



Original Investigation | Cardiology

Ultraprocessed Food Intake and Adiposity, Vascular Brain Injury, and Cognition in Middle-Aged Adults

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Abstract

IMPORTANCE Ultraprocessed foods (UPFs) account for a substantial and increasing proportion of dietary intake in Canada. Although UPFs are consistently associated with adiposity and cardiometabolic disease, their associations with subclinical vascular brain injury (VBI) and cognitive performance in midlife are unclear.

OBJECTIVE To evaluate associations of UPF consumption with adiposity, magnetic resonance imaging (MRI)-defined VBI, and cognitive performance in middle-aged adults in Canada.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study included 8783 adults aged 35 to 69 years without cardiovascular disease who were enrolled in the Canadian Alliance for Healthy Hearts and Healthy Minds (CAHHM) and Prospective Urban and Rural Epidemiology-MIND (PURE-MIND) studies. Participants from CAHHM were recruited from January 1, 2014, to December 31, 2018, and participants from PURE-MIND were recruited from January 1, 2010, to December 31, 2018. Data analyses were conducted between July 16, 2024, and August 16, 2026.

EXPOSURES UPF consumption assessed using previously validated semiquantitative food frequency questionnaires and expressed as servings per 2000 kcal/d.

MAIN OUTCOMES AND MEASURES The main outcomes were body fat (BF) percentage (bioelectrical impedance), visceral adipose tissue (VAT) volume, hepatic fat fraction (HFF), VBI defined as covert brain infarcts or high white matter hyperintensities (HWMHs) (measured by MRI), and cognitive performance measured by the Montreal Cognitive Assessment (MOCA) and the Digital Symbol Substitution Test (DSST).

RESULTS In this cross-sectional study of 8783 participants (mean [SD] age, 57.7 [8.7] years; 4917 females [56.6%]), those in the highest quartile of UPF intake had a BF percentage that was 1.7 (95% CI, 1.2-2.2) percentage points higher and a 5.7 (95% CI, 3.2-8.3) mL greater VAT volume compared with those in the lowest quartile, but no significant difference in HFF. Compared with the lowest quartile, the highest UPF quartile had higher odds of VBI (adjusted OR, 1.40; 95% CI, 1.10-1.77; *P* for trend = .009). No significant associations were observed between UPF intake and MOCA or DSST performance.

CONCLUSIONS AND RELEVANCE In this cross-sectional study of middle-aged adults in Canada, higher UPF intake was associated with greater adiposity and higher odds of MRI-defined VBI but not cognitive performance. Associations with VBI were sensitive to UPF exposure definition. Longitudinal studies are needed to establish temporality.

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Key Points

Question Is higher consumption of ultraprocessed foods associated with adiposity, subclinical vascular brain injury, and cognitive performance among middle-aged adults in Canada?

Findings In this cross-sectional study of 8783 adults, higher ultraprocessed food intake was associated with greater percentage of body fat and visceral adipose tissue and with higher odds of magnetic resonance imaging-defined vascular brain injury. Ultraprocessed food intake was not associated with cognitive performance.

Meaning In this study, higher ultraprocessed food intake was associated with markers of adiposity and subclinical cerebrovascular injury that may precede detectable cognitive deficits, but longitudinal studies are needed to establish temporality.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Introduction

Ultraprocessed foods (UPFs), as defined by the NOVA classification, now contribute more than half of daily energy intake in many high-income countries and have been increasingly implicated in adverse cardiometabolic outcomes.¹⁻³ The Canadian food environment is characterized by high availability and affordability of UPFs, which affects habitual intake patterns.^{4,5} Growing evidence suggests that UPF consumption may also influence brain health, but the pathways linking UPFs to early cerebrovascular changes remain uncertain and incompletely studied.⁵⁻⁹

Subclinical vascular brain injury (VBI), including white matter hyperintensities (WMHs) and covert brain infarcts (CBIs), reflects early cerebrovascular disease that develops years before clinically detectable cognitive decline and may represent a modifiable target for prevention.¹⁰⁻¹⁵ UPF intake is associated with obesity and visceral adiposity,¹⁶⁻¹⁹ which are associated with cerebrovascular injury^{20,21} through metabolic dysfunction, inflammation, and vascular damage.²² UPFs may also influence brain health independent of adiposity²³ because they are characterized by high glycemic load, added sugars, sodium, saturated fats, and food additives^{1,2} that may promote endothelial dysfunction and systemic inflammation.^{20,24-27} However, few studies have concurrently evaluated UPF intake, detailed adiposity phenotypes,²⁸ and magnetic resonance imaging (MRI)-defined VBI, and most have focused on cognitive decline or dementia^{27,29-32} rather than early structural markers of cerebrovascular disease.

To address these gaps, we examined the cross-sectional associations between UPF intake and body fat (BF) percentage, visceral adipose tissue (VAT) volume, hepatic fat fraction (HFF), MRI-defined VBI, as well as cognitive performance on standardized tests in a large, well-characterized cohort of middle-aged adults in Canada. We hypothesized that higher UPF intake would be associated with greater adiposity and a higher burden of VBI and that associations with VBI would occur before detectable differences in cognitive performance.

Methods

Study Design and Population

This secondary analysis used data from the Canadian Alliance for Healthy Hearts and Minds (CAHHM) and Prospective Urban and Rural Epidemiology-MIND (PURE-MIND) studies, described previously.^{28,33} CAHHM enrolled adults aged 35 to 69 years from Canadian cohorts and included cardiovascular phenotyping and brain MRI, whereas PURE-MIND enrolled adults aged 35 to 70 years without stroke, dementia, or neurological disease.³³⁻³⁵ Some country-specific food frequency questionnaires (FFQs) used in PURE-MIND had differential capacity to capture UPF intake (eg, six UPF items in China). The present analyses included only CAHHM and PURE-MIND participants from Canada because the same FFQs were used in both of these cohorts, enabling consistency of UPF classification.³⁶ Participants self-identified as male or female. CAHHM participants were recruited from January 1, 2014, to December 31, 2018. PURE-MIND participants were recruited from January 1, 2010, to December 31, 2018. Ethics approval was obtained from the Hamilton Integrated Research Ethics Board and all participating sites, and all participants provided written informed consent. Data were deidentified before analyses, which were conducted between July 16, 2024, and August 16, 2026. Because the NOVA classification was developed after cohort data collection, UPF intake was not prespecified in the original study protocols for CAHHM or PURE-MIND. We followed the Strengthening the Reporting of Observational Studies in Epidemiology-Nutritional Epidemiology (STROBE-nut) reporting guideline for cross-sectional studies.³⁷

Diet and UPF Assessment

Validated ethnicity-specific FFQs were used to assess habitual food and beverage intake over the previous year. Additional details regarding questionnaire development, validation, and NOVA classification procedures are provided in the eMethods in [Supplement 1](#).^{28,38}

Adiposity Measures

BF percentage was measured using a Tanita Ironman Innerscan BC-554 bioelectrical impedance analyzer (Tanita Corporation) according to a standardized protocol across study sites.²⁸ Participants were measured barefoot and in light clothing, and BF percentage was estimated using validated manufacturer equations based on measured electrical impedance. VAT volume was quantified from standardized axial T1-weighted MRI at the L4-L5 level by a central core laboratory. HFF was measured using dual- and triple-echo gradient-recalled echo MRI sequences.²⁸

Brain MRI Outcomes

MRI protocols for CAHHM and PURE-MIND have been published previously.^{28,33,34} Neurologists (including E.E.S.) at a central core facility, blinded to participant data, adjudicated all scans. VBI was defined as the presence of a CBI or high WMH burden. CBI was defined as 1 or more infarcts. WMH burden was graded using the Fazekas scale; HWMH was defined a priori as a Fazekas score 4 or higher (sum of periventricular and subcortical grades), indicating beginning confluent or confluent WMH and identifying clinically meaningful covert cerebrovascular disease.²⁸

Cognitive Outcomes

Cognition was assessed using the Montreal Cognitive Assessment (MOCA)³⁹ and the Digit Symbol Substitution Test (DSST).⁴⁰ The MOCA (score range: 0-30) evaluates multiple cognitive domains; scores 26 or higher denote normal cognitive performance. The DSST (score range: 0-133, with higher scores indicating better cognitive performance) captures psychomotor speed, attention, and working memory.

Covariates

Participant-reported sociodemographic and health characteristics were collected using standardized questionnaires. Covariates included age, self-identified ethnicity, household income, education level, physical activity, smoking status, and histories of hypertension, diabetes, and dyslipidemia (eMethods in [Supplement 1](#)). Case record forms collected self-reported ethnicity only; this variable was included in the analysis given known ethnic variations in various cardiometabolic traits. Ethnic categories analyzed were White European and all other self-reported ethnicities, including Black, East Asian, Indigenous, South Asian, and other ethnicity not further specified. The other self-reported ethnicity group was combined because sample sizes of the individuals groups were small. Height and weight were measured directly, and total energy intake was derived from the food-frequency questionnaire.

Statistical Analyses

All measures were collected at a single baseline visit; therefore, this analysis was cross-sectional. Participants with baseline cardiovascular disease, implausible energy intake (<500 or >5000 kcal/d), or missing exposure, outcome, or covariate data were excluded from the analysis (**Figure 1**). UPF intake was expressed as servings per 2000 kcal/d and categorized into quartiles (1 as the lowest quartile and 4 as the highest).^{41,42}

Multivariable linear regression was used for continuous outcomes (BF percentage, VAT volume, HFF, MOCA, and DSST) and logistic regression for VBI composite outcomes (VBI, CBIs, and HWMHs), with a random intercept for study center. UPF intake was modeled as quartiles and continuously. Analyses were restricted to complete cases, defined as participants with nonmissing data for UPF intake, outcomes, and all covariates included in the fully adjusted model; all sequential models were fit using the same analytic sample. Sequential models adjusted for: (1) age, sex, and study center; (2) self-identified ethnicity, income, and education; (3) physical activity and smoking; (4) diabetes, hypertension, and dyslipidemia; and (5) total energy intake. Adiposity and cardiometabolic risk factors may lie on the pathway between UPF intake and VBI; therefore, models including these

variables were interpreted as estimating associations independent of adiposity and traditional vascular-metabolic pathways. A directed acyclic graph is provided in eFigure 1 in Supplement 1.

Dietary misreporting is possible, particularly for UPF. Therefore, exclusion of implausible energy intakes and 6 prespecified sensitivity analyses were used to assess robustness: (1) redefining exposure as percentage of energy from UPFs or percentage of total food servings; (2) evaluating percentage of energy from UPFs in a subset with available data; (3) restricting analyses to participants without diabetes, hypertension, or dyslipidemia; (4) additionally adjusting VBI models for VAT volume and BF percentage; (5) additionally adjusting cognitive models for VAT volume, BF percentage, and VBI; (6) examining odds of low cognition (MOCA score <26 or MOCA or DSST <1 SD below the cohort mean). Because no calibration substudy or recovery biomarkers were available, formal measurement-error correction was not performed. However, exclusion of implausible energy intakes and multiple sensitivity analyses were used to evaluate the potential influence of dietary measurement error and exposure misclassification on study findings. Additional exploratory analyses included repeating analyses after inclusion of participants with prevalent cardiovascular disease and modeling UPF intake as a continuous variable (per 5 servings per 2000 kcal/d and per 5% energy from UPFs).

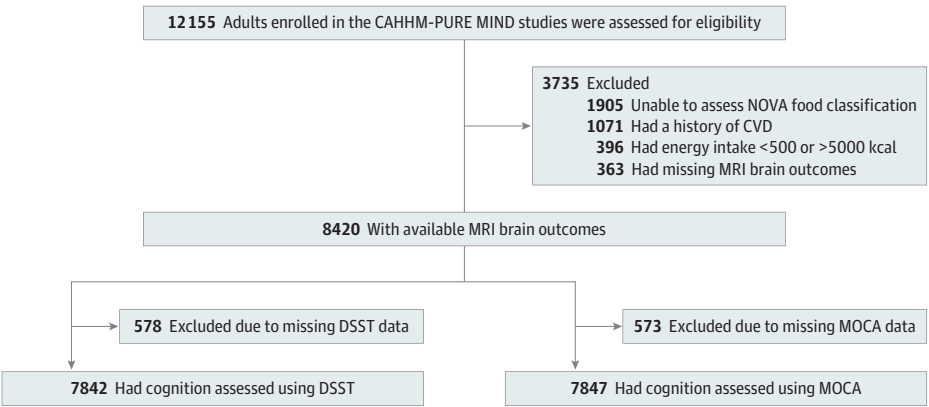
Linear trends across UPF quartiles were tested by modeling quartiles as an ordinal variable. Effect modification by sex was evaluated by including a sex × UPF interaction term in the regression models. Two-sided *P* < .05 were considered statistically significant. All analyses were conducted using SAS, version 9.4 (SAS Institute). Data were analyzed between July 16, 2024, and August 16, 2026.

Results

Cohort Characteristics

The demographic characteristics of participants are shown in Table 1. Among the 8783 individuals included, 4917 (56.6%) were females, 3866 (43.4%) were males, and the mean (SD) age was 57.7 (8.7) years. The mean body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) was 27.0 (5.1), and mean (SD) BF percentage was 31.0% (9.2%). Cognitive performance was normal, with mean (SD) MOCA and DSST scores of 27.0 (2.3) and 73.2 (15.7), respectively. A total of 3276 participants (37.3%) reported hypertension, 426 (4.9%) diabetes, and 1460 (16.6%) dyslipidemia. On MRI, 772 participants (9.2%) had evidence of VBI, including 467 (4.3%) with HWMHs and 363 (5.5%) CBIs. Participants consumed a mean (SD) of 42.2% (14.2%) of daily caloric intake from UPFs.

Figure 1. Flow Diagram for Single Baseline Visit Determination of Enrollment and Analysis



CAHHM indicates Canadian Alliance for Healthy Hearts and Minds; CVD, cardiovascular disease; DSST, Digital Symbol Substitution Test; MOCA, Montreal Cognitive Assessment; MRI, magnetic resonance imaging; PURE MIND, Prospective Urban and Rural Epidemiology-MIND.

Higher UPF intake was associated with less favorable socioeconomic, lifestyle, and cardiometabolic profiles, greater energy intake, and differences in overall dietary composition (Table 1 and **Table 2**). Across increasing UPF quartiles, the proportion of daily food servings derived from UPFs increased from 16.5% to 45.0% (difference, 28.5 [95% CI, 28.1-29.0] percentage points), whereas the proportion derived from minimally processed foods decreased from 68.6% to 41.5% (difference, -27.1 [95% CI, -27.7 to -26.4] percentage points).

Adiposity Outcomes

In model 5, participants in the highest vs lowest quartile of UPF intake had a higher BF percentage (1.7 [95% CI, 1.2-2.2] percentage points) and greater VAT volume (5.7 [95% CI, 3.2-8.3] mL). HFF did not

Table 1. Participant Characteristics by Quartile of Servings Per 2000 kcal/d From UPF

Characteristic	Participants by quartile of UPF consumption, No. (%)			
	1 (n = 2196)	2 (n = 2196)	3 (n = 2196)	4 (n = 2195)
UPF servings per 2000 kcal/d	3.1 (0.1-5.4)	6.6 (5.4-7.7)	8.8 (7.7-10.1)	12.8 (10.1-43.3)
Sex ^a				
Female	1244 (56.6)	1286 (58.6)	1187 (54.1)	1200 (54.7)
Male	952 (43.4)	909 (41.4)	1009 (45.9)	995 (45.3)
Urban residence ^b	2090 (98.6)	2114 (96.6)	2018 (92.4)	1940 (88.7)
Self-identified ethnicity				
White European	1532 (69.8)	1736 (79.1)	2005 (91.3)	2054 (93.6)
All other self-identified ethnicity ^c	664 (30.2)	460 (20.9)	191 (8.7)	141 (6.4)
Educational level ^d				
Primary/none/unknown/high school or less	261 (12.1)	253 (11.8)	319 (14.8)	514 (23.9)
Trade or vocational	266 (12.3)	131 (6.1)	201 (9.3)	232 (10.8)
College or university	1627 (75.5)	1757 (82.1)	1636 (75.9)	1402 (65.3)
Annual income level, \$ ^e				
<60 000	431 (21.4)	305 (15.2)	361 (17.8)	4921 (24.5)
60 000 to <120 000	767 (38.0)	742 (37.1)	864 (42.6)	914 (45.6)
≥120 000	819 (40.6)	955 (47.7)	803 (39.6)	598 (29.9)
Current smoker (%) ^f	105 (4.8)	96 (4.4)	131 (6.0)	181 (8.3)
Physical inactivity (%) ^g	896 (41.0)	781 (36.1)	909 (42.1)	1090 (50.8)
BMI ^h				
<25.0	999 (45.6)	948 (43.4)	787 (36.2)	615 (28.6)
25.0 to <30.0	822 (37.5)	842 (38.5)	852 (39.2)	825 (38.4)
≥30.0	369 (16.8)	396 (18.1)	535 (24.6)	711 (33.1)
History of hypertension ⁱ	813 (37.0)	740 (33.7)	850 (38.7)	873 (39.8)
History of diabetes ^j	104 (4.7)	74 (3.4)	84 (3.8)	164 (7.5)
History of dyslipidemia	350 (15.9)	306 (13.9)	352 (16.0)	452 (20.6)
Brain measures				
CBI	73 (3.4)	74 (3.5)	89 (4.2)	127 (6.1)
HWMH	111 (5.2)	115 (5.4)	115 (5.5)	126 (6.1)
Vascular brain injury	173 (8.1)	173 (8.2)	192 (9.1)	235 (11.3)
Age, mean (SD), years ^k	58.2 (8.5)	57.1 (8.9)	57.8 (8.8)	57.7 (8.8)
Cognitive scores, mean (SD)				
MOCA ^l	27.1 (2.4)	27.1 (2.3)	27.0 (2.3)	26.8 (2.4)
DSST ^m	73.3 (16.2)	74.9 (15.4)	72.8 (15.5)	71.9 (15.5)
Adiposity measures, mean (SD)				
BMI	26.1 (4.6)	26.3 (4.6)	27.3 (5.1)	28.4 (5.7)
Body fat % ⁿ	29.7 (8.8)	30.3 (8.9)	31.2 (9.3)	32.9 (9.6)
WHR ^o	0.87 (0.08)	0.87 (0.08)	0.87 (0.09)	0.88 (0.09)
VAT, mL ^p	69.4 (36.6)	65.7 (32.6)	73.4 (37.8)	79.2 (38.8)
HFF, % ^q	5.5 (5.7)	5.4 (5.6)	5.7 (5.6)	6.1 (6.1)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CBI, covert brain infarct; DSST, digital symbol substitution test; HFF, hepatic fat fraction; HWMH, high white matter hyperintensity; MOCA, Montreal Cognitive Assessment; VAT, visceral adipose tissue; WHR, waist-to-hip ratio.

^a Missing data for sex: n = 1.

^b Missing data for urban residence: n = 102.

^c Combined due to small sample sizes for each ethnicity, which included Black, East Asian, Indigenous, South Asian, or other ethnicity not further specified.

^d Missing data for educational level: n = 184.

^e Missing data for income: n = 733.

^f Missing data for smoking status: n = 20.

^g Missing data for physical activity: n = 127.

^h Missing data for BMI: n = 82.

ⁱ Missing data for history of hypertension: n = 2.

^j Missing data for history of diabetes: n = 3.

^k Missing data for age: n = 62.

^l Missing data for MOCA: n = 17.

^m Missing data for DSST: n = 23.

ⁿ Missing data for body fat percentage: n = 328.

^o Missing data for WHR: n = 89.

^p Missing data for VAT: n = 2214.

^q Missing data for HFF: n = 2498.

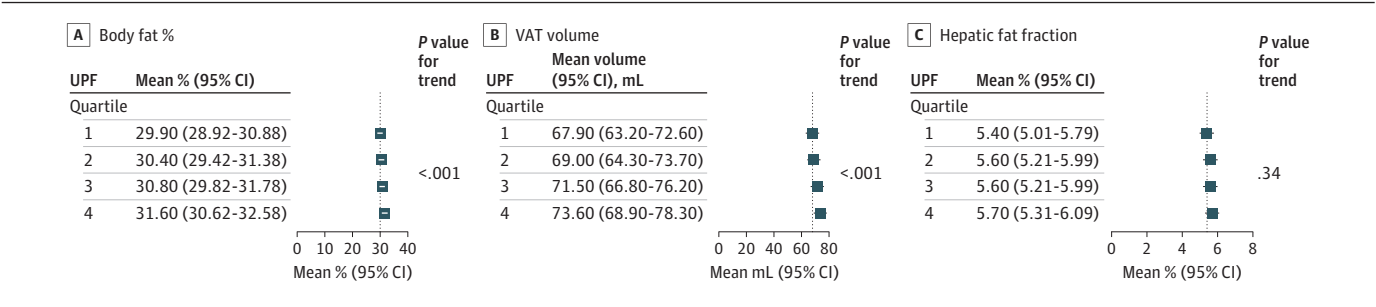
significantly differ between the 2 quartiles (difference, 0.3 [95% CI, -0.2 to 0.8] percentage points) (Figure 2; eTable 1 in Supplement 1). Associations were strongest among participants with obesity (BMI ≥30.0), with progressively higher BF percentages (38.9%-40.1%; *P* < .001) and modestly higher VAT volume (103.9-110.7 cm³; *P* = .009) across UPF quartiles, whereas HFF did not differ significantly across quartiles (9.5%, 10.7%, 10.0%, and 10.1%; *P* = .76). Results were similar when

Table 2. Dietary Intake of UPF

Variable	Mean (SD) by quartile			
	1 (n = 2196)	2 (n = 2196)	3 (n = 2196)	4 (n = 2195)
Energy intake, kcal/d	1850 (717)	1877 (662)	2041 (740)	2163 (855)
Food type, No. of servings/d				
Fruit	2.1 (1.8)	2.3 (1.5)	2.1 (1.4)	1.7 (1.2)
Vegetables	4.5 (3.9)	5.2 (4.3)	5.6 (4.8)	5.7 (4.9)
Legumes	0.5 (0.7)	0.6 (0.6)	0.5 (0.6)	0.5 (0.6)
Nuts	0.9 (3.5)	1.5 (4.1)	1.5 (4.0)	1.5 (4.1)
Whole grains	0.5 (1.0)	1.2 (1.3)	1.9 (2.1)	2.2 (2.5)
Fish	0.2 (0.3)	0.3 (0.3)	0.3 (0.3)	0.2 (0.2)
Dairy	2.3 (2.6)	3.7 (2.9)	4.1 (3.0)	4.1 (3.4)
Unprocessed red meat	0.4 (0.6)	0.6 (0.6)	0.8 (0.9)	1.1 (1.2)
Processed meat	0.1 (0.2)	0.3 (0.3)	0.3 (0.3)	0.4 (0.4)
Macronutrients, % E				
Carbohydrate	49.6 (8.0)	50.8 (7.0)	52.1 (6.7)	53.0 (7.0)
Protein	17.4 (3.8)	17.6 (3.1)	17.1 (2.7)	16.2 (2.6)
Total fat	32.0 (7.1)	30.8 (6.0)	30.5 (5.6)	31.0 (5.9)
Monounsaturated fat	12.9 (3.4)	11.7 (2.8)	11.3 (2.5)	11.7 (2.7)
Saturated fatty acids	9.8 (2.8)	10.1 (2.6)	10.3 (2.7)	10.0 (2.6)
Polyunsaturated fat	6.2 (1.9)	5.5 (1.6)	5.2 (1.4)	5.4 (1.5)
Sodium, mg/d	2675 (1381)	2308 (1056)	2442 (996)	2754 (1212)
NOVA classification, No. of servings/d				
Minimally processed foods	12.1 (7.7)	14.3 (6.0)	13.7 (6.0)	12.8 (6.0)
Processed culinary ingredients	0.7 (1.4)	1.6 (1.9)	1.8 (2.0)	2.0 (2.4)
Processed foods	2.0 (1.8)	2.7 (1.8)	2.6 (1.6)	2.2 (1.4)
Ultraprocessed foods	2.8 (1.9)	6.2 (2.3)	9.0 (3.4)	13.8 (6.1)
NOVA classification, % of total daily food servings				
Minimally processed foods	68.6 (12.4)	57.5 (9.8)	50.3 (9.4)	41.5 (10.4)
Processed culinary ingredients	2.9 (4.9)	5.9 (6.0)	6.3 (6.3)	6.2 (6.2)
Processed foods	12.1 (9.0)	10.9 (5.8)	9.7 (5.0)	7.3 (4.1)
Ultraprocessed foods	16.5 (8.1)	25.6 (5.8)	33.7 (6.5)	45.0 (9.9)

Abbreviations: Kcal, kilocalories; % E, percentage of energy.

Figure 2. Dot Plots of Multivariable-Adjusted Mean Adiposity Measures Across Quartiles of Ultraprocessed Food (UPF) Consumption



Adjusted least-squares means are reported for body fat percentage (A), visceral adipose tissue (VAT) volume (B), and hepatic fat fraction (C) by quartile of UPF intake (servings per 2000 kcal/d). Models are adjusted for age, sex, study center (random effect), self-identified ethnicity, income, education, physical activity, smoking status, and histories of diabetes, hypertension, and dyslipidemia, and total energy intake. *P* for trend values represent linear trend tests across quartiles and are shown in each panel.

UPF intake was modeled continuously. In the adjusted model 5, each 5-serving per 2000 kcal/d higher UPF intake was associated with a higher BF percentage (0.9 [95% CI, 0.7-1.1] percentage points) and higher VAT volume (4.0 [95% CI, 2.8-5.2] mL), but not a higher HFF. No meaningful patterns were observed among participants with BMI less than 25.0, and there was no association with BMI 25.0 to 29.9.

VBI Outcomes: Composite, WMHs, CBIs

Higher UPF intake was associated with greater odds of composite VBI (OR for quartile 4 vs quartile 1, 1.40; 95% CI, 1.10-1.77; *P* for trend = .009) (Figure 3; eTable 2 in Supplement 1). Associations for the individual components were directionally consistent but less robust, with similar patterns observed for both WMHs and CBIs, although these patterns did not consistently reach statistical significance. VBI prevalence was 8.1% in the lowest UPF quartile vs 11.3% in the highest quartile.

Cognitive Outcomes

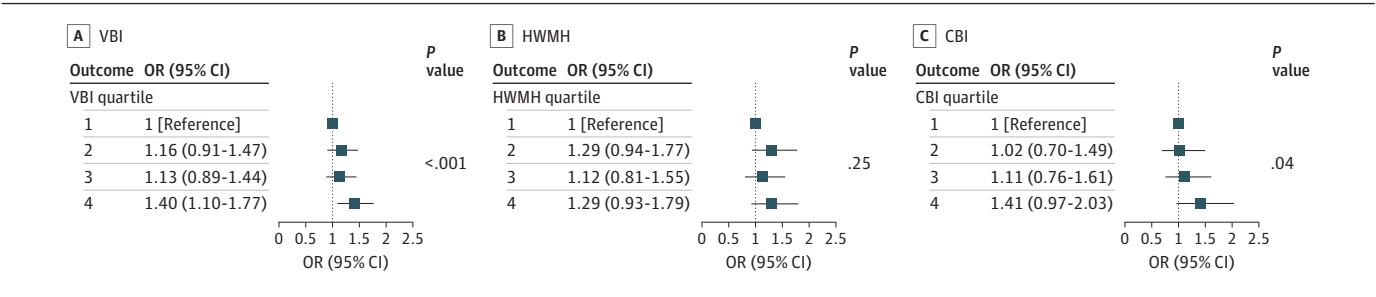
UPF intake was not associated with cognitive performance. In model 5, there was no association between UPF intake and DSST scores (quartile 4 minus quartile 1 = 1.0 [95% CI, -0.01 to 2.1] points; *P* for trend = .19) or MOCA scores (quartile 4 minus quartile 1 = 0.2 [95% CI, -0.01 to 2.1] points; *P* for trend = .09) (eTable 3 in Supplement 1). Cognitive scores remained high with minimal variation across UPF quartiles.

Sensitivity Analyses

Redefining UPF exposure as the percentage of total daily food servings or as the percentage of total energy intake from UPFs was not associated with VBI, and no linear trends were observed (eTables 4 and 5 in Supplement 1). Associations between UPF servings per 2000 kcal/day and the composite VBI outcome were directionally similar to the main analyses but were not statistically significant (eTable 6 in Supplement 1). Additional adjustment for VAT volume and/or BF percentage did not materially alter the magnitude or direction of the associations between UPF intake and VBI (eTable 7 in Supplement 1).

Adjustment of the associations between UPF intake and cognitive scores for VAT volume, BF percentage, and/or VBI yielded a statistically significant association with higher MOCA scores (from 27.0 [0.2] in Q1 to 27.2 [0.1] in Q4; *P* = .01) but not DSST scores (from 73.4 [1.0] in Q1 to 74.4 [1.0] in Q4; *P* = .08) (eTable 8 in Supplement 1). Dichotomizing cognitive performance produced results consistent with the quartile analyses. Higher UPF consumption was associated with lower odds of low cognitive performance across several secondary analyses, although most associations were not statistically significant. Comparing quartile 4 with quartile 1, the ORs were 0.88 (95% CI, 0.73-1.07) for MOCA scores less than 26 (*P* for trend = .13), 0.80 (95% CI, 0.63-1.01) for MOCA scores less than 1 SD below the mean (*P* for trend = .04), and 0.76 (95% CI, 0.61-0.96) for DSST scores less than 1 SD

Figure 3. Dot Plots of Multivariable-Adjusted Odds Ratios for Vascular Brain Injury (VBI) Across Quartiles of Ultraprocessed Food Consumption



Odds ratios (ORs) are presented relative to quartile 1 of ultraprocessed food intake (servings per 2000 kcal/d; reference). Models are adjusted for age, sex, study center (random effect), self-identified ethnicity, income, education, physical activity, smoking status, and histories of diabetes, hypertension, and dyslipidemia, as well as total energy intake. *P* for trend values represent linear trend tests across quartiles and are shown below each panel. CBI indicates covert brain infarct; HWMH, high white matter hyperintensity.

below the mean (P for trend = .11) (eFigure 2 and eTable 9 in [Supplement 1](#)). In an additional sensitivity analysis including participants with prevalent cardiovascular disease (eTable 10 in [Supplement 1](#)), and diet quality indicators (eTable 11 in [Supplement 1](#)), associations between UPF intake and VBI were materially unchanged.

Results were also consistent when UPF intake was modeled as a continuous exposure. For each 5-serving per 2000 kcal/d higher UPF intake, the BF percentage was 0.9 (95% CI, 0.7-1.1) percentage points higher, VAT volume was 4.0 (95% CI, 2.8-5.2) mL higher, and odds of VBI were higher (OR, 1.16; 95% CI, 1.05-1.28). Higher continuous UPF intake was also associated with greater odds of CBI (OR, 1.21; 95% CI, 1.04-1.42) but not HWMH burden (OR, 1.06; 95% CI, 0.92-1.22). When UPF intake was modeled as percentage of total energy intake, associations with VBI, CBI, and HWMH burden were not statistically significant. Continuous analyses of cognitive outcomes were largely null: per 5-serving per 2000 kcal/d higher UPF intake, there were no associations with DSST (β = 0.14; 95% CI, -0.31 to 0.59) and MOCA (β = 0.05; 95% CI, -0.02 to 0.13) scores. Modeling UPF as percentage of total energy intake yielded a direct association with DSST (β = 0.17; 95% CI, 0.05-0.30) but not with MOCA (β = 0.01; 95% CI, -0.01 to 0.03) performance.

Sex-Stratified Analyses

The association between UPF intake and BF percentage differed by sex. For each 1-quartile higher UPF intake, BF percentage was 0.7 (95% CI, 0.5-1.0) percentage points higher among females and 0.4 (95% CI, 0.1-0.6) percentage points higher among males (P for interaction <.001). For VAT volume, each 1-quartile higher UPF intake was associated with 2.7 (95% CI, 1.8-3.7) mL greater volume among females but not among males (0.8 mL; 95% CI, -0.6 to 2.2) (P for interaction = .10). UPF intake was directly associated with HFF among females (0.2 [95% CI, 0.0-0.4] percentage points per quartile) but not among males (-0.1 [95% CI, -0.3 to 0.1] percentage points per quartile) (P for interaction = .02) (eTable 12 in [Supplement 1](#)). For VBI, there was evidence that associations differed by sex (P for interaction = .04). Higher UPF intake was associated with greater odds of VBI among females (OR for quartile 4 vs quartile 1, 1.78; 95% CI, 1.27-2.48; P for trend = .002), whereas no association was observed among males (OR for quartile 4 vs quartile 1, 1.08; 95% CI, 0.76-1.54; P for trend = .84) (eTable 13 in [Supplement 1](#)). There was no evidence that associations between UPF intake and cognitive performance differed by sex (MOCA P for interaction = .08; DSST P for interaction = .38) (eTable 14 in [Supplement 1](#)).

Discussion

In this cross-sectional study of middle-aged adults in Canada without cardiovascular disease, higher intake of UPF was associated with greater total and visceral adiposity and with higher odds of MRI-defined VBI. These associations were most pronounced and consistent for adiposity, persisting across quartile- and continuous-exposure analyses. In contrast, associations with VBI were of lower magnitude and were sensitive to the definition of UPF intake. Associations were observed when UPF intake was expressed as servings per 2000 kcal/d but not consistently when expressed as percentage of energy intake or percentage of total food servings. UPF intake was not associated with cognitive performance in minimally adjusted models, although some associations emerged after further adjustment. These findings suggest that metabolic and cerebrovascular changes related to UPF consumption may appear earlier in the life course than observable cognitive decline.

The graded associations between UPF intake and BF percentage and VAT align with accumulating evidence of associations between UPFs and adiposity and metabolic dysfunction.^{15-18,43-51} These associations were more pronounced among individuals with obesity; for example, among participants with BMI 30. No association was observed among participants with BMI less than 25. UPFs may promote excess energy intake and impair appetite regulation^{19,52} consistent with evidence of amplified inflammatory and endocrine responses to poor-quality diets in

metabolically compromised states.¹⁹ Together, these findings support adiposity as a plausible pathway for an association between UPF exposure and downstream cerebrovascular injury.

The association between UPF intake and VBI suggests a potential cerebrovascular consequence of high UPF consumption; however, attenuation in sensitivity analyses warrants cautious interpretation. Although WMHs and CBIs are not identical lesions, both are manifestations of covert cerebrovascular disease and share major vascular risk factors. Both are often discussed in relation to cognitive aging and are established factors in future clinical stroke and other adverse cerebrovascular outcomes, highlighting their relevance as early markers of vascular risk.^{53,54} WMHs are generally considered markers of diffuse cerebral small-vessel disease characterized by chronic hypoperfusion, endothelial dysfunction, blood-brain barrier disruption, and neuroinflammation, whereas CBIs may arise from small-vessel occlusion, embolic phenomena, or large-artery atherosclerotic disease. Higher UPF consumption may contribute to both lesion types through mechanisms involving adiposity, metabolic dysfunction, inflammation, and vascular injury, providing biological support for the observed association with the composite VBI outcome.

In contrast, UPF intake was not consistently associated with cognitive performance. This pattern may reflect ceiling effects in a cognitively healthy cohort, the earlier emergence of subclinical cerebrovascular injury relative to deficits detectable by brief cognitive screens, or cognitive reserve in this highly educated sample (>73% with postsecondary education).³⁵ MOCA cut points may also be insufficiently sensitive in ethnoculturally and linguistically diverse populations, potentially leading to differential misclassification of cognitive impairment^{55,56}; particularly given the higher proportion of White European participants in the highest UPF intake category.

After additional adjustment for VAT volume, BF percentage, and VBI, direct associations between MOCA scores and UPF intake across quartiles reached statistical significance; however, absolute differences were minimal. The adjusted variables may represent intermediates on the pathway between diet and cognition, such that adjustment could introduce overadjustment or collider bias. The unexpected direction of the association may also reflect residual confounding, measurement error, ceiling effects, or chance findings arising from multiple comparisons. Consistent with this interpretation, the primary analyses using continuous MOCA and DSST scores were null, and the apparent inverse associations were observed only in selected secondary analyses based on dichotomized cognitive outcomes. Accordingly, these results should be interpreted cautiously and should not be taken as evidence that higher UPF intake is associated with better cognitive performance. Conversely, the absence of consistent associations with cognitive performance should not be interpreted as evidence of no neurological consequences, because structural cerebrovascular injury may be detectable before measurable impairment on brief cognitive tests. Longitudinal analyses are needed to clarify whether adiposity and cerebrovascular injury mediate any associations between UPF intake and later cognitive decline.

These findings extend previous studies on the association of UPF intake with adverse brain health outcomes by incorporating detailed adiposity phenotyping and MRI-defined vascular brain injury in the same cohort. Differences in study design, UPF definitions, dietary assessment methods, and outcome ascertainment limit direct comparison with prior reports.^{27,29-32} Associations with VAT volume, HFF, and VBI differed by sex, with associations generally observed among females but not males. The apparent sex differences should be interpreted cautiously because sex-stratified analyses were exploratory and were not prespecified primary analyses. Prior studies have reported mixed findings,^{57,58} although studies have similarly reported associations between UPF intake and visceral adiposity or metabolic-associated steatotic liver disease that were observed primarily among women rather than men.^{18,59} Potential explanations include differences in body fat distribution, hormonal milieu, inflammatory responses, dietary patterns, or residual confounding, although these possibilities could not be evaluated in the current study.⁶⁰⁻⁶² Replication in other cohorts is needed to investigate whether these observed sex differences are reproducible.

The higher proportion of White European participants among high UPF consumers raises the possibility of residual confounding by social, cultural, and food-environment factors and may limit

generalizability to other populations.^{63,64} Higher UPF intake clustered with adverse socioeconomic, lifestyle, and cardiometabolic characteristics, suggesting that it may identify individuals with an accumulation of vascular and cognitive health risks in midlife. Nevertheless, associations persisted after adjustment for adiposity and cardiometabolic factors, suggesting that pathways related to food processing itself may also contribute.⁹ Notably, higher UPF intake was not characterized by lower vegetable consumption and was accompanied by higher intakes of several foods generally considered healthful, suggesting that findings are unlikely to be explained solely by differences in specific food groups.

Strengths and Limitations

Strengths of this study include the large sample, validated dietary assessment, detailed MRI protocols, and standardized adiposity and cognition measures. Study limitations include the cross-sectional design, which precludes assessment of temporality and limits causal inference. Because dietary intake, adiposity, VBI, and cognitive outcomes were measured at the same visit, reverse causation remains possible. Several covariates included in adjusted models, including diabetes, hypertension, dyslipidemia, and adiposity, may reflect cumulative effects of prior dietary exposures rather than baseline confounders, leaving residual confounding and incomplete exchangeability between exposure groups possible. Additional limitations include the absence of formal measurement-error correction, potential misclassification arising from application of the NOVA classification framework to food frequency questionnaire data, and the limited sensitivity of cognitive tests in midlife. UPFs represent a heterogeneous exposure rather than a single well-defined intervention, as lower UPF intake could be achieved through multiple dietary substitutions with differing health implications. Finally, dietary intake was assessed using a single food frequency questionnaire capturing habitual intake over the preceding year, whereas adiposity and VBI likely reflect cumulative exposures over longer periods.

Conclusions

In this cross-sectional study of middle-aged adults in Canada, higher UPF intake was consistently associated with greater adiposity and was associated with subclinical vascular brain injury using the primary exposure definition, although the latter finding was sensitive to alternative exposure definitions. UPF intake was not associated with cognitive performance. Longitudinal studies are needed to establish temporality and clarify the clinical significance of these findings.

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REFERENCES

1. Monteiro CA, Cannon G, Levy RB, et al. Ultra-processed foods: what they are and how to identify them. *Public Health Nutr*. 2019;22(5):936-941. doi:[10.1017/S1368980018003762](https://doi.org/10.1017/S1368980018003762)
2. Monteiro CA, Levy RB, Claro RM, Castro IR, Cannon G. A new classification of foods based on the extent and purpose of their processing. *Cad Saude Publica*. 2010;26(11):2039-2049. doi:[10.1590/S0102-311X2010001100005](https://doi.org/10.1590/S0102-311X2010001100005)
3. Nilson E, Hamel V, Wahrhaftig J, Rezende L, Polsky JY, Moubarac JC. What proportion of cardiovascular disease burden in Canada is attributable to ultra-processed foods? Université de Montréal. February 1, 2025. Accessed August 16, 2026. <https://coilink.org/20.500.12592/7n2x426>

4. Nardocci M, Polsky JY, Moubarac JC. Consumption of ultra-processed foods is associated with obesity, diabetes and hypertension in Canadian adults. *Can J Public Health*. 2021;112(3):421-429. doi:[10.17269/s41997-020-00429-9](https://doi.org/10.17269/s41997-020-00429-9)
5. Moubarac JC, Batal M, Martins AP, et al. Processed and ultra-processed food products: consumption trends in Canada from 1938 to 2011. *Can J Diet Pract Res*. 2014;75(1):15-21. doi:[10.3148/75.1.2014.15](https://doi.org/10.3148/75.1.2014.15)
6. Pagliai G, Dinu M, Madarena MP, Bonaccio M, Iacoviello L, Sofi F. Consumption of ultra-processed foods and health status: a systematic review and meta-analysis. *Br J Nutr*. 2021;125(3):308-318. doi:[10.1017/S0007114520002688](https://doi.org/10.1017/S0007114520002688)
7. Monteiro CA, Louzada ML, Steele-Martinez E, et al. Ultra-processed foods and human health: the main thesis and the evidence. *Lancet*. 2025;406(10520):2667-2684. doi:[10.1016/S0140-6736\(25\)01565-X](https://doi.org/10.1016/S0140-6736(25)01565-X)
8. Vandevijvere S, Jaacks LM, Monteiro CA, et al. Global trends in ultraprocessed food and drink product sales and their association with adult body mass index trajectories. *Obes Rev*. 2019;20(suppl 2):10-19. doi:[10.1111/obr.12860](https://doi.org/10.1111/obr.12860)
9. Lane MM, Gamage E, Du S, et al. Ultra-processed food exposure and adverse health outcomes: umbrella review of epidemiological meta-analyses. *BMJ*. 2024;384:e077310. doi:[10.1136/bmj-2023-077310](https://doi.org/10.1136/bmj-2023-077310)
10. Vermeer SE, Prins ND, den Heijer T, Hofman A, Koudstaal PJ, Breteler MM. Silent brain infarcts and the risk of dementia and cognitive decline. *N Engl J Med*. 2003;348(13):1215-1222. doi:[10.1056/NEJMoa022066](https://doi.org/10.1056/NEJMoa022066)
11. Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA. Religious orders study and Rush Memory and Aging Project. *J Alzheimers Dis*. 2018;64(s1):S161-S189. doi:[10.3233/JAD-179939](https://doi.org/10.3233/JAD-179939)
12. Kapasi A, Schneider JA. Vascular contributions to cognitive impairment, clinical Alzheimer's disease, and dementia in older persons. *Biochim Biophys Acta*. 2016;1862(5):878-886. doi:[10.1016/j.bbadis.2015.12.023](https://doi.org/10.1016/j.bbadis.2015.12.023)
13. Iadecola C, Duering M, Hachinski V, et al. Vascular cognitive impairment and dementia: JACC Scientific Expert Panel. *J Am Coll Cardiol*. 2019;73(25):3326-3344. doi:[10.1016/j.jacc.2019.04.034](https://doi.org/10.1016/j.jacc.2019.04.034)
14. Schnabel L, Kesse-Guyot E, Allès B, et al. Association between ultraprocessed food consumption and risk of mortality among middle-aged adults in France. *JAMA Intern Med*. 2019;179(4):490-498. doi:[10.1001/jamainternmed.2018.7289](https://doi.org/10.1001/jamainternmed.2018.7289)
15. Srour B, Fezeu LK, Kesse-Guyot E, et al. Ultraprocessed food consumption and risk of type 2 diabetes among participants of the NutriNet-Santé Prospective Cohort. *JAMA Intern Med*. 2020;180(2):283-291. doi:[10.1001/jamainternmed.2019.5942](https://doi.org/10.1001/jamainternmed.2019.5942)
16. Konieczna J, Morey M, Abete I, et al; PREDIMED-Plus investigators. Contribution of ultra-processed foods in visceral fat deposition and other adiposity indicators: prospective analysis nested in the PREDIMED-Plus trial. *Clin Nutr*. 2021;40(6):4290-4300. doi:[10.1016/j.clnu.2021.01.019](https://doi.org/10.1016/j.clnu.2021.01.019)
17. Liu J, Steele EM, Li Y, Yi SS, Monteiro CA, Mozaffarian D. Consumption of ultraprocessed foods and body fat distribution among U.S. adults. *Am J Prev Med*. 2023;65(3):427-438. doi:[10.1016/j.amepre.2023.03.012](https://doi.org/10.1016/j.amepre.2023.03.012)
18. Fridén M, Kullberg J, Ahlström H, Lind L, Rosqvist F. Intake of ultra-processed food and ectopic-, visceral- and other fat depots: a cross-sectional study. *Front Nutr*. 2022;9:774718. doi:[10.3389/fnut.2022.774718](https://doi.org/10.3389/fnut.2022.774718)
19. Hall KD, Ayuketah A, Brychta R, et al. Ultra-processed diets cause excess calorie intake and weight gain: an inpatient randomized controlled trial of ad libitum food intake. *Cell Metab*. 2019;30(1):67-77.e3. doi:[10.1016/j.cmet.2019.05.008](https://doi.org/10.1016/j.cmet.2019.05.008)
20. Anand SS, Friedrich MG, Lee DS, et al; Canadian Alliance of Healthy Hearts and Minds (CAHHM) and the Prospective Urban and Rural Epidemiological (PURE) Study Investigators. Evaluation of adiposity and cognitive function in adults. *JAMA Netw Open*. 2022;5(2):e2146324. doi:[10.1001/jamanetworkopen.2021.46324](https://doi.org/10.1001/jamanetworkopen.2021.46324)
21. Cui C, He C, Sun Q, et al. Association between visceral adiposity index and incident stroke: data from the China Health and Retirement Longitudinal Study. *Nutr Metab Cardiovasc Dis*. 2022;32(5):1202-1209. doi:[10.1016/j.numecd.2022.01.031](https://doi.org/10.1016/j.numecd.2022.01.031)
22. Tchernof A, Després JP. Pathophysiology of human visceral obesity: an update. *Physiol Rev*. 2013;93(1):359-404. doi:[10.1152/physrev.00033.2011](https://doi.org/10.1152/physrev.00033.2011)
23. Morys F, Kanyamibwa A, Fängström D, et al. Ultra-processed food consumption affects structural integrity of feeding-related brain regions independent of and via adiposity. *NPJ Metab Health Dis*. 2025;3(1):13. doi:[10.1038/s44324-025-00056-3](https://doi.org/10.1038/s44324-025-00056-3)
24. Xu Q, Zhang S, Gu Y, Wang P, Zhang Q, Shan C. Interaction of high-sugar diet and history of stroke with risk of cognitive decline in older adults. *Med Sci Monit*. 2022;28:e937572. doi:[10.12659/MSM.937572](https://doi.org/10.12659/MSM.937572)
25. Miller AA, Spencer SJ. Obesity and neuroinflammation: a pathway to cognitive impairment. *Brain Behav Immun*. 2014;42:10-21. doi:[10.1016/j.bbi.2014.04.001](https://doi.org/10.1016/j.bbi.2014.04.001)

26. Poulouse SM, Miller MG, Scott T, Shukitt-Hale B. Nutritional factors affecting adult neurogenesis and cognitive function. *Adv Nutr*. 2017;8(6):804-811. doi:10.3945/an.117.016261
27. Gomes Gonçalves N, Vidal Ferreira N, Khandpur N, et al. Association between consumption of ultraprocessed foods and cognitive decline. *JAMA Neurol*. 2023;80(2):142-150. doi:10.1001/jamaneurol.2022.4397
28. Anand SS, Tu JV, Awadalla P, et al; CAHHM Study Investigators. Rationale, design, and methods for Canadian alliance for healthy hearts and minds cohort study (CAHHM) - a Pan Canadian cohort study. *BMC Public Health*. 2016;16:650. doi:10.1186/s12889-016-3310-8
29. Li H, Li S, Yang H, et al. Association of ultraprocessed food consumption with risk of dementia: a prospective cohort study. *Neurology*. 2022;99(10):e1056-e1066. doi:10.1212/WNL.0000000000200871
30. Bhavé VM, Oladele CR, Ament Z, et al. Associations between ultra-processed food consumption and adverse brain health outcomes. *Neurology*. 2024;102(11):e209432. doi:10.1212/WNL.0000000000209432
31. R Cardoso B, Machado P, Steele EM. Association between ultra-processed food consumption and cognitive performance in US older adults: a cross-sectional analysis of the NHANES 2011-2014. *Eur J Nutr*. 2022;61(8):3975-3985. doi:10.1007/s00394-022-02911-1
32. Weinstein G, Vered S, Ivancovsky-Wajcman D, et al. Consumption of ultra-processed food and cognitive decline among older adults with type-2 diabetes. *J Gerontol A Biol Sci Med Sci*. 2023;78(1):134-142. doi:10.1093/gerona/glac070
33. Smith EE, O'Donnell M, Teo KK, et al. Rationale, design and preliminary findings of the prospective urban-rural epidemiologic mind (Pure-Mind) MRI Study: abstracts from the 2nd Canadian Stroke Congress, 2011. *Stroke*. 2011;42(11):e587. doi:10.1161/STR.Ob013e3182301bf4
34. Smith EE, O'Donnell M, Dagenais G, et al; PURE Investigators. Early cerebral small vessel disease and brain volume, cognition, and gait. *Ann Neurol*. 2015;77(2):251-261. doi:10.1002/ana.24320
35. Durrani R, Friedrich MG, Schulze KM, et al. Effect of cognitive reserve on the association of vascular brain injury with cognition: analysis of the PURE and CAHHM Studies. *Neurology*. 2021;97(17):e1707-e1716. doi:10.1212/WNL.0000000000012765
36. Dehghan M, Mente A, Rangarajan S, et al; Prospective Urban Rural Epidemiology (PURE) study investigators. Ultra-processed foods and mortality: analysis from the Prospective Urban and Rural Epidemiology study. *Am J Clin Nutr*. 2023;117(1):55-63. doi:10.1016/j.ajcnut.2022.10.014
37. Lachat C, Hawwash D, Ocké MC, et al. Strengthening the reporting of observational studies in epidemiology-nutritional epidemiology (STROBE-nut): an extension of the STROBE Statement. *PLoS Med*. 2016;13(6):e1002036. doi:10.1371/journal.pmed.1002036
38. Kelemen LE, Anand SS, Vuksan V, et al; SHARE Investigators. Development and evaluation of cultural food frequency questionnaires for South Asians, Chinese, and Europeans in North America. *J Am Diet Assoc*. 2003;103(9):1178-1184. doi:10.1016/S0002-8223(03)00985-4
39. Rossetti HC, Lacritz LH, Cullum CM, Weiner MF. Normative data for the Montreal Cognitive Assessment (MoCA) in a population-based sample. *Neurology*. 2011;77(13):1272-1275. doi:10.1212/WNL.Ob013e318230208a
40. Wechsler D. *The Measurement and Appraisal of Adult Intelligence*. Williams & Wilkins; 1958.
41. Tomova GD, Arnold KF, Gilthorpe MS, Tennant PWG. Adjustment for energy intake in nutritional research: a causal inference perspective. *Am J Clin Nutr*. 2022;115(1):189-198. doi:10.1093/ajcn/nqab266
42. Willett WC, Stampfer M, Tobias DK. Re: Adjustment for energy intake in nutritional research: a causal inference perspective. *Am J Clin Nutr*. 2022;116(2):608-609. doi:10.1093/ajcn/nqac114
43. Mendonça RD, Lopes AC, Pimenta AM, Gea A, Martínez-González MA, Bes-Rastrollo M. Ultra-processed food consumption and the incidence of hypertension in a Mediterranean cohort: The Seguimiento Universidad de Navarra Project. *Am J Hypertens*. 2017;30(4):358-366. doi:10.1093/ajh/hpw137
44. Shim SY, Kim HC, Shim JS. Consumption of ultra-processed food and blood pressure in Korean adults. *Korean Circ J*. 2022;52(1):60-70. doi:10.4070/kcj.2021.0228
45. González-Palacios S, Oncina-Cánovas A, García-de-la-Hera M, et al; PREDIMED-PLUS Trial investigators. Increased ultra-processed food consumption is associated with worsening of cardiometabolic risk factors in adults with metabolic syndrome: longitudinal analysis from a randomized trial. *Atherosclerosis*. 2023;377:12-23. doi:10.1016/j.atherosclerosis.2023.05.022
46. Rezende-Alves K, Hermisdorff HHM, Miranda AEDS, et al. Effects of minimally and ultra-processed foods on blood pressure in Brazilian adults: a two-year follow up of the CUME Project. *J Hypertens*. 2023;41(1):122-131. doi:10.1097/HJH.0000000000000311

47. Scaranni PODS, Cardoso LO, Chor D, et al. Ultra-processed foods, changes in blood pressure and incidence of hypertension: the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). *Public Health Nutr.* 2021;24(11):3352-3360. doi:10.1017/S136898002100094X
48. Chen Z, Khandpur N, Desjardins C, et al. Ultra-processed food consumption and risk of type 2 diabetes: three large prospective U.S. cohort studies. *Diabetes Care.* 2023;46(7):1335-1344. doi:10.2337/dc22-1993
49. Delpino FM, Figueiredo LM, Bielemann RM, et al. Ultra-processed food and risk of type 2 diabetes: a systematic review and meta-analysis of longitudinal studies. *Int J Epidemiol.* 2022;51(4):1120-1141. doi:10.1093/ije/dyab247
50. Nouri M, Davies IG, Webb RJ, et al. The association between ultra-processed foods and conventional markers of cardiovascular risk in an adult Iranian population. *Nutr Metab Cardiovasc Dis.* 2023;33(10):1951-1959. doi:10.1016/j.numecd.2023.06.009
51. Canhada SL, Vigo Á, Luft VC, et al. Ultra-processed food consumption and increased risk of metabolic syndrome in adults: The ELSA-Brasil. *Diabetes Care.* 2023;46(2):369-376. doi:10.2337/dc22-1505
52. Valicente VM, Peng CH, Pacheco KN, et al. Ultraprocessed foods and obesity risk: a critical review of reported mechanisms. *Adv Nutr.* 2023;14(4):718-738. doi:10.1016/j.advnut.2023.04.006
53. Merino JG. White matter hyperintensities on magnetic resonance imaging: what is a clinician to do? *Mayo Clin Proc.* 2019;94(3):380-382. doi:10.1016/j.mayocp.2019.01.016
54. Meinel TR, Kaesmacher J, Roten L, Fischer U. Covert brain infarction: towards precision medicine in research, diagnosis, and therapy for a silent pandemic. *Stroke.* 2020;51(8):2597-2606. doi:10.1161/STROKEAHA.120.030686
55. Milani SA, Marsiske M, Cottler LB, Chen X, Striley CW. Optimal cutoffs for the Montreal Cognitive Assessment vary by race and ethnicity. *Alzheimers Dement (Amst).* 2018;10:773-781. doi:10.1016/j.dadm.2018.09.003
56. Stimmel MB, Orkaby AR, Ayers E, Verghese J, Nsubayi CK, Weiss EF. Is the Montreal cognitive assessment culturally valid in a diverse geriatric primary care setting? Lessons from the Bronx. *J Am Geriatr Soc.* 2024;72(3):850-857. doi:10.1111/jgs.18705
57. Juul F, Martinez-Steele E, Parekh N, Monteiro CA, Chang VW. Ultra-processed food consumption and excess weight among US adults. *Br J Nutr.* 2018;120(1):90-100. doi:10.1017/S0007114518001046
58. Sung H, Park JM, Oh SU, Ha K, Joung H. Consumption of ultra-processed foods increases the likelihood of having obesity in Korean women. *Nutrients.* 2021;13(2):698. doi:10.3390/nu13020698
59. Kwan BS, Ko NG, Park JE. Sex differences in the association between ultra-processed food consumption and NAFLD: an analysis of KNHANES 2013-2021 data. *J Clin Med.* 2025;14(22):7930. doi:10.3390/jcm14227930
60. Smyth A, Hankey GJ, Damasceno A, et al. Carbonated beverage, fruit drink, and water consumption and risk of acute stroke: the INTERSTROKE Case-Control Study. *J Stroke.* 2024;26(3):391-402. doi:10.5853/jos.2024.01543
61. Morgenstern LB, Escobar JD, Sánchez BN, et al. Fast food and neighborhood stroke risk. *Ann Neurol.* 2009;66(2):165-170. doi:10.1002/ana.21726
62. Kim K, Hyeon J, Lee SA, et al. Role of total, red, processed, and white meat consumption in stroke incidence and mortality: a systematic review and meta-analysis of prospective cohort studies. *J Am Heart Assoc.* 2017;6(9):e005983. doi:10.1161/JAHA.117.005983
63. Olstad DL, Nejatnamini S, Blanchet R, et al. Protecting traditional cultural food practices: Trends in diet quality and intake of ultra-processed foods by Indigenous status and race/ethnicity among a nationally representative sample of adults in Canada. *SSM Popul Health.* 2023;24:101496. doi:10.1016/j.ssmph.2023.101496
64. Pachipala K, Shankar V, Rezler Z, et al. Acculturation and associations with ultra-processed food consumption among Asian Americans: NHANES, 2011-2018. *J Nutr.* 2022;152(7):1747-1754. doi:10.1093/jn/nxac082

SUPPLEMENT 1.

eMethods

eTable 1. Association of UPF (servings per day/2000kcal) with measures of adiposity.

eTable 2. Association of UPF with MRI-defined vascular brain injury

eTable 3. Association of UPF with cognitive function test scores

eTable 4. Association of UPF with MRI-defined vascular brain injury, using percentage energy from UPF

eTable 5. Association of UPF with MRI-defined vascular brain injury, using percentage of total food servings from UPF

eTable 6. Association of UPF with brain outcomes, stratified by metabolic health history (i.e., presence of diabetes, dyslipidemia, or hypertension)

- eTable 7.** Association of UPF with brain outcomes after additional adjustment for adiposity measures
- eTable 8.** Association of UPF with cognitive function test scores after additional adjustment for adiposity measures and vascular brain injury
- eTable 9.** Association of UPF with odds of low cognitive performance
- eTable 10.** Association of UPF with brain outcomes including participants with prevalent cardiovascular disease
- eTable 11.** Association of UPF with study outcomes after adjustment for minimally processed food intake, polyunsaturated-to-saturated fat ratio, and fruit and vegetable intake
- eTable 12.** Association of UPF with adiposity measures, stratified by sex and BMI
- eTable 13.** Association of UPF with vascular brain injury, high white matter hyperintensity burden, and covert brain infarction, stratified by sex
- eTable 14.** Association of UPF with cognitive function test scores, stratified by sex and BMI
- eFigure 1.** Directed acyclic graph illustrating hypothesized relationships among ultra-processed food intake (dark blue), adiposity (orange), cardiometabolic risk factors (orange), vascular brain injury (green), cognition (green), and measured confounders (light blue).
- eFigure 2.** Multivariable adjusted odds ratios for low cognitive score across quartiles of UPF consumption.
- eReferences**

SUPPLEMENT 2.
Data Sharing Statement