ONLINE SUPPLEMENTARY MATERIALS

Pathways explaining racial/ethnic and socio-economic disparities in dementia incidence: The UK Biobank Study

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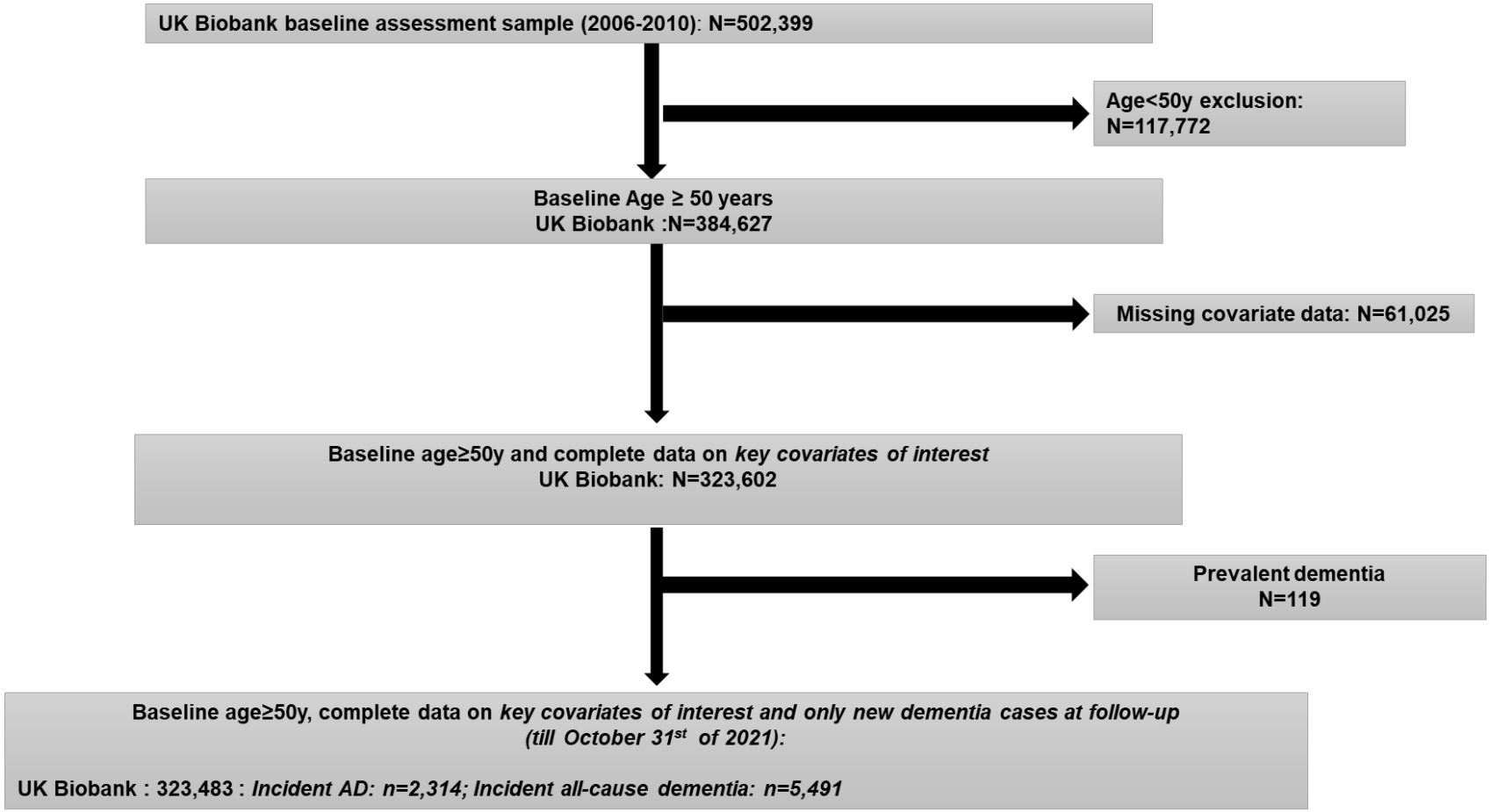
Supplementary Figure 1. Participant Flowchart: The UK Biobank 2006-2021



Abbreviations: AD=Alzheimer's Disease; N=Sample size; UK=United Kingdom.

Supplementary Table 1. Proration of mediators including LE8 sub-scales

Items	Number of missing items/participant allowed for prorating
1	0
2	1
3	1
4	2
5	2
6	3
7	3
8	4
9	4
10	5
11	5
12	6

Supplementary Method 1: Dietary intake and other lifestyle factors

The touchscreen questionnaire of the UKB main study included twenty-nine questions regarding diet and eighteen questions related to alcohol. The touchscreen questionnaire inquired about food consumption frequency and nature, over the past year of the following food groups: cooked vegetables, salad/raw vegetables, fresh fruit, dried fruit, oily fish, other fish, processed meats, poultry, beef, lamb, pork, cheese, salt added to food, tea, water, as well as questions on the type of milk most commonly consumed, type of spread most commonly consumed, number of slices and type of bread most commonly consumed, number of bowls and type of breakfast cereal most commonly consumed, cups of coffee and type most commonly consumed, as well as questions on the avoidance of specific foods and food groups (eggs, dairy products, wheat, sugar), age last ate meat (for participants who reported never consuming processed meats, poultry, beef, lamb or pork), temperature preference of hot drinks, changes in diet in the past 5 years, and variation in diet. Four of the dietary questions originally utilized in the pilot trial were slightly altered for the main assessment phase: these were the items related to avoiding specific foods and food groups; spread type; bread type; and variation in diet.

The Healthy Diet Index (HDI) score combined several food groups in terms of quantity and frequency of consumption per week, when available to reflect the guidelines listed in **Supplementary Table 2**. However, those criteria were modified to fit the availability of data in the UK Biobank. **Supplementary Table 3** represents the food groups that were selected, their respective coding scheme and the scoring system to reflect better diet quality, approximating the criteria in **Supplementary Table 2**. The touchscreen questionnaire was later validated against the 24-hr recall that was administered over time to UK Biobank participants and has shown adequate agreement in terms of ranking for each food group of interest[1].

Supplementary Table 2. Goals and guidelines used to construct the Healthy Diet Score

Consume more	Goal*	One Serving Equals…
Fruits	3 servings/d	1 medium-sized fruit; ½ cup of fresh, frozen, or unsweetened canned fruit; ½ cup of dried fruit; ½ cup of 100% juice
Nuts, seeds	4 servings/wk	1 ounce
Vegetables, including legumes (excluding russet or white potatoes)	3 servings/d	1 cup of raw leafy vegetables; ½ cup of cut-up raw vegetables, cooked vegetables, or 100% vegetable juice
Whole grains†	3 servings/d, in place of refined grains	1 slice of whole-grain bread; 1 cup of high-fiber, whole-grain cereal; ½ cup of cooked whole-grain rice, pasta, or cereal
Fish, shellfish	≥2 servings/wk	3.5 ounces (100 g)
Dairy products, especially yogurt and cheese ‡	2–3 servings/d	1 cup of milk or yogurt; 1 ounce of cheese
Vegetable oils	2–6 servings/d	1 teaspoon oil, 1 tablespoon vegetable spread
Consume less		
Refined grains, starches, added sugars†	No more than 1–2 servings/d	
Processed meats	No more than 1 serving/wk	1.75 ounces (50 g)
Unprocessed red meats	No more than 1–2 servings/wk	3.5 ounces (100 g)
Industrial trans fat §	Don’t eat	Any food containing or made with partially hydrogenated vegetable oil
Sugar-sweetened beverages	Don’t drink	8 ounces of beverage; 1 small sweet, pastry, or dessert
Sodium	No more than 2000 mg/d	n/a

Source: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.115.018585#d3e341

* Based on a 2000 kcal/d diet. Servings should be adjusted accordingly for higher or lower energy consumption.
† As a practical rule-of-thumb for selecting healthful whole grains and avoiding carbohydrate-rich products high in starches and added sugars, the ratio of total carbohydrate to dietary fiber (g/serving of each) appears useful. Foods with ratios <10:1 are preferable; ie, food containing at least 1 g of fiber for every 10 g of total carbohydrate. In addition, minimally processed whole grains (eg, steel-cut oats, stone-ground bread) are generally preferable to finely milled whole grains (eg, many commercial whole-grain breads and breakfast cereals) because of the larger glycemic responses of the latter.
‡ Current evidence does not permit clear differentiation of whether low-fat or whole-fat products are superior for cardiometabolic health. Other characteristics, such as probiotic content or fermentation, may be far more relevant than fat content.
§ The US Food and Drug Administration recently ruled that the use of partially hydrogenated vegetable oils is no longer "generally regarded as safe,"384 which should effectively eliminate the majority of industrial trans fats from the US food supply. Several countries including Denmark, Argentina, Austria, Iceland, and Switzerland have effectively eliminated the use of partially hydrogenated vegetable oils through direct legislation on the amounts of allowable trans fats in foods. Small amounts of certain trans fatty acids may be formed through other industrial processes, including oil deodorization and high-temperature cooking; the health effects of these trace industrial trans fats require careful investigation.

Supplementary Table 3. Healthy Diet Index, HDI, using touchscreen questionnaire in the UK Biobank study

Food group/nutrient item	UKB fields used	Definition of meeting criterion	Criteria and scoring
Consume more			
Fruits, fresh or dried	1309 and 1319	≥3 servings per day including fresh and dried fruits 1 piece of dried fruit (e.g. apricot)~=2.5 TBSP, 1 TBSP= 0.063 cups; ½ cup of dried fruit (1 serving) is 3 pieces of dried fruit. 1 medium sized fruit is one serving.	1=meets criterion, 0=does not meet criterion
Vegetables, salad/cooked	1289 and 1299	≥3 servings per day Including salad, raw and cooked 1 cup of raw leafy vegetables is 16 TBSP. ½ cup of cooked or non-leafy raw vegetables is 8 TBSP. 1 serving of raw leafy or non-leafy vegetables is on average ~=12 TBSP; 1 serving of cooked vegetables is ~=8 TBSP	1=meets criterion, 0=does not meet criterion
Whole grains		≥3 servings per day	1=meets criterion, 0=does not meet criterion
Slices of bread	1438 and 1448	Daily slices of wholemeal or wholegrain bread (servings per day), convert from weekly slices.	
Cereal	1458 and 1448	Daily bowls of whole wheat cereal as servings/day (bran	

		cereal, biscuit cereal, oat cereal and muesli), convert from weekly bowls.	
Fish shellfish	1329 and 1339	Sum weekly frequencies to obtain total servings/week. ≥2 servings/wk	1=meets criterion, 0=does not meet criterion
Oily fish	…	…	
Non-oily fish	…	…	
Dairy products	6114, 1408 and 1418	Reporting consumption of two milk items and eating cheese once a day to meet the 2-3 servings/day criterion.	1=meets criterion, 0=does not meet criterion
Milk	…		
Cheese	…		
Vegetable oil	2654	Reporting use of olive oil or polyunsaturated/sunflower oil (yes=1, 0=no)	1=meets criterion, 0=does not meet criterion
Consume less			
Refined grains, starches, added sugars†	1438 and 1448	Follow a similar coding scheme as for whole grains but select non-whole grains; <1.5 servings per day	1=meets criterion, 0=does not meet criterion
Processed meats	1349	Once a week or less would meet the criterion.	1=meets criterion, 0=does not meet criterion
Unprocessed red meats	1369, 1379, and 1389	Summation of frequency of consumption across three types of red meats (lamb/mutton, beef or pork). <3 on the summation corresponds to the criterion of <1-2 servings per week.	1=meets criterion, 0=does not meet criterion
Industrial trans fat §	1428	Never use spread, e.g. butter or margarine etc. would meet the criterion	1=meets criterion, 0=does not meet criterion
Sugar-sweetened beverages	6144	Never eat sugar or food/drink containing sugar would meet the criterion	1=meets criterion, 0=does not meet criterion

Sodium	1478	Salt added to food, never or rarely would meet the criterion	1=meets criterion, 0=does not meet criterion

Source: https://biobank.ndph.ox.ac.uk/showcase/label.cgi?id=100052.

Stata code can be made available upon request.

Smoking

We utilized several fields of data to generate three tobacco exposure variables, based on the touchscreen questionnaire at the assessment centre visit, namely smoking status, environmental tobacco smoke and pack-years of smoking. Those three constructs were transformed into standardized z-scores which were then averaged into the latent construct SMOKING.

Alcohol

The touchscreen questionnaire also provided several questions related to alcohol consumption, which were quantity-frequency in nature. One question asked “About how often do you drink alcohol?” with 6 possible responses that were reverse coded to the following: 0 "never" 1 "special occasions only" 2 "1-3 times per month" 3 "1-3 times per week" 4 "3-4 times per week" 5 "daily or almost daily". The construct ALCOHOL was the standardized z-score for this item.

Physical activity

Physical activity (PA) was operationalized using a set of self-reported responses that can be used to assess mild (i.e. walking), moderate and vigorous activities based on the short form of the International Physical Activity Questions[2] in terms of frequency (# of days) per week and number of minutes per day. Those were then combined to generate MET.min/week for each category of physical activity intensity. Finally, the MET.min/week values were added together. Given that missing data does exist, addition was made on the imputed data, whereby MET.min/week per intensity were imputed where missing using chained equations. This single measured variable reflecting total MET.min/week was transformed into a standardized z-score, labelled PA and used in our pathway analyses.

Diet quality

We utilized the dietary questionnaire data category, based on a set of questions administered at the assessment visit. A measure of diet quality was constructed to approximate dietary recommendations listed in **Supplementary Table 2**. The criteria applied to each food or nutrient item derived the food frequency questionnaire (FFQ) to obtain an overall measure of diet quality is described in **Supplementary Table 3**. The resulting z-score was used to obtain the DIET construct.

Nutritional biomarkers

Vitamin D was additionally selected from the list as a nutritional biomarker that was previously shown to be inversely associated with cognitive aging[3-6]. Of the long list of hematological factors, we selected red cell distribution width (RDW) as an additional nutritional biomarker, reflecting iron metabolism, as it was previously shown to be directly associated with cognitive aging[7-9]. Thus, the z-score of RDW was multiplied by -1. The average of the two z-scores was used reflect nutritional biomarkers, or NUTR.

Social Support

Three social support variables were used to operationalize SS standardized z-score. The first variable pertained to the question: “How often do you visit friends or family or have them visit you?”, with potential responses reverse coded to range from 1=”No friends/family” to 7=”Almost daily”. Intermediate responses were “Never or almost never”, “Once every few months”, “About once a month”, “About once a week” and “2-4 times a week”. Similarly, another question asked: “How often are you able to confide in someone close to you?” With no reverse coding necessary, the responses ranged from 0=”Never or almost never” to

5=”almost daily” and intermediate responses being “Once every few months”, “About once a month”, “About once a week” and “2-4 times a week”. Finally, a third question asked “Which of the following do you attend once a week or more often?” and was used to count leisure and social activities among “sports and club or gym”, “pub or social club”, “religious group”, “adult education class” and “other group activity”. These three measures were then transformed into a standardized z-score and averaged into the SS measure.

Supplementary Method 2: Life’s Essential 8

Life’s Essential 8 was computed using guidelines from **Supplementary Table 4** and all available data fields that correspond to these guidelines, while ensuring maximal sample preservation. The HDI was used for the dietary quality component, while other criteria were used that fit the guidelines well. In order to further preserve the sample and increase statistical power, two methods were available. The first one was multiple imputations using chained equations. Given the large sample to be used, this method was deemed infeasible as a main tool for the analysis. Another method that is widely used in the social science is proration[10, 11], with general guidelines for large sample to allow for up to 50% of the items to be missing per observation, as shown in **Supplementary Table 1**. Beyond this threshold, the entire observation was dropped from analysis. For scales that relied on totals (e.g. LE8), the row means were multiplied by the total number of items (4 for the LE8 sub-scales and 8 for the total score). This method was also applied to SES, DIET, SMOKING, ALCOHOL, NUTR, SS and HEALTH. COGN score was obtained using principal components analysis with complete cases and thus proration was not needed. In the final sample, 99.9% of participants had 2 items or less missing on the LE8 total score.

Supplementary Table 4. Definition and scoring approach for quantifying cardiovascular health, as per the American Heart Association's Life's Essential 8 score [12, 13], and as applied in the National Health and Nutrition Examination Surveys, 2013-2018

Domain	CVH Metric	Method of Measurement	Quantification of CVH Metric - Adults (≥20 Years)
Health Behaviors	**Diet**	**Measurement: Self-reported daily intake of a DASH-style eating pattern** **Example tools for measurement: DASH diet score (populations)**	Quantiles of DASH-style diet adherence **Scoring(Population):** Points Quantile 100 ≥95th %ile (top/ideal diet) 80 75th – 94th %ile 50 50th – 74th %ile 25 25th – 49th %ile 0 1st – 24th %ile (bottom/least ideal quartile)
	Physical activity	**Measurement: Self-reported minutes of moderate or vigorous physical activity per week** **Example tools for measurement:** NHANES PAQ-K questionnaire	**Metric: Minutes of moderate (or greater) intensity activity per week** **Scoring:** Points Minutes 100≥150 90 120 – 149 80 90 – 119 60 60 – 89 40 30 – 59 20 1 – 29 0 0
	Nicotine exposure	**Measurement:** Self-reported use of cigarettes or inhaled nicotine- delivery system **Example tools for measurement:** NHANES SMQ	**Metric: Combustible tobacco use and/or inhaled NDS use; or secondhand smoke exposure** **Scoring:** Points Status 100 Never smoker 75Former smoker, quit≥5 yrs 50 Former smoker, quit 1 - <5 yrs

			25 Former smoker, quit <1 year, or currently using inhaled NDS 0 Current smoker Subtract 20 points (unless score is 0) for living with active indoor smoker in home
	Sleep health	**Measurement:** Self-reported average hours of sleep per night **Example tools for measurement:** "On average, how many hours of sleep do you get per night?" Consider objective sleep/actigraphy data from wearable technology, if available	**Metric:** Average hours of sleep per night **Scoring:** Points Level 100 7 – <9 90 9 - <10 70 6 - <7 40 5 -<6 or≥10 20 4 - <5 0 <4
Health Factors	**Body mass index**	**Measurement:** Body weight (kg) divided by height squared (m2) **Example tools for measurement:** Objective measurement of height and weight	**Metric :Body mass index (kg/m^2)** **Scoring:** Points Level 100 <25 70 25.0 – 29.9 30 30.0 – 34.9 15 35.0 – 39.9 0≥40.0

	Blood lipids	**Measurement:** Plasma total and HDL-cholesterol with calculation of non-HDL-cholesterol **Example tools for measurement:** Fasting or non-fasting blood sample	**Metric :Non-HDL-cholesterol (mg/dL)** **Scoring:** Points Level 100 <130 60 130 – 159 40 160 – 189 20 190 – 219 0 ≥220 If drug-treated level, subtract 20 points
	Blood glucose	**Measurement: Fasting blood glucose or casual hemoglobin A1c Example tools for measurement: Fasting (FBG, HbA1c) or non-fasting (HbA1c) blood sample**	**Metric: Fasting blood glucose (mg/dL) or Hemoglobin A1c (%)** **Scoring:** Points Level 100 No history of diabetes and FBG <100 (or HbA1c < 5.7) 60 No diabetes and FBG 100 – 125 (or HbA1c 5.7-6.4) (Pre-diabetes) 40 Diabetes with HbA1c <7.0 30 Diabetes with HbA1c 7.0 – 7.9 20 Diabetes with HbA1c 8.0 – 8.9 10 Diabetes with Hb A1c 9.0 – 9.9 0 Diabetes with HbA1c ≥10.0
	Blood pressure	**Measurement:** Appropriately measured systolic and diastolic blood pressure **Example tools for measurement:** Appropriately sized blood pressure cuff	**Metric:** Systolic and diastolic blood pressure (mm Hg) **Scoring:** Points Level 100 <120/<80 (Optimal) 75 120-129/<80 (Elevated) 50 130-139 or 80-89 (Stage I HTN) 25 140-159 or 90-99 0≥160 or≥100

Supplementary Method 3: Health-related factors

Blood biochemistry was conducted at baseline assessment the full list of markers, included markers for liver and kidney function, systemic inflammation, lipid metabolism, glucose homeostasis and calcium metabolism among others. Some of these markers were included into the measure of allostatic load, including albumin, C-reactive protein, total cholesterol, HDL-cholesterol, and glycated hemoglobin (HbA1c). Clinical criteria summarized in **Supplementary Table 5** were used to obtain risk indicators. Glycosylated hemoglobin was measured in mmol/mol and converted to %, with a cutoff of 6.4% corresponding to 41.8 mmol/mol, using high performance liquid chromatography, Bio-Rad Variant II. Nurses and phlebotomists collected blood and urine samples from participants at the assessment center after an overnight fast, which was determined largely compliant based on the pilot testing phase[14]. Among blood measures, we used total cholesterol (mg/dl), HDL-cholesterol (mg/dl), CRP (mg/dl), albumin (g/dl) and glycosylated hemoglobin (%) which were analyzed by contract laboratories[14]. Specifically, blood lipids were measured using direct enzymatic methods (Konelab, Thermo Fisher Scientific, Waltham, Massachusetts). Using standard protocols, waist-to-hip ratio, radial pulse (beats/min), and systolic and diastolic blood pressure (mmHg) were measured by trained examiners. Specifically, both blood pressure and pulse rate were measured using the Omron HEM-7015IT digital blood pressure monitor[14].

BMI

The body mass index was computed at baseline assessment measured weight in kilograms divided by measured height-squared in squared-meters.

Allostatic Load (AL)

Using a method described previously, [15] AL total score is an index that adds up with equal weighting (range: 0-9), cardiovascular (systolic and diastolic blood pressure, pulse rate), metabolic (total cholesterol, HDL-cholesterol, glycosylated Hb, sex-specific waist-to-hip ratio) and inflammatory (albumin and C-reactive protein (CRP)) risk indicators.

Co-morbidity index

Two data fields (134 and 135) were used to construct a variable for cancer and non-cancer co-morbidity index at the baseline assessment. These are based on self-reported data on pre-existing co-morbidities.

Self-rated health

Self-rated health (or overall health rating) was obtained as part of the touchscreen questionnaire at baseline assessment the UK Biobank. Possible responses were: 1. Excellent, 2. Good, 3. Fair, 4. Poor. The coding was left as is to reflect poorer health with higher score.

Supplementary Table 5 Allostatic load indicator criteria[15]

	High-risk clinical
Albumin (g/dL)	< 3.8 [16]
C-reactive protein (mg/dL)	≥ 0.3 [17]
Waist:Hip Ratio	>0.9 for males; > 0.85 for females [18]
Total cholesterol (mg/dL)	≥240[19]
HDL-C (mg/dL)	<40[19]
Glycated hemoglobin (%)	≥6.4[20, 21]
Resting heart rate (beat/min)	≥90[22]
Systolic BP	≥140[23]
Diastolic BP	≥90[23]

Abbreviations: BP=Blood Pressure; HDL=High Density Lipoprotein-Cholesterol

Supplementary method 4: Cognitive test performance: assessment and scoring

The UK Biobank performed touchscreen computer assessment of cognitive performance on all participants in the case of the pairs memory test and the reaction time test. A sub-sample also completed the numeric memory test, a prospective memory task and a numeric and verbal reasoning test [24, 25]. Those tests were shown to correlate with general cognitive ability (R^2: 0.3-0.6), though generally had a lower test-retest reliability compared to reference cognitive tasks (R^2 varied from 0.4 to 0.6) [24, 25]. For our purpose, we used a total of three cognitive test scores from the pairs memory test (two scores) an the reaction time test (one score), to preserve the final sample size.

Visual memory

The visual memory task involved memorizing positions of pairs of cards, followed by successfully matching them after the cards have been turned face down on the screen. In the first round, participants had 3 pairs to remember, while in the second round, they were asked to remember 6 pairs. The number of incorrect matches were of interest and Cronbach α reliability = 0.62[26]. We have focused on the 6 pair version due to its greater difficulty. In addition, the time to complete the visual memory test was also of interest in this study.

Reaction time

Participants completed a touch screen version of the game snap and the time to match each symbol was recorded. They completed twelve rounds with the reaction time averaged across rounds. Cronbach α reliability = 0.85[26].

Supplementary Table 6. Study sample characteristics by sex: The UK Biobank 2006-2021

	Males, n=148,958				Females, n=173,525				P_{sex}
Study sample characteristics	**All males**	**White**	**Non-White**	**P**	**All females**	**White**	**Non-White**	**P**	
Socio-demographic									
Baseline age, y	60.7±5.4	60.8±5.4	59.1±5.7	<0.001	60.1±5.4	60.2±5.4	58.1±5.5	<0.001	**<0.001**
Sex, % female	0.0	0.0	0.0	__	100.0	100.0	100.0	__	__
Race/ethnicity				__				__	
White	96.4	100.0	0.0	__	96.4	100.0	0.0	__	<0.001
Black	0.8	0.0	22.6	__	1.0	0.0	27.5	__	__
South Asian	1.4	0.0_	39.8	__	1.0	0.0	28.3	__	<0.001
Other	1.4	0.0	37.6	__	1.6	0.0	44.2		0.45
Household size	2.3±1.2	2.3±1.1	2.9±1.5	<0.001	2.2±1.2	2.1±1.1	2.6±1.7	<0.001	<0.001
Socio-economic status									
Education									
Low	24.1	24.2	21.6	__	19.8	19.6	24.9	__	__
Intermediate	34.8	35.1	27.9	0.001	43.7	44.2	32.1	<0.001	<0.001
High	41.1	40.7	51.4	<0.001	36.5	36.2	43.0	<0.001	<0.001
Income				<0.001				<0.001	<0.001
Less than £18,000	22.6	22.4	28.1	__	27.8	27.7	32.3	__	__
£18,000–£29,999	26.9	26.9	27.3	__	29.0	29.0	28.3	__	__
£30,000–£51,999	25.8	25.9	22.8	__	24.0	24.0	22.2	__	__
£52,000–£100,000	19.5	19.6	16.7	__	15.5	15.5	13.6	__	__
greater than £100,000	5.2	5.2	5.1	__	3.7	3.7	3.6		
TDI	-1.54±2.99	-1.62±2.9	0.41±3.53	<0.001	-1.57±2.91	-1.65±2.85	0.53±3.43	<0.001	0.013
SES z-score	-0.01±0.73	0.00±0.72	-0.23±0.80	<0.001	-0.05±0.68	-0.03±0.68	-0.33±0.78	<0.001	<0.001
Lifestyle factors									
Smoking									
Smoking status									
Never	78.5	78.4	81.4	__	83.8	83.6	89.9	__	__
Former	10.6	10.8	5.4	<0.001	8.5	8.7	3.1	<0.001	<0.001
Current	10.9	10.8	13.2	<0.001	7.7	7.8	7.1	0.001	<0.001
Environmental tobacco smoke	0.97±5.4	0.97±5.4	1.02±4.72	0.48	0.81±5.1	0.80±5.1	1.04±4.73	<0.001	<0.001
Pack-years of tobacco smoke	0.10±0.30	0.10±0.30	0.07±0.22	<0.001	0.07±0.22	0.07±0.22	0.04±0.16	<0.001	<0.001
SMOKING z-score	-0.002±0.481	-0.000±0.482	-0.050±0.454	<0.001	-0.008±0.405	-0.008±0.406	-0.004±0.383	0.51	<0.001
Alcohol consumption									
Alcohol consumption frequency									
0 "never"	5.5	4.9	21.2	____	8.8	8.1	27.4	__	__
1 "special occasions only"	6.8	6.5	16.5	<0.001	14.8	14.2	30.0	<0.001	<0.001
2 "1-3 times per month"	8.0	8.0	10.1	<0.001	12.5	12.5	11.6	<0.001	0.020
3 "1-3 times per week"	24.5	24.6	21.4	<0.001	25.0	25.3	15.4	<0.001	<0.001
4 "3-4 times per week"	26.8	27.2	15.6	<0.001	21.6	21.5	8.9	<0.001	<0.001
5 "daily or almost daily"	28.4	28.9	15.2	<0.001	17.9	18.4	6.8	<0.001	<0.001

								<0.001	<0.001
ALCOHOL z-score	+0.20±0.94	0.23±0.92	-0.49±1.15	<0.001	-0.17±1.00	-0.14±1.00	-0.96±1.02	<0.001	<0.001
Physical activity, PA									
PA, Met.min.wk^{-1}	2,169±3.189	2,180±3,194	1,853±3,023	<0.001	1,787±2,437	1,790±2,431	1,703±2,580	0.005	
PA z-score	0.07±1.13	0.08±1.13	-0.039±1.07	<0.001	-0.06±0.86	-0.06±0.86	-0.09±0.92	0.005	<0.001
									<0.001
Diet quality									
HDI total score	4.81±1.56	4.79±1.57	5.13±1.49	<0.001	5.37±1.39	5.36±1.39	5.57±1.35	<0.001	<0.001
DIET z-score	-0.20±1.04	-0.21±1.04	+0.01±0.99	<0.001	+0.17±0.93	0.17±0.93	0.31±0.90	<0.001	<0.001
Nutritional Biomarkers									
25-hydroxyvitamin D	49.7±21.1	50.3±20.9	33.8±17.9	<0.001	49.6±20.7	50.0±20.6	36.9±18.1	<0.001	0.016
Red cell distribution width	13.5±0.9	13.5±0.9	13.7±1.1	<0.001	13.5±1.0	13.5±0.9	13.9±1.3	<0.001	0.002
NUTR z-score	0.004±0.733	+0.023±0.723	-0.500±0.823	<0.001	-0.005±0.777	0.013±0.766	-0.49±0.91	<0.001	0.001
Social Support									
"How often do you visit friends or family or have them visit you?"	5.09±1.16	5.10±1.16	4.81±1.20	<0.001	5.42±1.09	5.44±1.08	4.86±1.21	<0.001	<0.001
"How often are you able to confide in someone close to you?"	1.00±0.83	1.00±0.83	0.91±0.80	<0.001	1.08±0.90	1.08±0.90	0.98±0.85	<0.001	<0.001
"Which of the following do you attend once a week or more often?"	3.43±2.02	3.44±2.02	2.93±2.04	<0.001	3.65±1.76	3.67±1.75	3.12±1.92	<0.001	<0.001
SS z-score	-0.089±0.645	-0.082±0.642	-0.293±0.671	<0.001	0.075±0.614	0.086±0.609	-0.221±0.664	<0.001	<0.001
Cardio-metabolic and general health-related factors									
Body mass index, kg.m^{-1}	27.9±4.2	27.9±4.2	27.5±4.1	<0.001	27.2±5.1	27.1±5.0	28.1±5.6	<0.001	<0.001
Allostatic load	2.42±1.35	2.41±1.35	2.46±1.38	0.019	1.83±1.35	1.82±1.34	2.02±1.40	<0.001	<0.001
Co-morbidity index	2.07±1.86	2.07±1.86	2.08±1.84	0.91	2.15±2.00	2.15±2.01	2.16±1.98	0.50	<0.001
Self-rated health				<0.001				<0.001	<0.001
Excellent	15.8	16.0	11.9		17.1	17.4	10.7		
Good	56.9	57.0	52.4		60.8	61.1	53.9		
Fair	22.5	22.2	28.8		18.7	18.3	28.8		
Poor	4.9	4.8	6.9		3.4	3.3	6.6		
HEALTH z-score	0.077±0.660	0.076±0.661	0.117±0.650	<0.001	-0.066±0.704	-0.072±0.702	0.104±0.743	<0.001	<0.001
Cognitive performance									
Reaction Time	6.31±0.19	6.31±0.18	6.40±0.22	<0.001	6.34±0.18	6.34±0.18	6.42±0.22	<0.001	<0.001
Pairs matching, errors	0.71±0.71	0.70±0.70	1.00±0.75	<0.001	0.72±0.69	0.71±0.69	0.99±0.71	<0.001	<0.001
Pairs matching, time to complete	5.34±0.37	5.33±0.37	5.57±0.47	<0.001	5.36±0.37	5.35±0.36	5.58±0.46	<0.001	<0.001
COGN z-score	-0.043±0.764	-0.062±0.750	+0.456±0.940	<0.001	0.037±0.746	0.019±0.73	0.504±0.896	<0.001	<0.001

LE8									
Total score	493.3±93.0	493.7±93.0	483.7±94.0	<0.001	510.1±97.1	510.8±97.1	493.2±96.1	<0.001	<0.001
Biological score	243.7±62.0	243.8±61.9	239.5±64.3	<0.001	248.7±69.0	249.3±68.3	233.1±73.7	<0.001	<0.001
Lifestyle score	249.6±63.8	249.8±63.7	243.9±64.9	<0.001	261.2±62.3	261.3±62.3	258.7±60.8	0.001	<0.001
Incidence proportion									
All-cause dementia	1.99 (n=2,980)	1.99 (n=2,882)	1.81 (n=98)	0.34	1.45 (n=2,511)	1.46 (n=2,439)	1.14 (n=72)	0.040	<0.001
AD dementia	0.76 (n=1,147)	0.77 (n=1,111)	0.66 (n=36)	0.39	0.67 (n=1,167)	0.68 (n=1,134)	0.53 (n=33)	0.14	0.002
Incident rates, per 100,000 P-Y									
All-cause dementia	164	164	214 (Black) 132 (SA) 134 (Others)		117	117	130(Black) 74(SA) 85(Others)	—	—
AD dementia	63	63	69 (Black) 58 (SA) 45 (Others)		54	54	63 (Black) 41(SA) 32(Others)	—	—

Abbreviations: AD=Alzheimer's Disease; ALCOHOL=Alcohol consumption z-score; COGN=Poor cognitive performance z-score; DIET=diet quality z-score; HEALTH=Cardio-metabolic and general health z-score; PA=Physical Activity z-score; NUTR=Nutritional biomarker z-score; SES=Socio-economic status z-score; SMOKING=Smoking z-score; SS=Social Support z-score.

Supplementary Table 7. Generalized Structural Equations models (GSEM) for racial/ethnic disparities in all-cause dementia: mediation through SES, alternative lifestyle factors (LIFESTYLE), health-related factors (HEALTH) and cognitive performance (COGN): The UK Biobank 2006-2021

	LIFESYLTE					
	DIET	PA	SMOKING	ALCOHOL	NUTR	SS
Main pathway						
RACE_ETHN→SES (β_{12})	**-0.351±0.006*** **	**-0.351±0.006*** **	**-0.351±0.006*** **	**-0.351±0.006*** **	**-0.351±0.006*** **	**-0.351±0.006*** **
SES→LIFESTYLE (β_{23})	**+0.192±0.003*** **	**-0.059±0.003*** **	**-0.152±0.002*** **	**+0.305±0.002*** **	**+0.102±0.002*** **	**+0.086±0.002*** **
LIFESTYLE → HEALTH (β_{34})	**-0.081±0.001*** **	**-0.091±0.001*** **	**+0.046±0.002*** **	**-0.094±0.001*** **	**-0.168±0.002*** **	**-0.063±0.002*** **
HEALTH→COGN(β_{45})	-0.002±0.002	-0.001±0.002	-0.003±0.002	**-0.010±0.002*** **	**-0.007±0.002*** **	**-0.006±0.002*** **
COGN → DEMENTIA (β_{56})	**+0.416±0.017*** **	**+0.416±0.017*** **	**+0.416±0.017*** **	**+0.412±0.017*** **	**+0.414±0.017*** **	**+0.410±0.017*** **
Selected direct effects on final outcomes						
RACE_ETHN→DEMENTIA(β_{16})	**-0.167±0.080***	**-0.156±0.079***	**-0.157±0.079***	**-0.202±0.080***	**-0.209±0.080** **	**-0.184±0.079***
SES → DEMENTIA(β_{26})	**-0.220±0.020*** **	**-0.215±0.020*** **	**-0.216±0.020*** **	**-0.196±0.020*** **	**-0.209±0.020*** **	**-0.203±0.020***
LIFESTYLE → DEMENTIA(β_{36})	+0.026±0.014	+0.011±0.013	-0.004±0.019	**-0.075±0.014*** **	**-0.111±0.017*** **	**-0.163±0.021*** **
HEALTH → DEMENTIA(β_{46})	**+0.408±0.019*** **	**+0.407±0.019*** **	**+0.404±0.019*** **	**+0.388±0.019*** **	**+0.378±0.020*** **	**+0.395±0.019*** **
Other effects between endogenous variables						
SES→HEALTH (β_{24})	**-0.211±0.002*** **	**-0.232±0.002*** **	**-0.219±0.002*** **	**-0.198±0.002*** **	**-0.209±0.002*** **	**-0.221±0.002*** **
SES→COGN (β_{25})	**-0.135±0.002*** **	**-0.131±0.002*** **	**-0.136±0.002*** **	**-0.125±0.002*** **	**-0.132±0.002*** **	**-0.131±0.002*** **
LIFESTYLE→COGN (β_{35})	**+0.015±0.001*** **	**+0.016±0.001*** **	**-0.023±0.002*** **	**-0.029±0.001*** **	**-0.014±0.0017*** **	**-0.131±0.002*** **
Other direct effects of race						
RACE_ETHN→LIFESTYLE (β_{13})	**+0.257±0.009*** **	**-0.076±0.009*** **	**-0.103±0.007*** **	**-0.675±0.009*** **	**-0.482±0.007*** **	**-0.217±0.006*** **
RACE_ETHN→HEALTH(β_{14})	**+0.093±0.006*** **	**+0.065±0.006*** **	**+0.077±0.006*** **	+0.009±0.006	-0.009±0.006	**+0.059±0.006*** **
RACE_ETHN→COGN(β_{15})	**+0.523±0.007*** **	**+0.528±0.007*** **	**+0.524±0.007*** **	**+0.507±0.007*** **	**+0.521±0.007*** **	**+0.520±0.007*** **

Selected Indirect effects

RACE_ETHN → SES → DEMENTIA(β_A)	**+0.077±0.007*** **	**+0.075±0.007*** **	**+0.076±0.007*** **	**+0.068±0.007*** **	**+0.073±0.007*** **	**+0.071±0.007*** **
RACE_ETHN → SES → LIFESTYLE → DEMENTIA(β_B)	-0.002±0.001	+0.0002±0.0003	-0.0002±0.0010	**+0.0081±0.0015*** **	**+0.0040±0.0006*** **	**+0.0050±0.0006*** **
RACE_ETHN → SES → LIFESTYLE → HEALTH → DEMENTIA(β_C)	**+0.0022±0.0001*** **	**-0.00076±0.00005*** **	**+0.00099±0.00006*** **	**+0.0039±0.0002*** **	**+0.0023±0.0001*** **	**+0.00075±0.0000*** **
RACE_ETHN → SES → LIFESTYLE → HEALTH → COGN → DEMENTIA(β_D)	0.0000±0.0000	0.00000±0.00000	+0.0000±0.0000	**-0.00004±0.0000*** **	**-0.00002±0.00000*** **	**+0.0000±+0.0000** **
RACE_ETHN → SES → LIFESTYLE→ COGN → DEMENTIA(β_E)	**-0.00043±0.00004*** **	**0.000136±0.000014*** **	**-0.00051±0.00005*** **	**+0.00129±0.00008** ** *	**+0.00021±0.0000*** **	**+0.00039±0.00003*** **
RACE_ETHN → SES → COGN → DEMENTIA(β_F)	**+0.0197±0.0009*** **	**0.0191±0.0009*** **	**+0.0198±0.0009*** **	**+0.0181±0.0009*** **	**+0.0192±0.0009*** **	**+0.0188±0.0009*** **
TOTAL EFFECT OF RACE_ETHN	**+0.232±0.078** **	**+0.232±0.078** **	**+0.232±0.078** **	**+0.232±0.078** **	**+0.232±0.078** **	**+0.232±0.078** **

Abbreviations: AD=Alzheimer's Disease; ALCOHOL=Alcohol consumption z-score; COGN=Poor cognitive performance z-score; DIET=diet quality z-score; HEALTH=Cardio-metabolic and general health z-score; NUTR=Nutritional biomarker z-score; PA=Physical Activity z-score; RACE_ETHN=Race/ethnicity; SES=Socio-economic status z-score; SMOKING=Smoking z-score; SS=Social Support z-score.

[a] Values are path coefficients $\beta \pm$ SE or non-linear combinations of path coefficients to compute selected indirect effects. →DEMENTIA associations are interpreted as Log_e(HR) of these incident outcomes per unit exposure, as are total effects of RACE_ETHN.

*P<0.05 **P<0.01 ***P<0.001 for null hypothesis of β=0.

Supplementary Table 8. Generalized Structural Equations models (GSEM) models for racial/ethnic disparities in all-cause dementia: mediation through SES, alternative lifestyle factors (LIFESTYLE) and health-related factors (HEALTH): The UK Biobank 2006-2021

	LIFESYLTE					
	DIET	PA	SMOKING	ALCOHOL	NUTR	SS
Main pathway						
RACE_ETHN→SES (β_{12})	**-0.351±0.006*** **	**-0.350±0.006*** **	**-0.350±0.006*** **	**-0.351±0.006*** **	**-0.351±0.006*** **	**-0.351±0.006*** **
SES→LIFESTYLE (β_{23})	**+0.192±0.003*** **	**-0.059±0.003*** **	**-0.152±0.002*** **	**+0.305±0.002*** **	**+0.102±0.002*** **	**+0.086±0.002*** **
LIFESTYLE → HEALTH (β_{34})	**-0.081±0.001*** **	**-0.091±0.001*** **	**+0.046±0.002*** **	**-0.094±0.001*** **	**-0.168±0.002*** **	**-0.063±0.002*** **
HEALTH → DEMENTIA(β_{46})	**+0.408±0.019*** **	**+0.408±0.019*** **	**+0.404±0.019*** **	**+0.384±0.019*** **	**+0.376±0.020*** **	**+0.394±0.020*** **
Selected direct effects on final outcomes						
RACE_ETHN→DEMENTIA(β_{16})	+0.092±0.079	+0.104±0.078	+0.101±0.078	+0.048±0.079	+0.050±0.079	+0.067±0.079
SES → DEMENTIA(β_{26})	**-0.284±0.020*** **	**-0.278±0.020*** **	**-0.281±0.020*** **	**-0.255±0.020*** **	**-0.272±0.020*** **	**-0.265±0.020*** **
LIFESTYLE → DEMENTIA(β_{36})	**0.032±0.014***	+0.018±0.013	-0.017±0.020	**-0.091±0.014*** **	**-0.117±0.017*** **	**-0.184±0.021*** **
Other effects between endogenous variables						
SES→HEALTH (β_{24})	**-0.211±0.002*** **	**-0.232±0.002*** **	**-0.219±0.002*** **	**-0.198±0.002*** **	**+0.102±0.002*** **	**-0.221±0.002*** **
Other direct effects of race						
RACE_ETHN→LIFESTYLE (β_{13})	**+0.257±0.009*** **	**-0.076±0.009*** **	**-0.104±0.007*** **	**-0.675±0.009*** **	**-0.482±0.007*** **	**-0.217±0.006*** **
RACE_ETHN→HEALTH(β_{14})	**+0.093±0.006*** **	**+0.065±0.006*** **	**+0.077±0.006*** **	+0.009±0.006	-0.009±0.006	**+0.059±0.006*** **
Selected Indirect effects						
RACE_ETHN → SES → DEMENTIA(β_A)	**+0.0998±0.0073*** **	**+0.0977±0.0070*** **	**+0.0987±0.0073*** **	**+0.0896±0.0073*** **	**+0.096±0.007*** **	**+0.093±0.007*** **
RACE_ETHN → SES → LIFESTYLE → DEMENTIA(β_B)	**-0.0022±0.0009***	+0.0004±0.0003	-0.0009±0.0010	**+0.0097±0.0014*** **	**+0.0042±0.0006*** **	**+0.0055±0.0007*** **

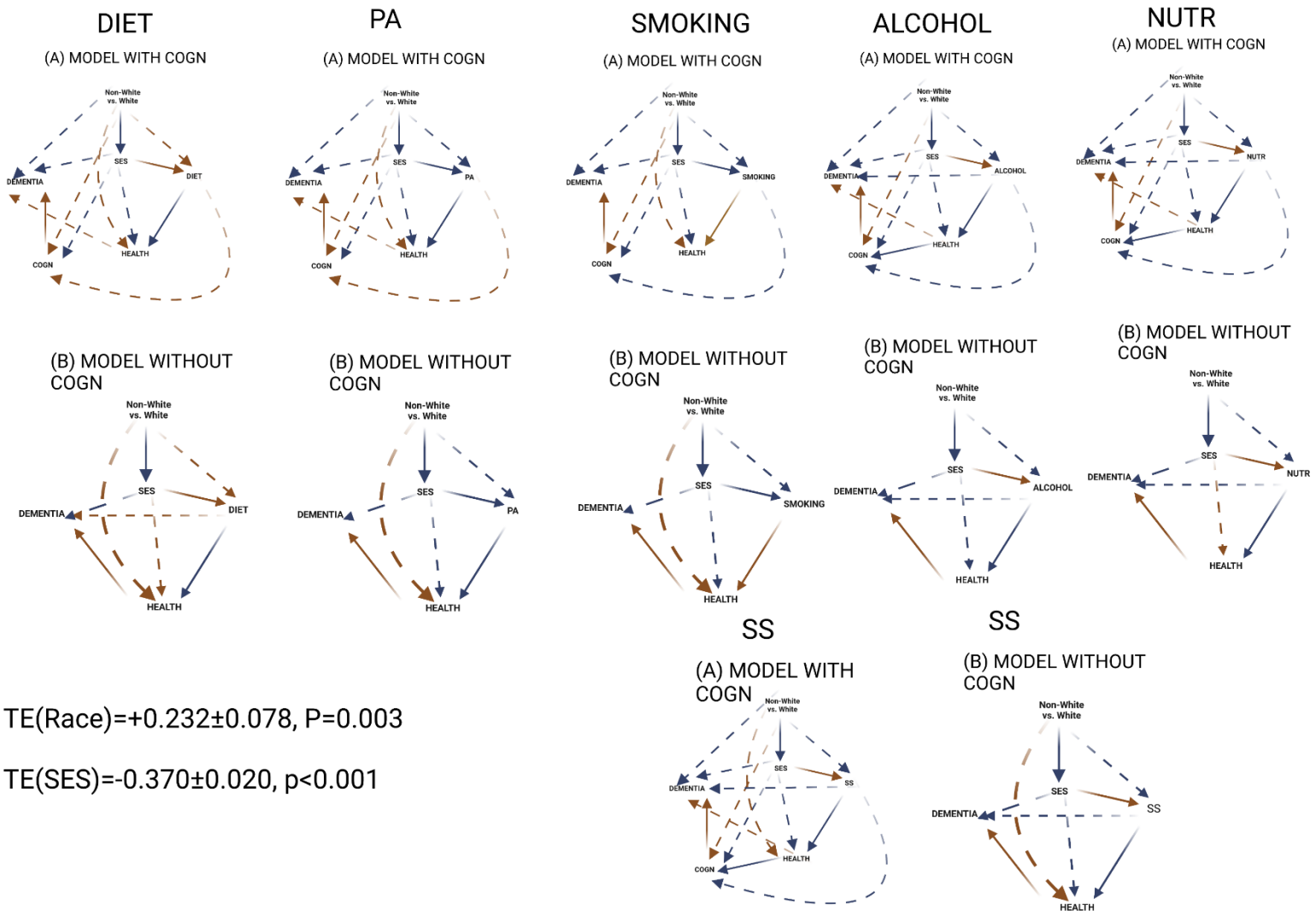
RACE_ETHN → SES → LIFESTYLE → HEALTH → DEMENTIA(β_C)	**+0.0022±0.0001*** **	**-0.00076±0.00005*** **	**+0.000991±0.00006*** **	**+0.0039±0.0002*** **	**+0.0023±0.0001*** **	**+0.00075±0.0000*** **
TOTAL EFFECT OF RACE_ETHN	**+0.232±0.078****	**+0.232±0.078****	**+0.232±0.078****	**+0.232±0.078****	**+0.232±0.078****	**+0.232±0.078****

Abbreviations: AD=Alzheimer's Disease; ALCOHOL=Alcohol consumption z-score; COGN=Poor cognitive performance z-score; DIET=diet quality z-score; HEALTH=Cardio-metabolic and general health z-score; NUTR=Nutritional biomarker z-score; PA=Physical Activity z-score; RACE_ETHN=Race/ethnicity; SES=Socio-economic status z-score; SMOKING=Smoking z-score; SS=Social Support z-score.

[a] Values are path coefficients $\beta \pm$ SE or non-linear combinations of path coefficients to compute selected indirect effects. →DEMENTIA associations are interpreted as Log_e(HR) of these incident outcomes per unit exposure, as are total effects of RACE_ETHN.

*P<0.05 **P<0.01 ***P<0.001 for null hypothesis of β=0.

Supplementary Figure 2. GSEM findings from models with alternative mediators, HEALTH and COGN



TE(Race)=+0.232±0.078, P=0.003

TE(SES)=-0.370±0.020, p<0.001

Abbreviations: AD=Alzheimer's Disease; ALCOHOL=Alcohol consumption z-score; COGN=Poor cognitive performance z-score; DIET=diet quality z-score; HEALTH=Cardio-metabolic and general health z-score; PA=Physical Activity z-score; NUTR=Nutritional biomarker z-score; SES=Socio-economic status z-score; SMOKING=Smoking z-score; SS=Social Support z-score;TE=Total Effect.

Supplementary results 1

The estimated incidence rate of all-cause dementia among men was 164 per 100,000 person-years (P-Y); among women it was 117 per 100,000 per year. For AD, incidence estimates were 63 per 100,000 P-Y among men and 54 per 100,000 P-Y among women. Dementia incidence rates for both sexes were greater among Black adults compared to White adults, which was the reverse for rates among SA and other ethnic groups. Racial/ethnic composition differed significantly across sexes, with greater percentage of Black adults among women compared to men (1.0% (F) vs. 0.8% (M)), coupled with a greater percentage SA among men vs. women (1.4% (M) vs. 1.0% (F)). Moreover, minority groups overall were younger than White adults in this sample (58.6 (NW) vs. 60.5y (W), mean age). Household size was larger in the minority group compared to White adults (2.7 (NW) vs. 2.2 (W)) in both sexes. Importantly, non-White adults had lower SES compared to White adults (z-score: -0.28 (NW), -0.02 (W)). There were both sex and racial differences in the smoking construct. The SMOKING z-score was lower among minority groups compared to White adults (-0.025 (NW) vs. -0.004 (W)), and higher among men (-0.002) compared to women (-0.008). In contrast, men tended to consume alcohol more frequently than women, and non-White adults were less heavy consumers compared to their White counterparts. Physical activity measured in $Met.min.wk^{-1}$ was lower among non-White adults vs. White adults, and among women compared to men. There were notable racial and ethnic differences in the NUTR z-score, owing mainly to reduced vitamin D level among non-White compared to White adults. Minority groups had poorer general and cardiometabolic health compared to White adults as did men compared with women. Minority groups combined and women performed worse on a set of cognitive test scores compared to their White and male counterparts. LE8 total, lifestyle and biological scores were markedly higher among White adults compared to non-White adults, and were also higher among women than men, suggesting a more optimal cardiovascular health among White adults and women.

Figure S2 illustrates the results of **Tables S7** and **S8**, which examined similar GSEM models by substituting $LE8_{LIFESTYLE}$ with other alternative LIFESTYLE factors (DIET, PA, SMOKING, ALCOHOL, NUTR and SS), and $LE8_{BIOLOGICAL}$ with the HEALTH score. The results were comparable to the LE8 findings. Focusing on **Model B**, NUTR and SS were among the key antecedent mediators to HEALTH explaining racial/ethnic and SES disparities in all-cause dementia risk, both of which by being associated with reduced risk. More specifically, `RACE_ETHN(-)→SES(+)→ NUTR(-)→DEMENTIA' and `RACE_ETHN(-)→ SES(+)→ SS(-)→ DEMENTIA' are pathways that explained 0.9% and 0.3% of the total effect RACE_ETHN→ DEMENTIA, respectively. This is in contrast with `RACE_ETHN(-)→ NUTR(-)→ DEMENTIA' and `RACE_ETHN(-)→ SS(-)→ DEMENTIA', which explained about 25% and 17% of the total effect, respectively. Nevertheless, the residual pathway `RACE_ETHN→ SES→DEMENTIA' in these models explained around half of the RACE_ETHN→ DEMENTIA total effect. Other notable pathways by which RACE_ETHN could adversely impact dementia risk included `RACE_ETHN(-)→ SES(+)→ DIET(-)→ HEALTH(+)→ DEMENTIA'; `RACE_ETHN(-)→ PA(-)→ HEALTH(+)→DEMENTIA';`RACE_ETHN(-)→SES(-)→SMOKING(+)→HEALTH(+)→ DEMENTIA'; and `RACE_ETHN(-)→ SES(-)→ HEALTH(+)→ DEMENTIA'.

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