<td>Fruits &gt;3/d</td>
<td>5</td>
<td>Other Vegetables ≥1/d</td>
<td>1</td>
</tr>
<tr>
<td>Dairy ≥2/d</td>
<td>1</td>
<td>Full-fat Dairy ≤10/wk</td>
<td>5</td>
<td>Berries ≥2/wk</td>
<td>1</td>
</tr>
<tr>
<td>Meat, poultry and fish ≤2/d</td>
<td>1</td>
<td>Red meat ≤1/wk</td>
<td>5</td>
<td>Red Meats and products &lt;4/wk</td>
<td>1</td>
</tr>
<tr>
<td>Nuts, seeds &amp; legumes ≥4/wk</td>
<td>1</td>
<td>Legumes, nuts &amp; beans &gt;6/wk</td>
<td>5</td>
<td>Fish ≥1/wk</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Poultry ≥2/wk</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Beans &gt;3/wk</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nuts ≥5/wk</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fast/fried food &lt;1/wk</td>
<td>1</td>
</tr>
<tr>
<td>Total fat ≤27% of kcal</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated fat ≤6% of kcal</td>
<td>1</td>
<td>Olive oil ≥1/d</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweets ≤5/wk</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium ≤2400 mg/d</td>
<td>1</td>
<td>Alcohol &lt;300 mL/d but &gt;0</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total DASH Score</td>
<td>10</td>
<td>Total MedDiet Score</td>
<td>55</td>
<td>Total MIND Score</td>
<td>15</td>
</tr>
</tbody>
</table>

Abbreviations: MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; DASH, Mediterranean-Dietary Approaches to Stop Hypertension.

2.5. Statistical analyses

We used proportional hazards models in SAS© to investigate the relationship between diet scores and time in years to the diagnosis of AD. We first examined the relations of the three dietary pattern scores in separate age-adjusted and basic-adjusted models. The basic model included potential confounders with the most established evidence for association with Alzheimer disease: age, sex, education, participation in cognitively stimulating activities, physical activity, and APOE ε4. Total energy intake was also included as a potential confounder in the basic model because of its relevance to diet. Further analyses added covariates to the basic-adjusted models: (1) cardiovascular conditions, which have high likelihood of mediating the diet effects on dementia, and (2) depression and weight measures which may act as effect mediators but in addition have complex cause and effect relations with dementia. The dietary scores were modeled both as continuous variables and in tertiles in each of these models with similar results. We present the results of the tertile analyses to enable the comparison of the dietary score associations with AD given the different dietary score ranges. We also report the P-value for linear trend based on a categorical variable of the tertiles with records in each tertile scored at the tertile median. The effect modification was investigated for the MIND diet score and each covariate by including a multiplicative term between the diet score and the potential effect modifier in the basic-adjusted model and testing at P < .05.

3. Results

A total of 144 incident cases of AD developed over an average follow-up of 4.5 years in the sample of 923 MAP
participants. The mean time to AD diagnosis from the date that diet was assessed was 3.8 years (range of 1–9, median 3.0). The average MIND diet score for the AD sample was 7.4 (15 possible) and ranged from 2.5 to 12.5. Participants with the lowest scores had lower education, were more likely to be obese and to have diabetes, and reported fewer hours of physical activity and more depressive symptoms (Table 2). Mean score for the DASH diet was 4.1 (10 possible; range 1.0–8.5) and for the MedDiet, 31.5 (55 possible; range 18–46). The MIND diet score was correlated with both the MedDiet ($r = 0.62$) and the DASH ($r = 0.50$) diet scores.

MIND diet score was linearly and statistically significantly associated with the lower risk of developing AD in the age-adjusted model (Table 3). In the basic model significantly associated with the lower risk of developing AD in adjusted for age, sex, education, $APOE$ score

Table 2  
Baseline characteristics of 923 MAP participants by tertile of MIND diet score

<table>
<thead>
<tr>
<th>Baseline characteristic</th>
<th>Tertile 1</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIND diet score, mean</td>
<td>5.6 (2.5, 6.5)</td>
<td>7.5 (7.0, 8.0)</td>
<td>9.6 (8.5, 12.5)</td>
</tr>
<tr>
<td>(minimum, maximum)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean years</td>
<td>81.7</td>
<td>81.4</td>
<td>80.4</td>
</tr>
<tr>
<td>Males, percent</td>
<td>26</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>Education, mean years</td>
<td>14.3</td>
<td>15.1</td>
<td>15.6</td>
</tr>
<tr>
<td>$APOE$ e4, percent</td>
<td>21</td>
<td>27</td>
<td>21</td>
</tr>
<tr>
<td>Total Energy Intake, mean</td>
<td>1644</td>
<td>1777</td>
<td>1792</td>
</tr>
<tr>
<td>calories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive activity frequency,</td>
<td>3.1</td>
<td>3.2</td>
<td>3.4</td>
</tr>
<tr>
<td>mean rating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity weekly,</td>
<td>2.5</td>
<td>3.5</td>
<td>4.3</td>
</tr>
<tr>
<td>mean hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms, mean</td>
<td>1.3</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>number</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent BMI $\leq 20$</td>
<td>9</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Percent BMI $&gt; 20$</td>
<td>31</td>
<td>22</td>
<td>24</td>
</tr>
<tr>
<td>Medical conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes, percent</td>
<td>24</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>Hypertension, percent</td>
<td>79</td>
<td>75</td>
<td>72</td>
</tr>
<tr>
<td>Hypertensive medication use,</td>
<td>57</td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td>percent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, percent</td>
<td>17</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Stroke, percent</td>
<td>10</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 2—Baseline characteristics of 923 MAP participants by tertile of MIND diet score. 

NOTE. All variables were age-standardized using 5-year age categories.

Participants with the lowest tertile of MIND diet scores also had a statistically significant 35% reduction in AD rate compared with those in the first tertile (HR = 0.65, 95% CI: 0.44, 0.98) (Table 3).

Only the highest tertiles of the DASH and MedDiet diet scores were significantly associated with incident AD compared with the lowest tertile scores (Table 3). The estimated effects were somewhat higher for the MedDiet diet (54% reduction in AD for tertile 3 vs tertile 1) than for the DASH diet (39% reduction for tertile 3 vs tertile 1) based on the basic-adjusted models (Table 3 and Fig. 1A-1C).

We investigated whether the MIND diet association could be attributed to diet effects on cardiovascular conditions that have been related to the increased risk of AD including diabetes, hypertension, stroke, and myocardial infarction. There was no evidence that the dietary pattern associations with AD were mediated by these conditions, as the hazard ratios from models adjusted for these cardiovascular conditions were very similar to the basic models (Table 3). Estimates of effects for the DASH and MedDiet diet scores on incident AD did not materially change in the analyses of the basic model plus covariates for depressive symptoms and low or high BMI (data not shown). However, the effect estimates were modified for the MIND diet score with further adjustment for depression and BMI (tertile 2 HR = 0.77 (95% CI: 0.51, 1.17); tertile 3 HR = 0.50 (95% CI: 0.30, 0.83); and P-value for trend = .006).

In an attempt to evaluate to what extent the observed effects of the MIND diet on AD could be due to dietary changes in participants with preclinical AD, we reanalyzed the data after eliminating 33 AD cases that were diagnosed under 2 years of follow-up, but there was no change in the overall results (tertile 2 HR = 0.62, $P = .04$; tertile 3 HR = 0.53, $P = .01$). Further elimination of 60 AD cases that were diagnosed within 3 years of follow-up had minimal impact on the estimated effects (tertile 2 HR = 0.63 [$P = .08$] and tertile 3 HR = 0.53 [$P = .04$]), although that for the second tertile was only marginally statistically significant.

In further analyses we found no statistical evidence that the association between the MIND diet and incident AD was modified by age, sex, education, physical activity, obesity, low BMI, or histories of stroke, diabetes, or hypertension. Marginally statistically significant interactions were observed for $APOE$ e4 (the MIND diet was less protective in e4 positive participants) and history of myocardial infarction (the MIND diet was more protective in participants with history); $P$-value for interaction = .06 for both interactive terms.

4. Discussion

This prospective study of the MIND diet score provides evidence that the greater adherence to the overall dietary pattern may be protective against the development of AD. The estimated effect was a 53% reduction in the rate of AD for persons in the highest tertile of MIND scores and a 35% reduction for the middle tertile of scores compared
with the lowest tertile. The estimated effect was independent of other healthy lifestyle behaviors and cardiovascular-related conditions. These data suggest that even modest adherence to the MIND diet score may have substantial benefits for the prevention of AD. By contrast, only the highest concordance to the DASH and MedDiet diets were associated with AD prevention.

The MIND diet pattern was developed \textit{à priori} to the analyses and independently of the MAP study data. It is a hybrid of basic components from the Mediterranean and DASH diets but with modifications based on comprehensive reviews of the literature on nutrition and the aging brain [17–19]. Unlike the Mediterranean and DASH diet scores, the MIND diet specifies the frequent weekly consumption of green leafy vegetables in addition to other types of vegetables. Two large U.S. cohort studies reported significantly slower cognitive decline with consumption of two or more daily servings of vegetables, with the strongest associations observed for six or more weekly servings of green leafy vegetables [20,21]. Furthermore, given that these [20,21] and other prospective [22–24] studies do not find association between fruits as a general category and cognitive decline, the MIND diet does not specify daily fruit servings as do the DASH and Mediterranean diets. However, the MIND diet has a separate score component for berry consumption to reflect the positive associations reported between intakes of blueberries and strawberries and slower cognitive decline in the Nurses’ Health Study [25]. This finding is supported by a number of rodent models showing better memory performance and brain neuroprotection from multiple types of berries [26–29]. The MIND diet is more similar to the DASH diet with regard to fish consumption, with an optimal serving of just one meal per week as opposed to six meals per week specified by the Mediterranean diet. This level of fish consumption reflects the findings of prospective epidemiological studies that examined its relation to AD prevention [30–32].

Whereas, high dietary concordance to the MIND and MedDiet diets were similarly protective against the risk of developing AD, even mild concordance to the MIND diet resulted in a statistically significant AD reduction. In a previous study we observed a stronger inverse association between the MIND diet and cognitive decline than for either the MedDiet or DASH diets [5]. This suggests that the MIND diet is not specific to the underlying pathology of AD but perhaps better overall functioning and protection of the brain.

Protective associations with higher DASH diet scores were more modest. This may indicate that the unique recommendations for dairy and low salt in the DASH diet are not of particular relevance for brain health. Whereas the Mediterranean diet pattern has been related to the lower risk of

Table 3
Proportional hazards ratios (HR) and 95% confidence intervals (CI) of estimated effects of MIND diet score on time to incident Alzheimer disease (AD) in age-adjusted (n = 923; 151 AD cases) and basic-adjusted* (n = 789; 135 AD cases) models in MAP participants over a mean 4.5 years of follow-up, 2004–2013

<table>
<thead>
<tr>
<th>Model</th>
<th>Tertile 1 Score range</th>
<th>Tertile 2 Score range</th>
<th>Tertile 3 Score range</th>
<th>P for linear trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIND diet score</td>
<td>2.5–6.5</td>
<td>7–8</td>
<td>8.5–12.5</td>
<td>.0006</td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.75 (0.52, 1.09)</td>
<td>0.47 (0.30, 0.73)</td>
<td>.0006</td>
</tr>
<tr>
<td>Basic-adjusted HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.65 (0.44, 0.98)</td>
<td>0.47 (0.29, 0.76)</td>
<td>.002</td>
</tr>
<tr>
<td>Basic-adjusted + cardiovascular conditions HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.64 (0.42, 0.97)</td>
<td>0.48 (0.29, 0.79)</td>
<td>.003</td>
</tr>
<tr>
<td>DASH diet score</td>
<td>1.0–3.5</td>
<td>4.0–4.5</td>
<td>5.0–8.5</td>
<td>.02</td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.93 (0.64, 1.36)</td>
<td>0.56 (0.36, 0.86)</td>
<td>.02</td>
</tr>
<tr>
<td>Basic-adjusted HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.98 (0.66, 1.46)</td>
<td>0.61 (0.38, 0.97)</td>
<td>.07</td>
</tr>
<tr>
<td>Basic-adjusted + cardiovascular conditions HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.98 (0.64, 1.46)</td>
<td>0.60 (0.37, 0.96)</td>
<td>.06</td>
</tr>
<tr>
<td>Med. diet score</td>
<td>18–29</td>
<td>30–34</td>
<td>35–46</td>
<td>.01</td>
</tr>
<tr>
<td>Age-adjusted HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.77 (0.54, 1.11)</td>
<td>0.46 (0.29, 0.74)</td>
<td>.01</td>
</tr>
<tr>
<td>Basic-adjusted HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.81 (0.54, 1.24)</td>
<td>0.46 (0.27, 0.79)</td>
<td>.01</td>
</tr>
<tr>
<td>Basic-adjusted + cardiovascular conditions HR (95% CI)</td>
<td>1.0 (referent)</td>
<td>0.81 (0.53, 1.21)</td>
<td>0.49 (0.29, 0.85)</td>
<td>.01</td>
</tr>
</tbody>
</table>

Abbreviations: MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; DASH, Mediterranean-Dietary Approaches to Stop Hypertension.

*Basic-adjusted model included terms for age, sex, education, APOE ε4 (any), participation in cognitively stimulating activities, physical activity, and total energy intake.
incident AD in some [1,33] but not all studies [34] to date there has not been another prospective study that has inves-
tigated the AD relation to the DASH diet. The study has a number of strengths that lend confidence
to the findings. First, selection bias is minimized by the
prospective study design whereby community residents
free of dementia at the beginning of the study are followed
for incident disease. Second, the diagnosis of AD was based
on annual neuropsychological testing and structured clinical
neurological evaluations by clinicians blinded to the dietary
pattern scores. Third, the diet pattern scores were based on a
comprehensive semiquantitative food frequency question-
naire that was validated for use in older community-
dwelling Chicago residents. These features reduce the
potential for biased and random misclassification of disease
status and diet exposures in the analyses. And finally, there
was little or no change in the estimates of dietary effects
on AD after statistical adjustment for many important risk
factors for AD, suggesting that confounding is not a likely
explanation for the observed associations.

The primary limitation of the study is that the observa-
tional study design precludes the interpretation of the
findings as cause and effect. Randomized dietary intervention
trials would be required to attribute causal effects of the diet
patterns to the development of the disease. Another limitation
is the reliance on limited information from the food frequency
questionnaire to determine the consumption of individual
food components in the diet scores. For example, the question
on berry consumption was based on a single item for straw-
berries (not other berry types) and the response options ranged
from “never” to “2 or more times per week” (not higher fre-
quency of consumption). Similarly, the assessment of olive
oil consumption was based on a single item on the type of
oil usually used at home. These constricted measures of berry
and olive oil consumption do not capture the full upper range
of intakes in the population. However, the under-assessment
of frequent berry and olive oil consumption is likely to nega-
tively bias the observed AD associations with the MIND diet
score—that is, toward the null of no effect. And finally, the
relatively short period (3.8 years on average) from diet assess-
tment to disease onset may be capturing diets in individuals
who have preclinical AD. This raises the possibility that at
the time of baseline assessment the incident cases had experi-
enced dietary changes as a result of the disease. We investi-
gated this issue by reanalyzing the data after eliminating
cases that occurred within the first 3 years of follow-up and
observed little diminishing in the estimated effect of the
MIND diet. In addition, in an earlier study of the MAP partic-
ipants we reported slower cognitive decline with higher
MIND scores over up to 10 years of follow-up [5].

Results of the study suggest that even modest adjustments
to the diet may help to reduce one’s risk of developing AD.
For example, the MIND diet score specifies just two vege-
table servings per day, two berry servings per week, and
one fish meal per week. These serving recommendations
are much lower than three to four daily servings each for
fruits and vegetables specified for a maximum score in the
DASH and MedDiet indices and six or more fish meals per
week in the MedDiet diet score.

Effective dietary recommendations have far-reaching
implications for the public health and the growing burden of
dementia in aging populations. A growing literature on the in-
dividual foods and nutrients related to brain neuroprotection
needs to be considered to specify the food groups and servings
that are most likely to protect against brain diseases. Based on
this study, high quality diets such as the Mediterranean and
DASH diets can be modified, such as in the MIND diet, to pro-
vide better protection against dementia.
Acknowledgments

The study was funded by grants (R01AG031553 and R01AG17917) from the National Institute on Aging. Potential conflicts of interest: The authors have no relevant disclosures of potential conflicts of interest.

RESEARCH IN CONTEXT

1. Systematic review: The Mediterranean-DASH Intervention for Neurodegenerative Delay, (MIND) diet, a hybrid of the cardiovascular Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets, was developed based on an exhaustive review of animal models, laboratory studies, and prospective epidemiological studies to identify the nutrients, foods, and dietary patterns related to brain health and dementia.

2. Interpretation: In a previous study the MIND diet was more predictive of slower cognitive decline than either the Mediterranean or DASH diets. In this study, we examined the relations of these diet patterns to incident Alzheimer’s disease (AD). The MIND and Mediterranean diets had comparable protective relations to AD suggesting that the MIND diet is not specific to the underlying pathology of AD.

3. Future directions: These studies indicate that a diet that is specific to brain health is possible but that further diet modifications can improve its role in AD prevention as new information on nutrition and dementia is acquired.

References

[3] Martinez-Lapiscina EH, Clavero P, Toledo E, Estruch R, Salas-Salvado J, San Julian B, et al. Mediterranean diet improves cognition: an old diet with new information on nutrition and dementia is specific to brain health is possible but that further diet modifications can improve its role in AD prevention as new information on nutrition and dementia is acquired.


