# MIND not Mediterranean diet related to 12-year incidence of cognitive impairment in an Australian longitudinal cohort study

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Review Article

# MIND not Mediterranean diet related to 12-year incidence of cognitive impairment in an Australian longitudinal cohort study

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**Abstract**

**Introduction:** Associations between the Mediterranean-DASH diet Intervention for Neurological Delay (MIND) diet and incidence of cognitive impairment have not been evaluated outside the United States.

**Methods:** We investigated MIND and Mediterranean diet relations with 12-year incidence of Alzheimer's disease/Vascular dementia (National Institute of Neurological Disorders criteria) and mild cognitive impairment (Winbald criteria) in the Personality and Total Health (PATH) Through Life cohort (n = 1220) set in Canberra, Australia: wave-1 2001-2002; wave-2 2005-2006; wave-3 2009-2010; and wave-4 2013-2014.

MIND diet and two alternate Mediterranean diet scores were calculated from the baseline food frequency questionnaire responses. Higher dietary scores signified greater adherence.

**Results:** In adjusted logistic regression models, MIND diet (OR = 0.47, 95% CI 0.24, 0.91), but not Mediterranean diet, was associated with reduced odds of 12-year cognitive impairment.

**Discussion:** Preliminary evidence suggests that protective effects of the MIND diet are geographically generalizable. Additional prospective studies are needed in diverse samples to determine the relative effects of the MIND and the Mediterranean diets against cognitive decline.

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## 1. Background

Diet may modify the risk of cognitive impairment and dementia, but evidence remains controversial. The hypothesized protective effects of a healthy dietary pattern such as the Mediterranean diet (MedDiet) occur via antioxidant and anti-inflammatory mechanisms and reduction of cardiovascular disease. A recent systematic review and meta-analysis of nine prospective cohort studies (n = 34,168) found those with the highest MedDiet consumption had 21% less risk of developing cognitive disorders than those with the lowest consumption over 2.2 to 12 years follow-up [1]. These findings are promising, but measurement bias and confounding limit the generalizability of associations between the MedDiet and risk of cognitive impairment or dementia. The MedDiet has been measured using multiple methodologies and the same MedDiet score across different samples is likely to represent varying levels of MedDiet adherence [2].

A new dietary pattern designed to reduce risk of cognitive impairment and dementia is the Mediterranean-DASH diet Intervention for Neurodegenerative Delay (MIND) diet. The MIND diet shares many food groups with the MedDiet but was developed specifically to be neuroprotective using evidence from epidemiological and animal studies. It differs from the MedDiet by allocating separate categories for green

leafy vegetables and berries, and a category for cakes and pastries. Unlike the MedDiet, fruit is not included and fish is not prescribed daily because evidence suggests 2-3 times a week is adequate for neuroprotective effects [3].

Across four studies, the MIND diet has been associated with reduced Alzheimer's disease (AD) risk [4] and better cognitive performance [5,6] but inconsistently with cognitive decline [3,6]. To date, the cognitively protective effect of the MIND diet has not been tested or compared with the MedDiet outside the United States; two of the four MIND diet studies were conducted in the same sample, the Chicago-based Memory and Aging Project (MAP).
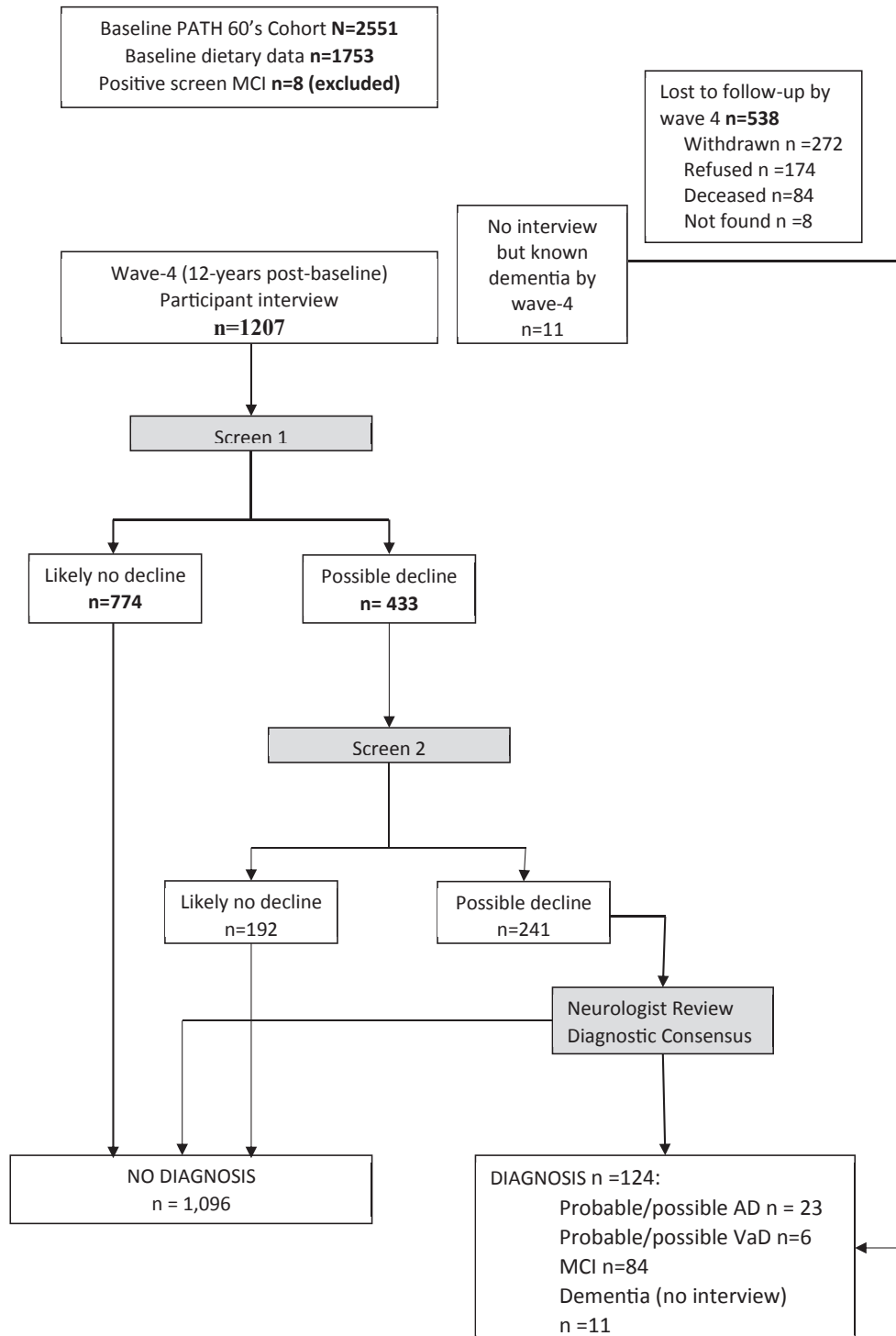


Fig. 1. Flow of participants in the PATH Through Life study and diagnoses outcomes.

Cross-country variation in food supply, dietary behaviours, and other lifestyle factors undermine the generalizability of dietary effects on risk for cognitive impairment and dementia. Clearly, studies of the MIND diet are required in other populations and geographic locations to further evaluate its protective effects.

The aim of the present study was two-fold. First, to investigate whether the cognitively protective effect of the MIND diet generalizzed from the United States to an Australian population; second, to compare the MIND diet with two alternate MedDiets to reduce risk for cognitive decline or dementia. The most commonly used MedDiet methodology [7] has not been compared previously with the MIND diet, and rarely compared with the alternate Greek MedDiet [8] to reduce risk of cognitive impairment or dementia.

## 2. Methods

### 2.1. Participants

Participants were drawn from the 60's cohort of the Personality and Total Health (PATH) Through Life study, a large 12-year longitudinal cohort study of health and aging originally situated in Canberra/Queanbeyan, Australia [9]. PATH participants were recruited via simple random sampling from the local area electoral rolls. Electoral roll registration is legally required for Australian adults over 18 years. At the baseline (2001-2002), participants were 60-64 years and subsample (n = 1753) provided dietary information. Those with baseline cognitive impairment [10] were excluded from subsequent analyses because cognitive impairment compromises the reliability of dietary recall. Follow-up interviews and cognitive assessment sessions were carried out at 3-time time points: in 2005-2006 (wave-2), 2009-2010 (wave-3), and in 2013-2014 (wave-4). The study analysis sample was n = 1220. The flow of participants from the PATH cohort into the present study is presented in Fig. 1. The study was approved by the Australian National University Human Research Ethics Committee, and all participants gave written informed consent.

### 2.2. Mild cognitive impairment and dementia

The diagnoses of 12-year incidence of mild cognitive impairment (MCI) and dementia in the PATH study has been fully described previously [11]. Briefly, neuropsychological testing and the MMSE were administered across waves 1-4 of the study. At wave-4, when participants were 72-76 years, information on cognitive and functional change over time was obtained through informant interviews conducted with a consenting proxy nominated by the participant. The informant interview comprised the Bayer Instrumental Activities of Daily Living [12] and the short 16-item Informant Questionnaire of Cognitive Decline in the Elderly [13]. Longitudinal assessment data were screened for cognitive impairment, defined as performance one standard deviation or more below sex- and education-

stratified sample means. Additional informant information for those who met screening criteria included medical and psychiatric history, neuropsychiatric symptoms and behavioural changes.

A casefile was collated for each participant who had cognitive impairment according to the screening criteria. Casefiles comprised PATH survey responses, cognitive testing data, and informant interview responses. Diagnosis of 'AD or vascular dementia (VaD) (according to National Institute of Neurological Disorders criteria [14,15]) or MCI (according to Winbald criteria [16]) were made according to casefile information. A research neurologist reviewed cases that met diagnostic criteria and a consensus diagnosis was reached with a senior clinician specializing in psychiatry [11]. The study outcome was any diagnoses of MCI or dementia.

### 2.3. Dietary assessment

At the baseline only, participants completed the Commonwealth Scientific and Industrial Research Organization semi-quantitative food frequency questionnaire (CSIRO-FFQ) [17] that assessed average dietary intake of 183 food items over the previous 12 months. Frequency options were the number of times a food was consumed per day, per week, per month, or if it was consumed rarely or never. Serving size information was also assessed. MIND diet and MedDiet scores were calculated from the baseline CSIRO-FFQ information.

#### 2.3.1. MIND diet

The MIND diet comprises 15 dietary components: ten brain healthy foods (green leafy vegetables, other vegetables, nuts, berries, beans, whole-grains, fish, poultry, olive oil, and wine) and five less healthy foods (red-meats, butter/margarine, cheese, pastries and sweets, and fried/fast food). Consumption of each MIND diet component was scored as 0, 0.5, or 1 and total MIND diet score was calculated by adding the individual component scores [3]. The CSIRO-FFQ did not include questions for butter/margarine consumption or olive oil consumption as separate items, so the maximum score possible in the current sample was 13.

#### 2.3.2. Mediterranean diet

Two Mediterranean diet scores were calculated. The first (developed by Trichopoulou [7]), regressed energy intake (kjs/day) on grams/day [18] of the following dietary categories: dairy, meat, fruits, vegetables, legumes, cereals, fish, ratio of mono to saturated fat, and alcohol intake. Sex-specific medians for the derived residuals of these categories were used as cutoffs. For beneficial components (fruits, vegetables, legumes cereals, fish, and ratio of mono to saturated fat), consumption below the median was assigned a value of 0; consumption at or above the median was assigned a value of 1. For detrimental components (meat & dairy), below-median consumption was assigned

a value of 1 and above-median consumption was assigned a value of 0. A score of 0 was assigned for no alcohol or for greater than moderate intake (moderate intake defined as greater or equal [GE] to 30 g/day; 3 standard drinks) and a score of 1 for less than 30 g/day. Possible MedDiet score ranged from 0 to 9 with a higher score equating to greater adherence.

The second Mediterranean dietary scoring method was described by Panagiotakos et al. [8] and includes 11 dietary components (nonrefined cereals, fruit, vegetables, legumes, potatoes, fish, meat and meat products, poultry, full fat dairy, olive oil, and alcohol intake). Components were scored 0-5 depending on adherence to quantities specific to the traditional Greek MedDiet. Alcohol intake was coded according to quantity of alcoholic beverages in milliliters per day, and scored nonlinearly with 0 being assigned to high consumption (>700 mL/day) or no consumption [8]. Possible score ranged from 0 to 55. Information on consumption frequency of olive oil was not available in the CSIRO-FFQ, so the maximum score was 50.

### 2.4. Covariates

Covariates replicated those used by Morris et al. [4] to optimize comparability between the current analyses and those undertaken previously in the United States. The following baseline measures were included: energy intake, age, sex, APOE ε4 status, years of education, self-report physical activity (categorized as mild, moderate, or vigorous according to the criteria from the Whitehall study [19]), mental activity participation (total number of mentally engaging activities undertaken across 6 months [20]), smoking history (never, past, current smoker), depressive symptoms (number of symptoms over the previous month [21]), and health status (i.e. self-report variables for BMI, heart disease, diabetes, stroke), and hypertension according to a systolic blood pressure (BP) reading of ≥140, diastolic BP ≥90, or self-report use of BP medication.

### 2.5. Analyses

Missing data patterns were investigated using logistic regression models to predict missingness on each variable by the other variables [22] (Appendix A) and analysis used complete cases as is appropriate in larger samples when covariate missingness is unrelated to the outcome [23]. Pearson's correlations assessed the strength of associations between the MIND diet and MedDiets. The independence of the continuous covariates was checked with Spearman's nonparametric correlations (Appendix B).

Logistic regression tested whether the dietary scores were associated with diagnoses of MCI/dementia (coded as a binary variable) 12 years after baseline. Model 1 (basic adjusted) included dietary score, energy intake, age, sex, and APOE ε4 status. Model 2 (lifestyle adjusted) included model 1 plus education, mental activity, physical activity,

smoking status, and depression. Model 3 additionally included cardiovascular-related diseases—diabetes, BMI, hypertension, heart disease, and stroke. The interaction term for the mean-centered dietary variable by APOE ε4 status was added as the final entry step. Separate models were estimated for diet scores as continuous variables and as tertiles, with low adherence as the reference category. All analyses were conducted using IBM SPSS Statistics v22.

### 3. Results

Approximately 10% (n = 124) of those who had baseline dietary data developed MCI or dementia by 12-year follow-up: MCI = 84; AD = 23; VaD = 6; any dementia = 11 (Fig. 1). The subsample of the PATH study who undertook the CSIRO-FFQ at wave-1 had significantly reduced odds of MCI/dementia at wave-4 (OR = 0.63, 95% CI 0.49, 0.82, $P = .001$). Those who were lost to follow-up over 12 years (n = 538) scored 0.32 of a point lower on the MMSE and had significantly lower baseline cognitive test scores ($P < .001$).

Table 1 presents baseline descriptive statistics for the sample according to tertile of dietary scores. Participants with greater adherence to any of the three dietary patterns were more educated, more engaged in mental activities, and had marginally lower BMI.

MIND diet scores ranged from 2.5 to 10.5 (M = 6.3, SD = 1.3). The 9-point MedDiet ranged from 0 to 9 (M = 4.6, SD = 1.7) and the Greek MedDiet score ranged from 17 to 43 (M = 30.0, SD = 4.2). In basic models adjusted for energy, age, sex, and APOE ε4 status, the MIND diet and the Greek MedDiet reduced odds of 12-year incidence of MCI/dementia. Associations remained only for the MIND diet with the inclusion of demographic, lifestyle, and cardiovascular variables. For every 1-point increase in MIND score, the odds of impairment decreased by 19% (Fig. 2). There were no associations between the 9-point MedDiet and incidence of MCI/dementia. Of the covariates, only APOE ε4 status and the mental activity variable made significant contributions to the model: OR = 2.20, 95% CI 1.33, 3.28 ($P = .001$) and OR 0.91, 95% CI 0.83, 0.99 ($P = .034$), respectively. The interaction term for MIND diet and APOE ε4 status was nonsignificant but attenuated the MIND diet estimate. Appendix C (Tables C1-C8) presents ORs, 95% CIs, and P values for all dietary variables and covariates in adjusted models.

In adjusted models, the highest tertile of MIND diet consumption was associated with a 53% reduction in the odds of impairment compared with medium and low levels of intake (Table 2). The interaction term for MIND diet and APOE ε4 status was not significant and did not attenuate the MIND diet estimate (Table C6). There were no associations between tertiles of MedDiet and MCI/dementia. The small number of AD and VaD participants precluded analyses according to diagnostic category, but in minimally adjusted

Table 1
Participant baseline characteristics according to tertiles of dietary scores*

| Sample N = 1220 | MIND diet score[†] | | | | Mediterranean diet tertile (9-point, Trichopoulou et al.)[†] | | | | Mediterranean diet tertile (Greek 55-point, Panagiotakos et al.)[†] | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Tertile 1 M = 5.28 SD = .95 | Tertile 2 M = 6.58 SD = .80 | Tertile 3 M = 7.82 SD = .80 | P value | Tertile 1 M = 2.44 SD = .73 | Tertile 2 M = 4.48 SD = .50 | Tertile 3 M = 6.68 SD = .79 | P value | Tertile 1 M = 25.3 SD = 2.45 | Tertile 2 M = 30.52 SD = 1.12 | Tertile 3 M = 35.02 SD = 1.92 | P value |
| Age mean (SD) | 62.4 (1.5) | 62.5 (1.5) | 62.5 (1.5) | 0.29 | 62.5 (1.5) | 62.4 (1.4) | 62.5 (1.5) | 0.77 | 62.3 (1.4) | 62.5 (1.5) | 62.5 (1.5) | 0.13 |
| Sex female % | 42 | 51 | 60 | <0.001 | 53 | 51 | 47 | 0.014 | 45 | 53 | 53 | 0.021 |
| APOE % ε4+missing = 62 | 25 | 25 | 27 | 0.77 | 20 | 30 | 25 | 0.006 | 23 | 25 | 30 | 0.05 |
| Total energy kj/day (SD)[†] | | | | | | | | | | | | |
| males | 9236 (2272) | 9125 (2361) | 8919 (2203) | 0.32 | 9352 (2553) | 8992 (2236) | 9112 (2143) | 0.48 | 9113 (2544) | 8933 (2175) | 9388 (2030) | 0.13 |
| females | 7783 (1956) | 7966 (2040) | 7930 (2013) | 0.57 | 7767 (1987) | 7873 (2855) | 8058 (1853) | 0.36 | 7580 (2095) | 7797 (1895) | 8350 (1975) | <0.001 |
| Education mean years (SD) missing = 1 | 13.5 (2.6) | 14.5 (2.5) | 14.7 (2.4) | <0.001 | 13.9 (2.6) | 14.2 (2.5) | 14.5 (2.4) | 0.003 | 13.5 (2.7) | 14.5 (2.4) | 14.8 (2.4) | <0.001 |
| Physical activity missing = 125[‡] | | | | | | | | | | | | |
| None/mild % | 45 | 42 | 39 | 0.09 | 45 | 45 | 37 | 0.023 | 47 | 43 | 36 | 0.001 |
| Moderate % | 30 | 35 | 35 | | 30 | 33 | 36 | | 31 | 33 | 36 | |
| Vigorous % | 12 | 13 | 15 | | 12 | 11 | 16 | | 10 | 12 | 18 | |
| Mental activities: mean undertaken in 6-ms missing = 2[§] | 7.8 (2.9) | 8.2 (2.7) | 8.7 (2.7) | <0.001 | 7.9 (2.9) | 8.1 (2.8) | 8.6 (2.7) | <0.001 | 7.7 (2.9) | 8.3 (2.7) | 8.7 (2.6) | <0.001 |
| BMI mean (SD) missing = 95[¶] | 27.2 (5.4) | 26.3 (4.7) | 25.9 (4.1) | <0.001 | 27.1 (5.3) | 26.5 (5.1) | 26.0 (4.1) | 0.025 | 27.6 (5.9) | 26.4 (4.3) | 25.4 (3.8) | <0.001 |
| Percent BMI ≤ 20 | 3.5 | 2.3 | 2.2 | 0.47 | 2.3 | 3.3 | 2.3 | 0.61 | 2.6 | 3.8 | 1.5 | 0.15 |
| Percent BMI ≥ 30 | 21 | 14 | 14 | 0.021 | 20 | 17 | 14 | 0.087 | 21 | 17 | 12 | 0.004 |
| Smoking % never; missing = 1 | 52 | 56 | 61 | 0.04 | 56 | 55 | 58 | 0.13 | 54 | 52 | 63 | 0.006 |
| Depressive symptoms %past month with none; missing = 2[#] | 32 | 35 | 41 | 0.03 | 36 | 32 | 39 | 0.15 | 31 | 38 | 38 | 0.06 |
| Heart condition % yes; missing = 1[**] | 13 | 11 | 14 | 0.32 | 10 | 12 | 15 | 0.10 | 14 | 9 | 14 | 0.037 |
| Stroke % yes[**] | 3 | 5 | 2 | 0.35 | 4 | 3 | 2 | 0.34 | 4 | 3 | 1 | 0.05 |
| Diabetes % yes[**] | 6 | 5 | 4 | 0.65 | 5 | 5 | 4 | 0.64 | 7 | 4 | 3 | 0.96 |
| Hypertension % yes[††] | 50 | 47 | 47 | 0.96 | 46 | 46 | 51 | 0.42 | 53 | 46 | 44 | 0.09 |

*For continuous variables, nonparametric tests compared distributions across the tertiles of dietary variables; chi-square tests were used for categorical variables.

[†]Calculated from the Commonwealth Scientific and Industrial Research Organization semi-quantitative food frequency questionnaire [17].

[‡]Self-report frequency and intensity categorized into mild, moderate, and vigorous according to Whitehall criteria [19].

[§]Assessed with the RIASEC activity scales [20].

[¶]Self-report kg/m$^2$.

[#]Goldberg Depression Scales [21].

[**]Self-reported: binary variable for does or does not have the condition.

[††]Systolic BP ≥140, diastolic BP ≥90, or self-report use of BP medication.
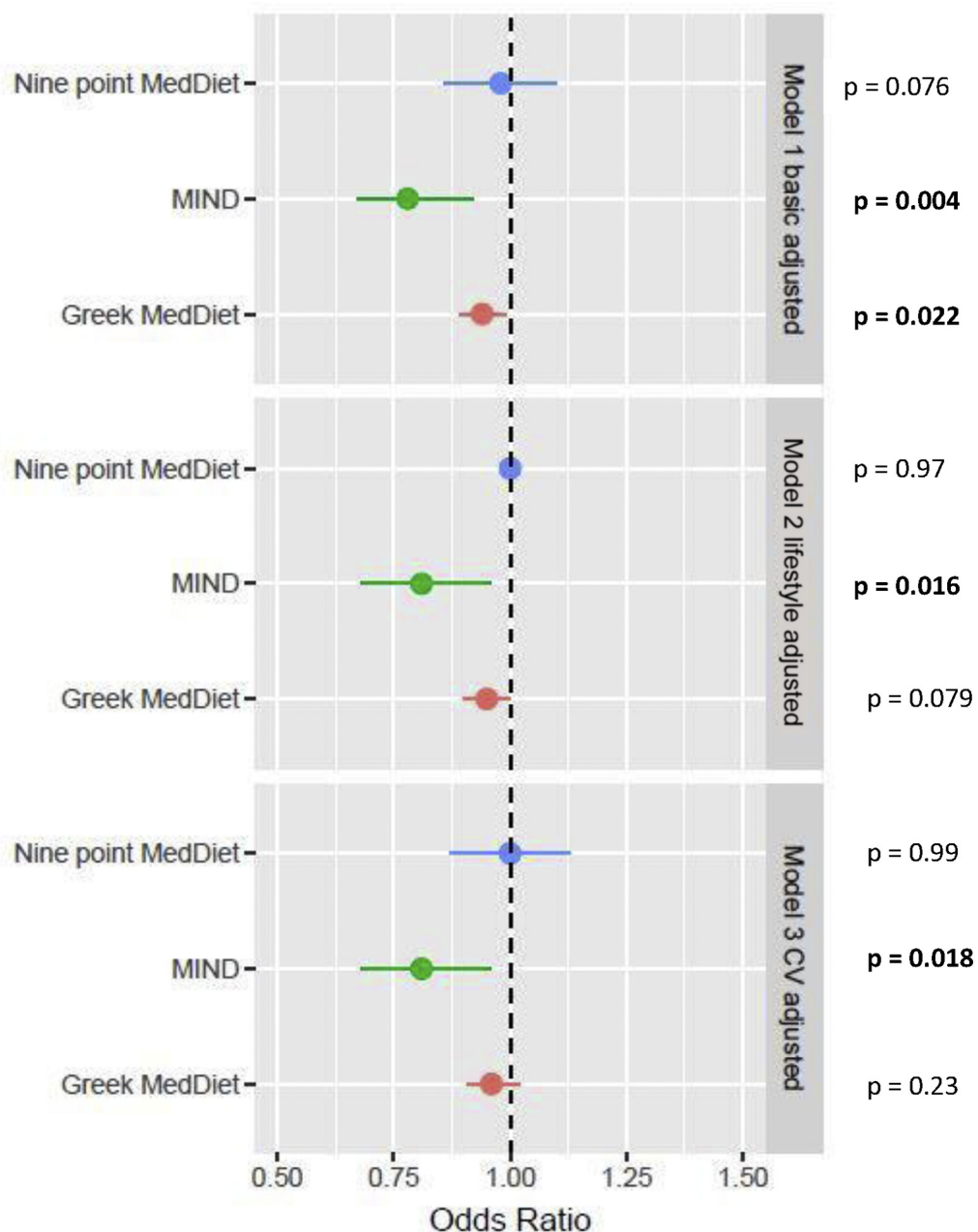
Fig. 2. Odds ratios (ORs) and 95% confidence intervals (CIs) of estimated effects of the MIND diet, the 9-point Mediterranean diet and the Greek Mediterranean diet on 12-year incidence of cognitive impairment in the PATH Through Life study.

models (age, sex, kilojoules/day), the MIND diet was protective against incidence of dementia (OR = 0.72, 95% CI 0.54, 0.95) but not MCI (OR = 0.85, CI 0.70, 1.0).

Post hoc analyses examined the relative importance of the individual MIND components (Appendix D). Separate MIND scores excluded each MIND dietary component while including this component as a covariate in fully adjusted logistic regression models [6]. Nuts was the only component independently associated with MCI/dementia.

Sensitivity analyses addressed potential reverse causality by excluding those who scored in the lowest 10% on the baseline cognitive measures. The strength of the associations did not change when removing low scorers for three of the four tasks. Results are presented in Appendix E.

## 4. Discussion

We have provided evidence that the cognitively protective effects of the MIND diet generalize to a population outside the United States. Greater MIND diet adherence was associated with 19% reduced odds of developing clinically diagnosed MCI/dementia after 12-years of follow-up

Table 2
Odds ratios (ORs) and 95% confidence intervals (CIs) of estimated effects for intake tertiles of the MIND diet, the 9-point Mediterranean diet and the Greek Mediterranean diet on 12-year incidence of cognitive impairment in the PATH Through Life study

| Dietary pattern (n = 961) | Tertile 1 lowest consumption | Tertile 2 medium consumption | Tertile 3 highest consumption | P for linear trend |
|---|---|---|---|---|
| MIND diet | | | | |
| Score range | | | | |
| *Model 1 basic adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.91(0.56, 1.47) | 0.42 (0.22, 0.79) | 0.008 |
| †Model 2 lifestyle adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.94 (0.57, 1.55) | 0.47 (0.24, 0.90) | 0.024 |
| ‡Model 3 CV adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.94 (0.57, 1.56) | 0.47 (0.24, 0.91) | 0.026 |
| 9-point MedDiet | | | | |
| Score range | | | | |
| *Model 1 basic adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.85 (0.46, 1.57) | 1.17 (0.72, 1.89) | 0.51 |
| †Model 2 lifestyle adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.88 (0.47, 1.63) | 1.30 (0.79, 2.13) | 0.28 |
| ‡Model 3 CV adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.87 (0.47, 1.62) | 1.30 (0.79, 2.15) | 0.29 |
| Greek MedDiet | | | | |
| Score range | | | | |
| *Model 1 basic adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.71 (0.43, 1.20) | 0.67 (0.38, 1.15) | 0.67 |
| †Model 2 lifestyle adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.75 (0.44, 1.27) | 0.75 (0.42, 1.33) | 0.33 |
| ‡Model 3 CV adjusted | | | | |
| OR (95% CI) | 1 (referent) | 0.77 (0.45, 1.30) | 0.77 (0.43, 1.39) | 0.40 |

*Model 1: MIND diet score, energy intake, age, sex, and *APOE ε4* status.

†Model 1, plus education, mental activity, physical activity, smoking status, and depression.

‡Model 3: Models 1 and 2 plus binary variables for diabetes, BMI, hypertension (systolic blood pressure (BP) reading of ≥140, diastolic BP ≥90 or use of BP medication), heart disease, and stroke.

with 53% reduction in the odds of impairment in the highest tertile of consumption.

In accord with others, we compared the effects of the MIND diet with those of the MedDiet [3–5]. Uniquely, however, we evaluated the MedDiet using two methodologies: the traditional Greek 55-point MedDiet [8] and the more common 9-point MedDiet [7] that has not been compared with the MIND diet previously. After covariate adjustment, no significant relationship existed between either version of the MedDiet and the odds of developing MCI/dementia.

Greek MedDiet adherence was comparable across the PATH and MAP cohorts, but protective effects in the MAP cohort [4] were not replicated in PATH. Multiple foods are consumed in Western-style diets that are not assessed in the MedDiet such as processed dairy products (ice cream, flavoured milk), salted biscuits and snacks, soft drinks, and processed meats (separate from red-meat) [24]. Consumption patterns of these non-Mediterranean foods within tertiles of Greek MedDiet consumption may have differed between PATH and MAP cohorts, so modifying MedDiet associations with cognitive health. The MIND diet, on the other hand, specifically includes items for "pastries and sweets" and "butter and margarine", and "fast fried foods". In the Nurses' Health Study, the lower consumption of pastries and sweets, and butter and margarine drove

cross-sectional association between the MIND diet and better verbal memory [6], which highlights the relevance of capturing consumption of these foods.

Associations between the MedDiet and incidence of cognitive impairment have been assessed primarily using the 9-point MedDiet score, and effects have been confined predominantly to the United States [1]. In PATH, an earlier study conducted 4 years after baseline found no associations between the 9-point MedDiet and cognitive decline or incidence of MCI [25]. Potentially, after 12-years, more participants would have developed impairment, thereby providing more power to detect associations with the 9-point MedDiet. As with the Greek MedDiet, the null result may be due to nonassessment of relevant foods, but also by the "floating metric of intake" [2] that occurs with the 9-point MedDiet when sample-specific medians are used to define scoring cutoffs, resulting in noncomparable findings.

Limitations of our study include lack of an item in the CSIRO-FFQ to assess if olive oil was the primary oil for cooking and eating. Olive oil is considered to drive MedDiet and MIND diet protective effects due to its antioxidant properties and its cardiovascular benefits [26]. Despite nonassessment of olive oil, the MIND diet score was protective against impairment in PATH. Possibly, high MIND diet consumers had relatively high olive oil consumption also, even if olive oil was not

captured by the FFQ; alternatively, olive oil may not be critical to the MIND diet's beneficial effect.

In our analyses, we were unable to evaluate dietary effects on time to MCI/dementia diagnoses. There were a relatively small number of MCI/dementia cases at wave-2 and wave-3, and these cases were not stable over time [27]. Our findings, therefore, are not directly comparable with those from the MAP cohort where proportional hazard models examined time in years to diagnosis of AD [4]. Sensitivity analysis suggested our choice to use complete cases did not bias estimates and effects were robust to the reduced sample size. Sensitivity analyses to test the impact of individual MIND diet components found nuts were the only item to independently predict odds of MCI/dementia. Nuts contain nutrients that benefit cardiometabolic and vascular health that in turn support brain health and cognitive function [28]. It should be highlighted, however, that the MIND diet's protective effects are likely to occur through the synergistic action of its components [4].

Generalizability of our study was limited due to dietary data being available for a subsample of the PATH cohort only. The stability of the MIND diet over follow-up was unknown, and we cannot discount the possibility that unmeasured confounding factors over time explained associations between MIND diet score and reduced odds of impairment. However, these same factors would likely have driven protective effects for the MedDiet also, given that the MedDiet and the MIND diet represent very similar healthful dietary lifestyles.

The study design precludes causal inferences regarding the protective effect of the MIND diet on incidence of MCI/dementia, but participants were relatively young at the baseline (aged 60-64 years) and the cohort was followed for 12 years, so reverse causation was unlikely to explain the observed associations. In addition, results remained substantially unchanged when the bottom 10% of cognitive scores were removed from the sample.

The small numbers of dementia cases prevented stratifying analyses by diagnoses, so distinguishing if the MIND diet was specifically protective against AD was impossible. Future randomized MIND diet interventions with vascular health and AD-relevant biomarkers as outcomes would elucidate the pathways and mechanisms by which the MIND diet may be protective of cognitive health.

Study strengths included a large population-based sample who had undergone comprehensive screening and diagnosis for cognitive impairment according to standard clinical criteria. Covariates replicated those used previously in a US-based study of MIND diet and incidence of AD which contributed to the comparability of findings across cohorts. Finally, we tested effects for both the Greek MedDiet and the 9-point MedDiet because outcomes may depend on MedDiet scoring methodology [2].

Dietary intake is a modifiable lifestyle factor that potentially mitigates risk of late-life cognitive impairment [29], but there is a need for consistent epidemiological evidence to inform dietary guidelines for cognitive health [30]. Our study has provided crucial evidence that the associations between the MIND diet and reduced risk of developing MCI/dementia are generalizable to a younger population geographically remote and culturally different from the United States. MIND diet adherence promotes consumption of additional dietary components to those assessed by the MedDiet, and is a promising approach to capturing dietary intake that may be specifically relevant to preventing cognitive decline.

## Acknowledgments

## Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jalz.2018.12.011.

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### RESEARCH IN CONTEXT

1. Systematic review: The MIND diet is a recently developed hybrid of the healthful DASH and Mediterranean diet (MedDiet) but incorporates foods specifically relevant to brain health. Initial studies found MIND diet was more effective than the MedDiet in reducing risk cognitive decline and had comparable relations with Alzheimer's disease (AD) risk.

2. Interpretation: To date, MIND diet has been evaluated in older Americans only. Our study tested if the effects of MIND diet generalized outside the United States and, uniquely, compared MIND with two versions of the MedDiet.

3. Future directions: Our study found the MIND diet, but neither of the MedDiets protected against 12-year incidence of MCI and dementia. Associations between diet and cognitive decline vary according to geographic, demographic, and cultural factors. MIND diet effects need replication in diverse populations. Importantly, RCTs of MIND diet on vascular health and AD-related biomarkers are required to identify its protective mechanisms and pathways.

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