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Original Article

Association between plant-based diets and incident dementia: results from prospective cohort studies and a meta-analysis

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ABSTRACT

Background: Plant-based diets are increasingly advocated for their health benefits, yet their associations with dementia risk remains inconclusive. We evaluated the associations between plant-based dietary patterns and dementia risk across three prospective cohorts and a meta-analysis.
Methods: Cohort analyses included the Health and Retirement Study (HRS; $N = 6642$), Framingham Heart Study Offspring cohort (FOS; $N = 3045$), and Whitehall II study (WHII; $N = 8219$). Participants were aged $\geq$45 years and free of dementia at baseline. The overall plant-based diet index (PDI), healthful plant-based diet index (hPDI) and unhealthful plant-based diet index (uPDI) were calculated from validated food frequency questionnaires. Further, a meta-analysis was conducted incorporating data from 5 cohort studies ($N = 207{,}981$).
Results: In the cohort analyses, 891 incident dementia cases were identified over 166,762 person-years. In multivariable-adjusted Cox proportional hazard models, higher scores in PDI and hPDI were associated with lower risk of dementia (highest vs. lowest tertile: pooled HR for PDI = 0.70, 95% CI, 0.53–0.92, p for trend <0.001; pooled HR for hPDI = 0.71, 0.48–1.06, p for trend = 0.03). Main contributors to lower risk were higher intake of vegetables, nuts, tea or coffee, and legumes. Conversely, higher uPDI was associated with higher dementia risk (highest vs. lowest tertile: pooled HR = 1.42, 1.19–1.70, p for trend <0.001). In the meta-analysis, individuals in the highest hPDI tertile had 21% lower dementia risk, and those in the highest uPDI tertile had 24% higher risk.
Conclusions: The healthful plant-based diet was associated with lower risk of dementia, whereas the unhealthful plant-based diet was linked to higher risk. These findings support recommendations to adopt diets rich in healthy plant foods for dementia prevention.

1. Introduction

The number of people living with dementia worldwide is estimated at 57 million and is projected to triple by 2050 [1]. Given the absence of cure to halt or reverse the course of dementia, preventive approaches have become increasingly crucial. Alzheimer's disease and related

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dementia (ADRD) are characterized by a prolonged pre-clinical stage before clinical onset [2], offering a critical window for preventive interventions through lifestyle modifications, particularly in dietary patterns, before clinical symptoms manifest.

Plant-based dietary patterns, characterized by higher intake of plant foods and lower consumption of animal foods, have been recommended by their dual health and environmental benefits [3,4]. Extensive studies have established their cardiometabolic benefits, demonstrating consistent associations between a plant-based diet and lower risks of cardiovascular disease (CVD) [5,6], type 2 diabetes [7], and overall mortality [8–10]. However, the neuroprotective potential of these dietary patterns remains unclear [11]. While some studies investigated associations between plant-based dietary patterns and cognitive function [12–14], cognitive decline [15], brain imaging biomarkers [16], and risk of dementia [17,18], the overall evidence remained limited and inconclusive. For instance, a prospective cohort study from the UK Biobankwith a median follow-up of 10 years reported that higher adherence to the healthful plant-based diet index (hPDI) was associated with a lower risk of dementia (hazard ratio [HR]for comparing extreme quintiles = 0.82, 95% CI, 0.68–0.98), whereas the unhealthful plant-based diet index (uPDI) was associated with a higher risk of dementia (HR = 1.29, 1.08–1.53) [17]. Conversely, the Rotterdam Study found no statistically significant associations between plant-based diets and incident dementia despite a mean follow-up of 14.5 years (HR = 0.89, 95% CI, 0.74–1.06 for hPDI; HR = 1.05, 0.87–1.26 for uPDI) [18]. These discrepancies may stem from variations in diet composition, diverse study populations, and the study design.

In the current study, we integrated three cohorts of middle-aged and older adults from the US and UK to examine the associations between three plant-based diet indices (the overall plant-based diet index [PDI], hPDI, and uPDI) and subsequent risk of dementia. Building upon these cohort analyses, we conducted a meta-analysis incorporating five Western cohort studies to enable a more robust investigation, while noting that their applicability to non-Western cultural contexts remains to be established.

2. Methods

2.1. Study population

This prospective study used data from three population-based cohorts: the Health and Retirement Study (HRS) [1], the Framingham Heart Study Offspring cohort (FOS) [2], and the Whitehall II study (WHII) [3]. The HRS is a national prospective cohort study of U.S. adults aged 51 years and older, initiated in 1992 [19,20]. As part of the 2013 Health Care and Nutrition Study (HCNS), 8035 HRS respondents completed dietary assessment [21], followed by cognitive assessments conducted approximately every two years. The Framingham Heart Study, established in 1948, is a community-based, prospective cohort study comprising six sub-cohorts [22]. The Framingham Heart Study Offspring cohort (FOS) enrolled 5124 offspring of the original cohort members and their spouses in 1971. Dietary assessments were administered during examinations 5 (1991–1995), 6 (1995–1998), and 7 (1998–2001), along with continuous dementia surveillance and diagnosis [23]. The WHII, initiated in 1985–1988, recruited 10,308 civil servants aged 35 to 55 years in the United Kingdom [24]. Dietary assessments were conducted during phases 3 (1991–1993), 5 (1997–1999), and 7 (2002–2004) [25,26] with dementia surveillance utilizing electronic health record linkage annually during follow up. Ethical approval for the protocols of all three studies was obtained from the respective institutional review boards (IRB) (University of Michigan for HRS, Boston University Medical Center for FOS, and the joint University College London and University College London Hospitals committee for WHII). All participants provided written informed consent prior to participation.

For the present analysis, we included HRS participants from the 2013 HCNS through 2020, FOS participants from examination 7 (1998–2001) through 2018, and WHII participants from phase 7 (2002–2004) through 2016. We included participants aged 45 years and older who completed one or more valid food frequency questionnaires (FFQs), defined as having reasonable daily energy intake of 500–4500 kcal to mitigate the influence of potential outliers. Participants with dementia at baseline or those who developed dementia within the first two years of follow-up were excluded to avoid reverse causality. Ultimately, the final analysis included 6642 HRS participants, 3045 FOS participants, and 8219 WHII participants (Fig. 1). This study was approved by IRB of Zhejiang University School of Public Health and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

2.2. Dietary assessment and plant-based diet indices calculation

Dietary information across all three cohort studies was collected using semi-quantitative FFQs, based on the extensively validated FFQ developed by Willett and colleagues [27]. The reliability and validity of the questionnaires have been previously described [25,28–30]. Participants were asked how often, on average, they consumed a standard portion size of each food item over the past year.

To assess adherence to plant-based dietary patterns, three plant-based diet indices were created, including the PDI, hPDI, and uPDI. The scoring methodology was based on the methods by Satija et al. [31], which has been widely applied in nutritional epidemiological studies [3,6,7]. A total of 18 food groups were included and categorized based on nutrient and culinary similarities, incorporating seven healthy plant food groups (whole grains, fruits, vegetables, nuts, legumes, tea or coffee, vegetable oils), five less healthy plant food groups (fruit juice, refined grains, potatoes, sugar sweetened beverages [SSB], sweets and desserts), and six animal food groups (animal fat, dairy, eggs, fish or seafoods, meat, miscellaneous animal-based foods). The 18 food groups were first ranked into quintiles of consumption. For certain food groups where quintile categorization was not feasible (e.g., nuts in FOS, SSB in HRS, nuts and potatoes in WHII), we implemented tertile-based categorization. For vegetable oils, participants were dichotomously classified based on whether they reported vegetable oil as their 'Primary cooking oil'. The indices were scored as follows: For PDI, participants received positive scores for each food item in plant food groups (5 for the highest quintile/tertile of consumption and 1 for the lowest), whereas reverse scores for each food item in animal food groups (1 for the highest consumption group and 5 for the lowest). For hPDI, positive scores were assigned to each food item in healthy plant food groups and reverse scores for each food item in less healthy plant food groups and animal food groups. Finally, for uPDI, positive scores were given to less healthy plant food groups, and healthy plant food groups and animal food groups received reverse scores. The 18 food group scores for an individual were summed to obtain the indices, with a total score range of 18 to 90. A higher score indicated greater adherence to the corresponding dietary pattern. In the WII cohort, information on vegetable oil consumption was not available. Therefore, the original score, ranging from 17 to 85, was rescaled to match the range of 18 to 90. Detailed components and scoring criteria are summarized in the **Supplemental Table 1**.

2.3. Ascertainment of dementia

The identification of incident all-cause dementia varied across the three cohorts. Briefly, HRS ascertained dementia using the Langa-Weir Classification algorithm [32,33], FOS conducted a dementia review panel for dementia identification [23], and WHII ascertained dementia through linkages to electronic health record databases [26]. Details are described in **Supplemental Methods**.

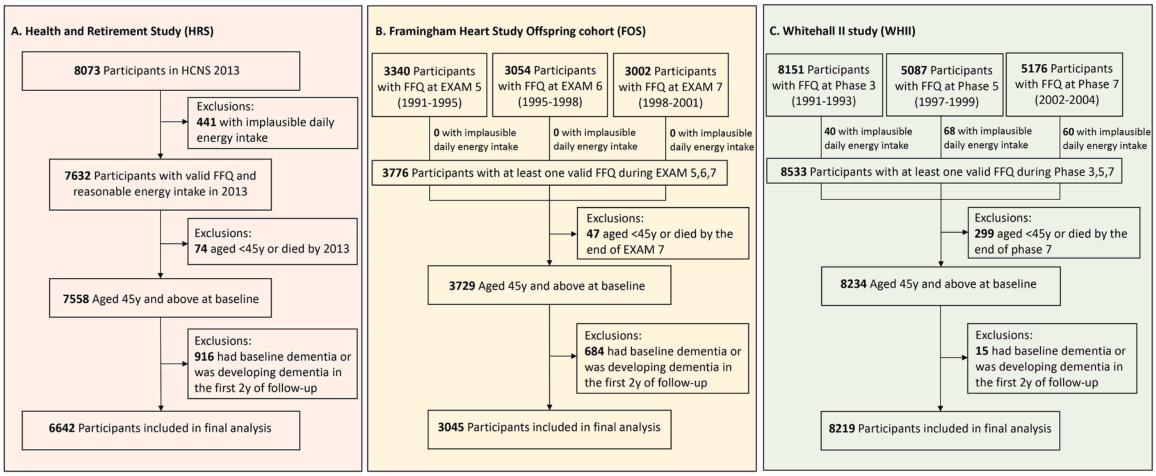

Fig. 1. Flowcharts of participants inclusion in the cohort analyses.

2.4. Assessment of covariates

Sociodemographic factors consisted of age, sex, race and ethnicity, years of education, household income (available in the HRS and FOS), and marital status. FOS did not take participant race into account because its racial makeup was predominantly White of European descent. Health behavioral factors consisted of current smoking status, current alcohol consumption, frequency of vigorous physical activity, body mass index (BMI) categories, and total energy intake. Health conditions included hypertension, diabetes, hypercholesterolemia (available in the FOS and WHII), CVD, stroke, and depressive symptoms. Details on the assessments of health conditions appear in the **Supplemental Methods**.

2.5. Statistical analysis

The baseline characteristics were presented for all participants and according to tertiles of PDI. To better reflect long-term dietary habits and to reduce within-person variation, we calculated the cumulative average diet indices by averaging the repeated FFQs in FOS (Exam 5–7) and WHII (Phase 3, 5, 7). The PDIs were grouped into tertiles to allow sufficient numbers of dementia cases in each category.

We used Cox proportional hazards models to examine the associations between the three plant-based diet indices and incident all-cause dementia. Person-years of follow-up were calculated from the study baseline to the date of incident dementia, death, loss to follow-up, or end of follow-up, whichever occurred first. Multivariable models adjusted for age, sex, race/ethnicity, total energy intake, years of education, household income, marital status, current smoking status, current alcohol consumption, BMI categories, frequency of vigorous physical activity, hypertension, diabetes, hypercholesterolemia, CVD, stroke, and depressive symptoms. The proportional hazards assumption was tested and verified using the Schoenfeld residuals. Missing values were imputed using single imputation with mode/median (for $<5\%$ missing value) or multiple imputation with the 'mice' package in R (for $\geq 5\%$ missing value). Three indices were modeled as categorical (in tertiles) and continuous (per 10-point increment) variables in the analysis. The linear trend across tertiles was conducted by assigning median values to each tertile of score and entering it as a continuous variable in the model. In the analysis of individual food groups, we included all individual food group variables simultaneously in the final adjusted models to allow mutual adjustment. All analyses were performed separately for each cohort and then the cohort-specific HRs were pooled with the use of random-effects models to account for between-study heterogeneity.

We conduced stratified analyses to examine potential effect modifications by key covariates, including age, sex, current smoking status, BMI categories, and history of major health conditions. The interactions between covariates and the diet indices were tested by adding the cross-product term and using the likelihood ratio test. Several sensitivity analyses were performed to assess the robustness of our findings. First, instead of using repeated dietary measurements, we reassessed the associations between baseline-only (recent) plant-based diet indices and incident dementia (in FOS and WHII). Second, we restricted the analyses to participants without stroke, diabetes, and CVD at baseline because dietary behaviors could be influenced by major chronic diseases. Third, given the long preclinical stage of dementia, we excluded events that occurred within the first 5 years of follow-up to minimize possible reverse causation. Fourth, based on previously documented beneficial effects of fish on health outcomes [34], we constructed a modified hPDI by assigning positive scores to fish and aquatic products [31]. Similarly, since poultry is relatively low in fats and cholesterol, we constructed another modified hPDI where poultry and other meat components were treated as two separate entities.

2.6. Meta-analysis

We performed a systematic search and meta-analysis, incorporating the present data along with previous prospective cohort studies that examined the association between PDIs and risk of dementia in the general population. The meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines (**Supplemental Figure 1**), and the systematic review protocol was registered on INPLASY [35]. The systematic search was completed on June 8th, 2025, using several online databases such as PubMed, Embase, and Web of Science.

Two authors (J.S and Y.G) independently performed the literature and data extraction. A detailed search strategy is provided in **Supplemental Table 2**. Eligibility criteria, based on PECOS framework, are displayed in **Supplemental Table 3**. Data were extracted from the included articles, including the name of first author, publication year, cohort name and study population, country where the cohort was conducted, baseline age ranges, follow-up duration, approaches for dietary assessment, methods for outcome ascertainment, as well as risk estimates and 95% CIs from adjustment for potential confounders.

We calculated the HRs for dementia risk associated with three plant-based diet indices for each study. Pooled risk estimates for the highest vs. lowest categories were computed using the random-effects models. Heterogeneity was examined using Cochran Q-test and the I^2 statistic (R 'meta' package). The Risk Of Bias (RoB) was assessed using the Risk Of Bias In Non-randomized Studies-of Exposures (ROBINS-E) tool. Two reviewers (J.S and Y.G) independently assessed RoB for each included study, with any disagreements resolved by consensus. The RoB assessment covered seven domains of bias: 1) Confounding, 2) measurement of exposure, 3) selection of participants into the study (or into the analysis), 4) post-exposure interventions, 5) missing data, 6) measurement of the outcome, and 7) selection of the reported results. Each domain as well as the overall RoB were judged as low, some concerns, or high.

All analyses were performed with the SAS version 9.4 (SAS Institute Inc) and R 4.1.0. We considered two-sided *P* values <0.05 to be statistically significant.

3. Results

3.1. Cohort analyses

The final study sample included 6642 participants from the HRS (mean [standard deviation, SD] baseline age, 66.4 [10.3] years; 2737 [58.8%] males), 3045 participants from the FOS (mean [SD] age, 64.4 [9.2] years; 1382 [45.4%] males), and 8219 participants from the WHII (mean [SD] age, 62.2 [6.0] years; 5687 [69.2%] males). In all cohorts, participants with higher PDI socres were more likely to be older, more physical active, more educated, non-current smokers, and to have a normal weight, higher total energy intake, and higher household income. Detailed baseline characteristics of all participants and according to PDI tertiles are presented in Table 1 and **Supplemental Table 4**.

The mean PDI scores were 53.1 (SD, 6.3) in HRS, 54.1 (SD, 6.8) in FOS, 54.1 (SD, 6.2) in WHII. Mean hPDI scores were 54.0 (SD, 8.3) in HRS, 53.8 (SD, 8.2) in FOS, 54.7 (SD, 7.4) in WHII. Detailed mean and standard deviation (SD) consumption of each food groups and diet indices for each cohort are presented in the **Supplemental Table 5**.

During a total of 166,762 person-years of follow-up across three cohorts, we documented 891 incident dementia cases (430 in HRS, 242 in FOS, and 219 in WHII). In multivariable-adjusted models, higher adherence to PDI and hPDI was associated with a lower risk of dementia, whereas uPDI was associated with a higher dementia risk (Table 2). Comparing the highest with the lowest tertiles, the pooled HRs for incident dementia were 0.70 (95% CI, 0.53–0.92) for the PDI, 0.71 (0.48–1.06) for the hPDI, and 1.42 (1.19–1.70) for the uPDI (all *p* for trend < 0.05).

Cohort-specific analyses demonstrated generally consistent patterns, with both PDI and hPDI being significantly associated with a lower risk of incident dementia in HRS (T3 vs T1: HR = 0.59, 95% CI, 0.45-0.77 for PDI; HR = 0.76, 0.59-0.99 for hPDI) and FOS (T3 vs T1: HR = 0.64, 0.46-0.89 for PDI; HR = 0.48, 0.34-0.70 for hPDI). Conversely, higher adherence to uPDI was significantly associated with 44% higher dementia risk in both HRS and FOS (T3 vs T1). However, the WHII cohort showed no significant associations between three plant-based diet indices and dementia risk (Table 2).

In the stratified analyses, the associations of PDI, hPDI and uPDI with dementia risk generally did not vary significantly across strata defined by age, sex, current smoking status, BMI categories, and history of major health conditions (**Supplemental Figure 2**). Notably, in the HRS, the inverse association between PDI and dementia was stronger among participants with hypertension ($HR_{T3\ vs\ T1} = 0.50$, 95% CI, 0.35-0.72) compared to those without hypertension (*p* for interaction = 0.01).

When evaluating the contributions of the three food categories in relation to dementia risk, a significant inverse association was found for the aggregated intake of all healthy plant foods category (pooled $HR_{T3\ vs\ T1} = 0.55$, 95% CI, 0.46-0.66) (Fig. 2). However, non-significant associations were observed for the aggregated intake of all less healthy plant foods and all animal foods categories. Potential individual contributors were higher consumption of tea or coffee, legumes, vegetables, and nuts (Fig. 2).

The results of main analyses remained generally consistent in sensitivity analyses, when using baseline-only (or recent) diet indices instead of the average of indices from repeated dietary assessments (**Supplemental Table 6**), when excluding dementia cases within the first five years to address potential reverse causation (**Supplemental Table 7**), as well as when applying two modified hPDI scoring methods (**Supplemental Table 8**). Although our modified hPDI scoring shares certain similarities with Mediterranean diets through its positive scoring of fish or poultry, it fundamentally retains the hPDI's distinctive emphasis on improving the quality of plant foods. Furthermore, consistent associations between PDIs and dementia risk were observed in all three cohorts, both among participants without chronic diseases and those with chronic diseases at the study baseline (**Supplemental Table 9**).

3.2. Meta-analysis

Our initial systematic review identified three eligible studies, two of which [17,18] were included in the final quantitative analysis. Specifically, after screening two studies from the UK Biobank [16,17], we included the one by Wu et al. due to its larger sample size and coverage of three plant-based diet indices. The HRs comparing the highest to lowest tertiles were derived from the original quintile comparisons in the source articles. The characteristics of the included studies are shown in the **Supplemental Table 10**. The risk of bias assessment of included studies (two eligible publications and three cohorts in present study) is provided in the **Supplemental Table 11**. All studies were rated as 'some concerns'.

The meta-analysis for the associations between three plant-based diet indices and the risk of dementia encompassed 207,981

Table 1
Baseline Characteristics of the study participants in three cohort studies.

	Health and Retirement Study	Framingham Heart Study	Whitehall II study
N	6642	3045	8219
Age group, y (%)			
45–59	2072 (31.2)	1020 (33.5)	2318 (28.2)
60–69	1944 (29.3)	1095 (36.0)	3852 (46.9)
70–79	1847 (27.8)	764 (25.1)	2049 (24.9)
80+	779 (11.7)	166 (5.5)	NA
Sex, Female (%)	3905 (58.8)	1663 (54.6)	2532 (30.8)
Race, White (%)	5169 (77.8)	NA	7476 (91.2)
Total energy, mean (SD), kcal/day	1782.3 (738.8)	1864.0 (553.1)	2021.5 (583.0)
Education duration, mean (SD), y	13.2 (2.8)	14.2 (2.6)	15.3 (4.0)
Household income (%)			
Tertile 1	1726 (26.0)	878 (40.0)	NA
Tertile 2	2359 (35.5)	708 (32.3)	NA
Tertile 3	2557 (38.5)	607 (27.7)	NA
Current smoker (%)	784 (11.9)	387 (12.7)	819 (10.0)
Current drinker (%)	2710 (40.9)	1901 (72.2)	6643 (81.2)
Body mass index (%)			
<25.0 kg/m^2	1419 (21.4)	941 (30.9)	3239 (39.4)
25.0-<30.0 kg/m^2	2240 (33.7)	1233 (40.5)	3546 (43.1)
≥30.0 kg/m^2	2983 (44.9)	871 (28.6)	1434 (17.4)
Vigorous physical activity (%)			
>1 times/week	1871 (28.2)	1396 (46.8)	1957 (23.8)
1–4 times/month	1467 (22.1)	495 (16.6)	1681 (20.5)
<1 time/month	3304 (49.7)	1095 (36.7)	4581 (55.7)
Hypertension (%)	3761 (56.6)	1620 (53.2)	4684 (57.0)
Hypercholesterolemia (%)	NA	1875 (61.6)	7334 (89.2)
Cardiovascular diseases (%)	1436 (21.6)	461 (15.1)	2821 (34.3)
Diabetes (%)	1356 (20.4)	299 (9.8)	1568 (19.1)
Stroke (%)	415 (6.2)	59 (1.9)	176 (2.1)
Depressive symptoms (%)	758 (11.4)	383 (12.8)	946 (11.5)
Follow-up durations, median (IQR), y	7.0 (5.0–7.0)	10.7 (7.4–14.3)	12.5 (11.9–12.7)

* NA, not applicable. The Framingham Study did not take participant race into account because its racial makeup was predominantly White of European descent.

Table 2
Hazard ratios for incident dementia according to the tertiles of plant-based diet indices.

	Health and Retirement Study			Framingham Heart Study			Whitehall II study			Pooled HR (95% CI) Random effect*
	Median score (IQR)	Cases / Total	HR (95% CI)	Median score (IQR)	Cases / Total	HR (95% CI)	Median score (IQR)	Cases / Total	HR (95% CI)	
PDI										
Tertile 1	47 (45–49)	177/ 2360	1 [Reference]	48 (45–50)	98/1097	1 [Reference]	49 (46–51)	87/3209	1 [Reference]	1 [Reference]
Tertile 2	54 (52–55)	151/ 2365	0.83 (0.66, 1.03)	54 (53–56)	78/1005	0.81 (0.59, 1.10)	55 (54–56)	66/2693	0.88 (0.63, 1.22)	0.84 (0.71, 0.98)
Tertile 3	60 (58–62)	102/ 1917	0.59 (0.45, 0.77)	61 (59–64)	66/943	0.64 (0.46, 0.89)	60 (59–64)	66/2317	0.94 (0.66, 1.33)	0.70 (0.53, 0.92)
Per 10-point increment			0.69 (0.59, 0.82)			0.71 (0.58, 0.87)			0.95 (0.75, 1.20)	0.77 (0.63, 0.92)
p-trend			<0.001			0.01			0.67	<0.001
hPDI										
Tertile 1	46 (43–48)	162/ 2288	1 [Reference]	46 (42–48)	85/1049	1 [Reference]	48 (44–51)	84/3143	1 [Reference]	1 [Reference]
Tertile 2	54 (52–56)	148/ 2150	0.92 (0.72, 1.16)	54 (52–56)	88/1101	0.68 (0.50, 0.94)	55 (54–57)	76/2661	1.12 (0.81, 1.55)	0.89 (0.68, 1.16)
Tertile 3	62 (60–66)	120/ 2204	0.76 (0.59, 0.99)	63 (60–65)	69/895	0.48 (0.34, 0.70)	62 (60–66)	59/2415	0.99 (0.69, 1.44)	0.71 (0.48, 1.06)
Per 10-point increment			0.82 (0.72, 0.94)			0.70 (0.94, 0.98)			1.10 (0.90, 1.36)	0.85 (0.67, 1.10)
p-trend			0.04			<0.001			0.97	0.03
uPDI										
Tertile 1	48 (44–50)	130/ 2401	1 [Reference]	47 (43–49)	66/1051	1 [Reference]	49 (46–51)	73/3135	1 [Reference]	1 [Reference]
Tertile 2	57 (54–58)	143/ 2217	1.20 (0.94, 1.54)	55 (53–57)	76/1080	0.99 (0.70, 1.39)	55 (54–56)	64/2387	1.19 (0.35, 1.68)	1.13 (0.93, 1.37)
Tertile 3	64 (62–68)	157/ 2024	1.44 (1.10, 1.87)	63 (60–66)	100/914	1.44 (1.03, 2.03)	61 (59–65)	82/2697	1.36 (0.93, 1.89)	1.42 (1.19, 1.70)
Per 10-point increment			1.22 (1.07, 1.40)			1.28 (1.07, 1.53)			1.14 (0.93, 1.38)	1.22 (1.11, 1.34)
p-trend			0.01			0.03			0.06	<0.001

Models were adjusted for age group (5-year groups), sex (male or female), race/ethnicity (white or non-white), total energy intake (in kcal), education (in years), household income (in tertiles, not available in WHII), marital status (married/partnered or not), current smoking status (yes or no), current alcohol consumption (yes or no), BMI categories (<25.0, 25.0-<30.0, or ≥30.0 kg/m^2), frequency of vigorous physical activity (<1 times/mo, 1–4 times/mo, or >1 times/week), hypertension (yes or no), hypercholesterolemia (yes or no, not available in HRS), diabetes (yes or no), stroke (yes or no), CVD (yes or no), and depressive symptoms (yes or no).
* Pooled HR: Random-effects models were used. Heterogeneity: $I^2 = 0.0\%$ for PDI (linear trend), $I^2 = 61.5\%$ for hPDI (linear trend), $I^2 = 0.0\%$ for uPDI (linear trend).

participants and 3855 incident dementia cases (Fig. 3). Pooled results revealed an inverse association between the hPDI and dementia risk (pooled $HR_{T3\ vs\ T1} = 0.79$, 95% CI, 0.65–0.98), whereas a higher risk for uPDI (pooled $HR_{T3\ vs\ T1} = 1.24$, 1.08–1.42). The overall PDI potentially exerted protective effect against dementia, although no statistically significant association was found (pooled $HR_{T3\ vs\ T1} = 0.84$, 0.66–1.06). The analyses showed moderate to substantial heterogeneity across studies.

4. Discussion

In three prospective cohort studies, greater adherence to overall and healthful plant-based diets was associated with a lower risk of all-cause dementia, whereas an unhealthful plant-based diet was linked to a higher dementia risk. These associations were consistently observed in both the HRS and FOS, though not in the WHII. Investigation of individual food categories revealed that healthier plant foods played a predominant role in reducing dementia risk, including vegetables, nuts, tea or coffee, and legumes. A meta-analysis incorporating five cohort studies further confirmed these findings, demonstrating robust associations for healthful (protective) and unhealthful (detrimental) plant-based dietary patterns. These results emphasize the importance of both the quantity and quality of plant-based diets for dementia prevention.

Only a limited number of population-based studies have explored the associations between predefined plant-based diet indices and cognitive outcomes in middle-aged and older populations. These include four studies on cognitive function [12–14,36], two on accelerated cognitive decline [15,37], one on brain imaging biomarkers [16], and two on dementia [17,18]. However, the evidence regarding the neuroprotective effects of plant-based diet indices remains inconclusive.

For instance, a study by Wu and colleagues [17], utilizing data from the UK Biobank ($N = 180{,}532$), reported an 18% (95% CI, 0.68–0.98) lower risk of dementia for hPDI and a 29% (95% CI, 1.08–1.53) higher risk for uPDI when comparing the highest with lowest quintile, whereas the association with the overall PDI was not significant. Similarly, another study [38] involving 5710 Taiwanese vegetarians reported a 33% lower risk of clinically overt dementia (95% CI, 0.45–0.99) among vegetarians compared to non-vegetarians. In contrast, a study among 9543 dementia-free participants from the Rotterdam Study found no association between three plant-based diet indices and the risk of dementia[18]. Our investigation across three well-established cohort studies yielded robust and consistent findings, demonstrating a potentially protective association for hPDI and a detrimental association for uPDI with dementia risk. These findings support dietary recommendations that advocate for diets rich in healthier plant foods while limiting the intake of less healthy plant foodsfor the prevention of age-related dementia and cognitive decline.

Notably, our meta-analysis revealed moderate to substantial heterogeneity in associations between PDIs and dementia risk across five cohorts. For example, while US cohorts (HRS/FOS) showed significant inverse associations between overall PDI and dementia risk, UK (UK Biobank and WHII) and Netherland (Rotterdam Study) cohorts reported null associations. This heterogeneity could be partially attributed to inter-cohort differences, such as in demographic characteristics (e.g., a younger age and lower proportion of women in the UK Biobank) and regional variations in dietary structure despite similar PDIs scoring. Furthermore, cross-population differences in dietary cultures and

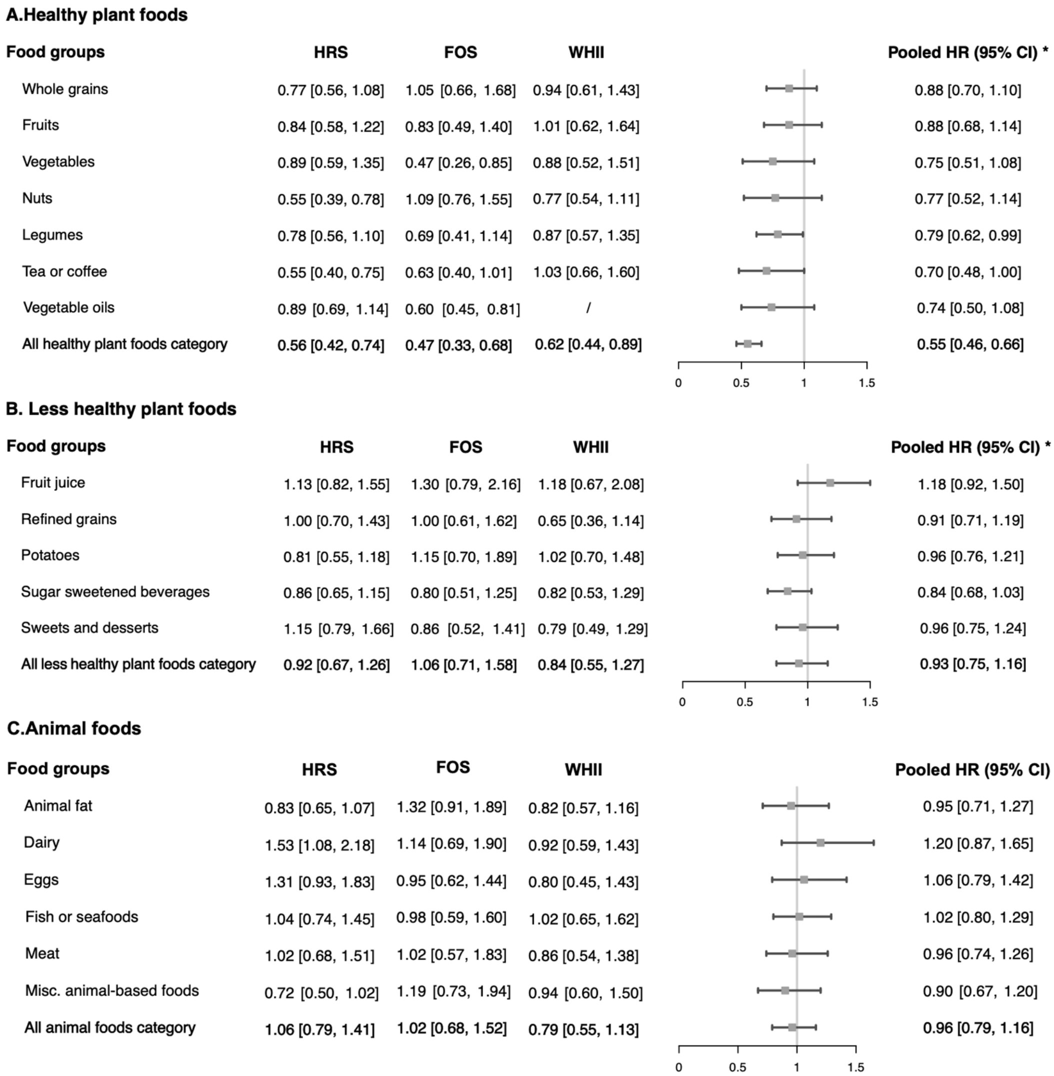

Fig. 2. Hazard ratios for incident dementia according to food groups.
* Pooled HR: Random-effects models were used. For each food group, HRs were estimated by comparing the highest to the lowest intake group for their association with dementia risk. Models were adjusted for age group (5-year groups), sex (male or female), race/ethnicity (white, non-white), total energy intake (in kcal), education (in years), household income (in tertiles) (not available in WHII), marital status (married/partnered or not), current smoking status (yes or no), current alcohol consumption (yes or no), BMI categories (<25.0, 25.0-<30.0, or ≥30.0 kg/m2), frequency of vigorous physical activity (<1 times/mo, 1–4 times/mo, >1 times/week), hypertension (yes or no), hypercholesterolemia (yes or no) (not available in HRS), diabetes (yes or no), stroke (yes or no), CVD (yes or no), and depressive symptoms (yes or no), and mutual adjustment for other individual food groups.

environmental contexts should be carefully considered in future nutritional studies. In addition, the WHII study comprised better-educated civil servants who were also relatively younger. Previous studies within WHII have indicated a lack of significant associations between other diet indices (such as the Alternate Healthy Eating Index [AHEI] [26] and the Mediterranean Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay [MIND] Diet [39]) and subsequent dementia risk. Observations suggest a slight decline in dietary quality prior to dementia in WHII participants, underscoring the need to investigate dietary changes in relation to cognitive ageing [26]. Moreover, the inconsistent findings across studies may partly be explained by differences in the length of follow-up periods. Given the long preclinical period of dementia [2,40], cognitive impairment may affect both the accuracy of dietary reporting and adherence to the diet itself. However, sensitivity analyses in our study excluding participants who developed dementia within the first two or five years of follow-up did not reveal significant evidence of reverse causality.

In general, our study highlights that healthier plant foods, including legumes, vegetables, nuts, tea or coffee, were associated with a lower risk of dementia, which is consistent with previous literatures. For example, recent meta-analyses reported an inverse association between habitual tea consumption and the risk of dementia or neurodegenerative cognitive disorders [41–43], with a non-linear relationship for coffee consumption [43]. Additionally, meta-analyses among older adults have shown that increased vegetables consumption was associated with a 25% decline in the odds of cognitive disorders [44,45]. Similarly, evidence from six randomized controlled trials indicated a benefitial effect of nuts intake on cognitive outcomes among individuals at higher risk of cognitive decline [46].

The biological mechanisms underlying these associations remain unclear. Consistent evidence suggested that healthy plant foods and nutrients possess anti-inflammatory and antioxidant properties [47,48], which may contribute to reducing amyloid accumulation, neuritic plaques, and neurofibrillary tangles in the brain [49]. Another potential pathophysiological mechanism linking plant-based diets and cognitive outcomes lies within the emerging field of the gut microbiome-brain axis [50,51]. Plant-dominant diets can substantially affect the intestinal environment and gut microbiome composition [52]. These shifts may

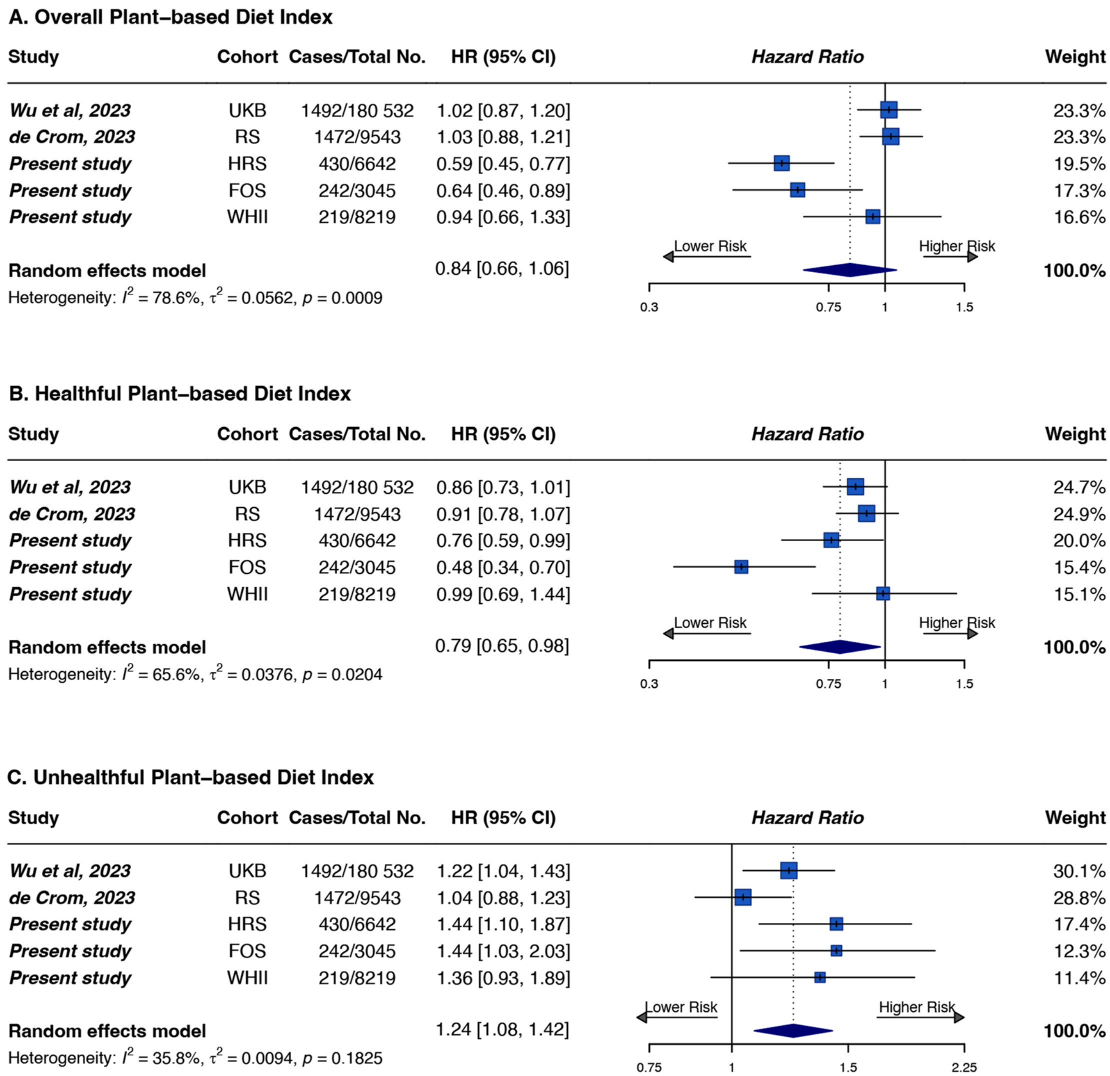

Fig. 3. Meta-analysis of multivariable-adjusted hazard ratios and 95% CI for incident dementia comparing the highest to the lowest tertile of plant-based diet indices. HR below 1.00 indicates a lower risk of dementia. We used random-effects models to pool the risk estimates comparing highest vs lowest tertiles of Plant-based diet indices. The I2 statistic was interpreted following the approximate guide from the Cochrane Handbook: 0% to 40% represents minor heterogeneity, 30% to 60% represents moderate heterogeneity, and 50% to 90% may represent substantial heterogeneity.

modulate intestinal permeability, influence immune system, and affect the hypothalamic–pituitary–adrenal axis, ultimately impacting the central nervous system [50].

This study has several major strengths, including its prospective design, long-term follow-up, and the use of validated methods to assess dietary intake across three well-established cohorts and a meta-analysis. Additionally, we conducted thorough sensitivity analyses to demonstrate the robustness of our findings. However, our results should be interpreted with caution due to some methodological limitations. First, dietary assessments relied on self-reporting, which may introduce the measurement error and misclassification. To mitigate this, we used cumulative dietary measures over time in the FOS and WHII to calculate average diet indices, reflecting long-term dietary habits and minimizing potential errors. Second, despite adjusting for numerous confounding factors, residual and unmeasured confounding may still exist. Third, the ascertainment of dementia cases varied across cohorts, with some relying on linkage to health electronic systems (e.g., WHII) and others using objective cognitive interviews (e.g., HRS), which may lead to outcome misclassification. Furthermore, we were unable to specifically assess the association between PDIs and different subtypes of dementia. Finally, the generalizability of our findings may be limited, as participants in all three studies were predominantly from Western populations. Variations in culture contexts and healthcare systems may further constrain the extrapolation of our findings to other settings.

5. Conclusion

Our study, integrating data from three prospective cohort studies and a comprehensive meta-analysis, demonstrated that greater adherence to the healthful plant-based diet was associated with lower risk of incident dementia, whereas an unhealthful plant-based diet was linked to higher risk. These findings suggest that dietary guidelines should recommend increasing consumption of healthier plant foods, which may contribute to preventing or delaying cognitive decline and dementia.

Ethical approvals and consents to participate

Ethical approval for the protocols of all three studies was obtained from the respective institutional review boards (IRB) (University of Michigan for HRS, Boston University Medical Center for FOS, and the joint University College London and University College London Hospitals committee for WHII). All participants provided written informed consent prior to participation.

Data sharing

This study is a secondary analysis of deidentified data that are publicly accessible online (https://www.ucl.ac.uk/epidemiology-health-care/research/epidemiology-and-public-health/research/whitehall-ii for the WHII, https://www.framinghamheartstudy.org/fhs-for-researchers/ for the FOS, and https://hrs.isr.umich.edu for the HRS). All human subjects provided informed consent.

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CRediT authorship contribution statement

Jie Shen: Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization. **Hui Chen:** Writing – review & editing, Writing – original draft, Formal analysis. **Yiying Gong:** Writing – review & editing, Formal analysis. **Yuhui Huang:** Writing – review & editing. **Minyu Wu:** Writing – review & editing. **Yuxuan Gu:** Writing – review & editing. **Tian Wang:** Writing – review & editing. **Luigi Fontana:** Writing – review & editing. **Shuang Rong:** Writing – review & editing. **Shujiao Qian:** Writing – review & editing. **Maurizio Tonetti:** Writing – review & editing. **Xiaoran Liu:** Writing – review & editing. **Changzheng Yuan:** Writing – review & editing, Conceptualization, Project administration, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tjpad.2025.100457.

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