The Journal of Prevention of Alzheimer's Disease 13 (2026) 100319

Contents lists available at ScienceDirect

The Journal of Prevention of Alzheimer's Disease

journal homepage: www.elsevier.com/locate/tjpad

Original Article

Dietary index for gut microbiota (DI-GM) and cognitive function: NHANES findings and validation in a Hong Kong cohort with metagenomic data

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ARTICLE INFO

Keywords:
Older adults
NHANES
Cognitive function
DI-GM
Fiber
Metagenomic

ABSTRACT

Background: The diet-gut-microbiota-brain axis is critical for maintaining brain health. The Dietary Index for Gut Microbiota (DI-GM), comprising beneficial and unfavorable components, may serve as a proxy for this connection, yet its association with cognition remains underexplored.

Methods: This study examined the relationship between DI-GM, its components, and cognitive function in older adults using data from the National Health and Nutrition Examination Survey (NHANES). Findings were validated in an independent Hong Kong osteoporosis cohort (OS cohort) with gut metagenomic data to assess of microbiota's mediating role in diet-cognition relationship. Cognitive assessment in NHANES utilized the Consortium to Establish a Registry for Alzheimer's Disease (CERAD), Animal Fluency Test (AFT), and Digit Symbol Substitution Test (DSST), while the OS cohort employed the Hong Kong version of the Montreal Cognitive Assessment (HK-MoCA). DI-GM was calculated from 24-hour dietary recalls. The diet-cognition associations were assessed by weighted multivariate regressions, supplemented by restricted cubic spline (RCS), subgroup, correlation network, and mediation analyses.

Results: Higher DI-GM was significantly associated with better performance on DSST (OR=0.90; 95 % CI: 0.82, 0.99; $p = 0.033$). The beneficial-to-gut-microbiota score (BGMS) associated with lower psychometric mild cognitive impairment (p-MCI) risk (OR=0.88; 95 % CI: 0.80, 0.98; $p = 0.022$) and better CERAD immediate and delayed recall and DSST (all $p < 0.05$). The beneficial-to-gut-microbiota components like dietary fiber demonstrated protective effects across cognitive domains, while refined grains was associated with poorer cognition. In the OS cohort, higher dietary fiber intake correlated with higher HK-MoCA score ($p < 0.05$) and increased abundance of fermenting bacteria. Among these species, *Eubacterium ventriosum* mediated the beneficial effect of dietary fiber intake on dementia risk reduction, with an indirect effect of -0.014 (95 % CrI: -0.040, -0.001), accounting for approximately 12.7 % of the total effect.

Conclusion: Higher adherence to beneficial-to-gut-microbiota dietary patterns, as reflected by DI-GM, was associated with better cognitive function in older adults. These findings highlight the importance of a gut-microbiota-targeted diet in maintaining cognitive health.

1. Introduction

With the world's population ageing rapidly, dementia is now a growing public health concern [1]. In the U.S. alone, over 7 million are living with Alzheimer's disease (AD), and the cost of illness amounts to 384 billion dollars [2]. Mild cognitive impairment (MCI) [3], a precursor to dementia, is estimated to affect roughly 8 % to 11 % of Americans aged 65 and older [2]. These figures highlight the urgent need to

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https://doi.org/10.1016/j.tjpad.2025.100319
Received 9 June 2025; Received in revised form 26 July 2025; Accepted 28 July 2025
Available online 5 August 2025

mitigate the growing burden of cognitive decline.

Growing evidence suggests that dementia is closely connected to dietary factors and gut microbiota. Studies have shown that diet can help slow cognitive decline, making them a promising preventive strategy [4,5]. Gut microbiota may affect cognitive function via its roles in systemic and neuroinflammation, blood-brain barrier integrity, and the generation of neuroactive metabolites [6,7]. In addition, diet plays a crucial role in shaping gut microbiota composition [8]. The interplay between diet and gut microbiota significantly influences health outcomes [9], shaping microbial balance and affecting metabolism and inflammation [10–12]. These interactions are key modulators of dementia risk, highlighting the potential of gut-microbiota-targeted dietary strategies.

To capture dietary patterns that promote a gut microbiota ecosystem beneficial to brain health, the Dietary Index for Gut Microbiota (DI-GM) was developed. Unlike established indices designed for broader health outcomes, such as the Dietary Approaches to Stop Hypertension (DASH) and the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND), DI-GM was constructed based on a systematic review of 106 studies, identifying 14 dietary components with consistent evidence of beneficial (e.g., fermented dairy, whole grains, fiber, green tea) or unfavorable (e.g., red and processed meats, refined grains) effects on gut microbiota [13]. This microbiota-targeted design provides a unique tool to investigate how diet influences cognition through the gut-microbiota-brain axis. Higher DI-GM scores, reflecting greater adherence to its microbiota-beneficial components, have been linked to reduced risk of brain diseases such as depression and stroke [14,15]. However, its association with cognitive function remains unexplored.

In this study, we aimed to investigate the association between the DI-GM and cognitive function using data from the National Health and Nutrition Examination Survey (NHANES). To validate part of our findings, we additionally analyzed data from an independent Hong Kong osteoporosis cohort (OS cohort), which included older adults with dietary records, cognitive assessments, and fecal metagenomic sequencing data. This enabled a focused evaluation of key DI-GM components, particularly dietary fiber, in relation to both cognitive function and gut microbial composition. By analyzing NHANES and validating key findings in the OS cohort, our study provided novel insights into the diet-gut microbiota-brain relationship.

2. Methods

2.1. Data source

This study was based on data from two complementary sources: [1] NHANES, and [2] OS cohort. NHANES served as the primary dataset for exploring associations between the DI-GM, its dietary components, and cognitive function. To strengthen and validate these findings, the OS cohort was additionally analyzed, with a particular focus on the associations of specific dietary components with both cognitive outcomes and gut microbiota.

NHANES is an ongoing survey conducted by the National Center for Health Statistics (NCHS) using a complex, stratified, multistage probability sampling method to assess the health and nutritional status of the non-institutionalized US national population. We utilized data from the 2011–2014 survey cycles, which included relevant dietary and cognitive assessments. All study protocols received approval from the NCHS Ethics Review Board, and written informed consent was obtained from all participants.

OS cohort is a community cohort of an ongoing study to examine the determinants of osteoporotic fractures in Hong Kong older adults initiated in 2001, with 2000 men and 2000 women recruited [16]. For the current analysis, we used data collected between 2022 and 2024, during which participants underwent the Hong Kong version of the Montreal Cognitive Assessment (HK-MoCA), completed 24-hour dietary recall interviews, and provided stool samples for metagenomic sequencing. This cohort was primarily used to validate key findings from the NHANES analysis, focusing particularly on the impact of dietary fiber and refined grains on both cognitive function and gut microbiota composition. All participants provided written informed consent, and the research protocol received approval from the Clinical Research Ethics Committee of the Chinese University of Hong Kong.

2.2. DI-GM

DI-GM is a literature-driven composite measure designed to assess how well an individual's dietary patterns support a healthy gut microbiota environment [13]. It was developed using the 24-hour dietary recall data from NHANES 2011–2014. Based on 14 food components, the index categorizes them into two groups: beneficial and unfavorable. For beneficial components including avocados, broccoli, chickpeas, coffee, cranberries, fermented dairy, fiber, green tea, soybeans and whole grains, a score of 1 was assigned if the individual's intake was equal to or above the sex-specific median; otherwise, a score of 0 was given. These scores were summed to calculate the Beneficial-to-Gut-Microbiota Score (BGMS), ranging from 0 to 10. For unfavorable components including refined grains, red or processed meats and high-fat diet, a score of 1 was assigned if the individual's intake of refined grains and red or processed meats was below the sex-specific median, and if fat contributed less than 40 % of total energy intake. These scores were summed to generate the Unfavorable-to-Gut-Microbiota Score (UGMS), ranging from 0 to 4. The DI-GM score ranges from 0 to 14, with higher scores representing diets that are more supportive of gut microbiota health. Based on the previous study, the total DI-GM score was categorized into four quartiles: 0–3, 4, 5, and 6 or more [14]. Detailed information regarding DI-GM was available in Supplementary Table S1.

2.3. Cognitive tests

In NHANES 2011–2014, cognition was evaluated using the Consortium to Establish a Registry for Alzheimer's Disease Immediate Recall (CERAD-IR) and Delayed Recall (CERAD-DR) [17], the Animal Fluency Test (AFT) [18], and the Digit Symbol Substitution Test (DSST) [19]. CERAD-IR involved three immediate recall trials, with the total score representing the sum of the correct words recalled across all trials, while CERAD-DR assessed delayed recall after an 8–10 min interval. The total CERAD score was the sum of CERAD-IR (maximum score of 30) and CERAD-DR (maximum score of 10). The AFT measured category fluency, with participants tasked to name as many animals as possible in one minute, and the DSST assessed processing speed, attention, and working memory through symbol-number matching. A composite cognitive score (Cognition-total) was derived by summing the individual scores of CERAD, AFT, and DSST. In the OS cohort, global cognition was assessed using HK-MoCA [20], which evaluated seven domains: visuospatial/executive, naming, attention, language, abstraction, delayed recall, and orientation, with a maximum score of 30.

Consistent with previous studies of NHANES [21–23], this study defined the cognitive outcomes as (i) classification into 'normal' and 'low performance' groups using the 25th percentile as the threshold, and (ii) psychometric mild cognitive impairment (p-MCI), based on a composite score more than 1 standard deviation (SD) below the mean [24].

2.4. Covariates

Based on previous NHANES studies [22,25], the potential covariates included age, sex, race, educational level, marital status, poverty income ratio (PIR), smoking status, drinking status, body mass index (BMI), hypertension, diabetes mellitus (DM), and hyperlipidemia. Detailed information regarding these covariates could be found in Supplementary Table S2. In contrast, in the analysis using data from the OS cohort, age and sex were included as covariates.

2.5. Metagenomic sequencing and profiling for OS cohort

Stool samples from participants in OS cohort were collected using the OMNIgene·GUT kit, which allowed for stable preservation of microbial DNA at room temperature. Upon receipt, samples were aliquoted and stored at −80 °C until further processing. Fecal DNA was extracted using the Qiagen PowerSoil Kit, and metagenomic sequencing libraries were prepared using standard protocols, with library preparation performed using the BGI Optimal DNA Library Prep Kit (BGI, Hong Kong, China). Genomic DNA was fragmented and size-selected with magnetic beads. The selected fragments underwent end repair, A-tailing, and adaptor ligation. The library was then amplified by PCR and subjected to quality control. The double-stranded library was denatured to single strands, followed by circularization to form single-stranded circular DNA. Any remaining linear DNA was digested, and the circular library was amplified using rolling circle amplification (RCA) to generate DNA nano balls (DNBs). These DNBs, carrying approximately 300 copies of the original single-stranded library, were loaded into a patterned nanoarray, and sequencing reads of PE150 bases were generated using the DNBSEQ-G400 platform (BGI, Hong Kong, China). Raw metagenomic sequencing data were processed using Kneaddata for quality control and MetaPhlAn4 for taxonomic profiling.

2.6. Statistical analysis

Statistical analyses were performed using R (version 4.3.3). The analysis followed NHANES guidelines by using survey weights (WTMEC2YR) to account for the complex sampling design. For combined data from 2011–2014, each cycle's weight was halved to ensure accurate population estimates. Demographics and cognitive scores were summarized using percentages for categorical variables and weighted means ± standard errors for continuous variables. Differences between groups were examined using either weighted *t*-tests or the Kruskal-Wallis test for continuous variables, and weighted Chi-squared tests for categorical variables. Weighted multivariable logistic regression models was employed to adjust for potential confounders: Model 1 (unadjusted), Model 2 (adjusted for age and sex), and Model 3 (fully adjusted for age, sex, race, educational level, marital status, PIR, smoking status, drinking status, BMI, hypertension, DM, and hyperlipidemia). We also employed restricted cubic spline (RCS) analysis to explore potential nonlinear associations between DI-GM, BGMS, and UGMS and the risk of p-MCI. For each predictor, three knots were placed at the 10th, 50th, and 90th percentiles of its distribution. The number of knots was determined using the Akaike Information Criterion (AIC) to ensure optimal model fit while avoiding overfitting. All RCS models were conducted adjusting for all covariates included in Model 3. Subgroup analyses were conducted by stratifying participants according to age, sex, race, educational level, marital status, PIR, smoking status, drinking status, BMI, hypertension, diabetes, and hyperlipidemia. All subgroup analyses used Model 3 for covariate adjustment, excluding the stratifying variable to avoid over-adjustment. Microbial diversity indices, including Shannon and Simpson, were calculated using the vegan package. Correlations among dietary fiber, refined grains, HK-MoCA, and gut microbiota in the OS cohort were visualized using the psych and igraph packages. Only bacterial taxa showing statistically significant Spearman correlations (adjusted $p < 0.05$) with dietary fiber or refined grains intake, which are the main dietary components of interest, were included in the network. Bayesian causal mediation analysis was performed using the brms package to quantify the mediating effects of gut microbial species significantly associated with dietary fiber intake on the relationship between fiber intake and dementia risk, adjusting for age and sex. Statistical significance was determined at a two-tailed p-value of <0.05.

3. Results

3.1. Study population

From the initial NHANES sample of 19,931 individuals, participants younger than 60 years were excluded, as cognitive assessments were only administered to those aged 60 and above in the 2011–2012 and 2013–2014 cycles. After further excluding individuals with missing cognitive or dietary data, the final analytical sample consisted of 2446 older adults (Fig. 1).

Participant characteristics were summarized in Table 1. Significant differences were observed across several variables among different DI-GM categories, including age, race, education level, marital status, PIR, smoking status, BMI, hypertension, and DM (all $p < 0.05$). The AFT, DSST, and Cognition-total scores increased significantly across DI-GM categories, with higher DI-GM scores associated with better cognitive function (all $p < 0.05$).

Additionally, significant differences in age, race, marital status, drink status, PIR, and hypertension were also observed between p-MCI and non-p-MCI groups (Supplementary Table S3). The p-MCI group had a significantly lower DI-GM score compared to the non-p-MCI group (5.27 ±0.08 vs. 5.47±0.06; mean±SE; $p = 0.041$). Besides, the p-MCI group had lower BGMS and higher UGMS ($p < 0.001$ and 0.006, respectively). In the NHANES cohort, the average intake of dietary fiber was 17.3 g, and refined grains 90.3 g (Supplementary Table S3).

The OS cohort included 252 participants (mean age 87.1 years; 53.6 % female) divided into three groups: healthy control (HC, $n = 125$), mild cognitive impairment (MCI, $n = 69$), and dementia (DEM, $n = 58$). The DEM group was older (mean age 89.6 years) and had a higher proportion of females (75.9 %) compared to HC (44.0 %) and MCI (52.2 %) groups. Mean HK-MoCA scores decreased from HC (24.3) to MCI (19.1) to DEM (12.1). Overall, the average intake of dietary fiber and refined grains in the OS cohort was 13.3 g and 295.7 g, respectively. Dietary fiber intake was highest in HC (14.5 g) and lowest in DEM (11.1 g), while refined grains intake was highest in MCI (340.9 g) and lowest in DEM (269.6 g) (Supplementary Table S4).

3.2. *Multivariate logistic regression analysis revealed association between DI-GM and its subcomponents with cognitive function*

Higher DI-GM scores were significantly associated with a lower risk of p-MCI and better performance on CERAD, AFT, DSST, and Cognitive-total in the unadjusted model (all $p < 0.05$). These associations remained significant after further adjustments for key covariates, including age and sex (Model 2). After further adjustment for age, sex, race, educational level, marital status, PIR, smoking status, drinking status, BMI, hypertension, DM, and hyperlipidemia, higher DI-GM was significantly associated with better performance on DSST (OR=0.90; 95 % Confidence Interval (CI): 0.82, 0.99; $p = 0.033$) (Table 2).

Additionally, higher BGMS was significantly associated with lower odds of p-MCI and better performance on CERAD-IR, CERAD-DR, DSST, and Cognition-total across all three models. In Model 3, higher BGMS was associated with lower odds of p-MCI (OR=0.88, 95 % CI: 0.80, 0.98, $p = 0.022$), and lower odds of poor performance on CERAD-IR (OR=0.90, 95 % CI: 0.82, 0.99, $p = 0.039$), CERAD-DR (OR=0.89, 95 % CI: 0.83, 0.97, $p = 0.011$), DSST (OR=0.82, 95 % CI: 0.74, 0.90, $p = 0.002$), and Cognition-total (OR=0.84, 95 % CI: 0.75, 0.94, $p = 0.008$). The association between BGMS and poor performance on AFT, however, did not reach statistical significance (OR=0.93, 95 % CI: 0.86, 1.00, $p = 0.059$) (Table 2).

Furthermore, higher UGMS was significantly associated with increased odds of p-MCI and poor performance on CERAD-IR and CERAD-DR across all three models. In Model 3, higher UGMS was associated with higher odds of p-MCI (OR=1.22, 95 % CI: 1.01, 1.48, $p = 0.045$), and higher odds of poor performance on CERAD-IR (OR=1.17, 95 % CI: 1.03, 1.33, $p = 0.023$) and CERAD-DR (OR=1.14, 95 % CI: 1.01,

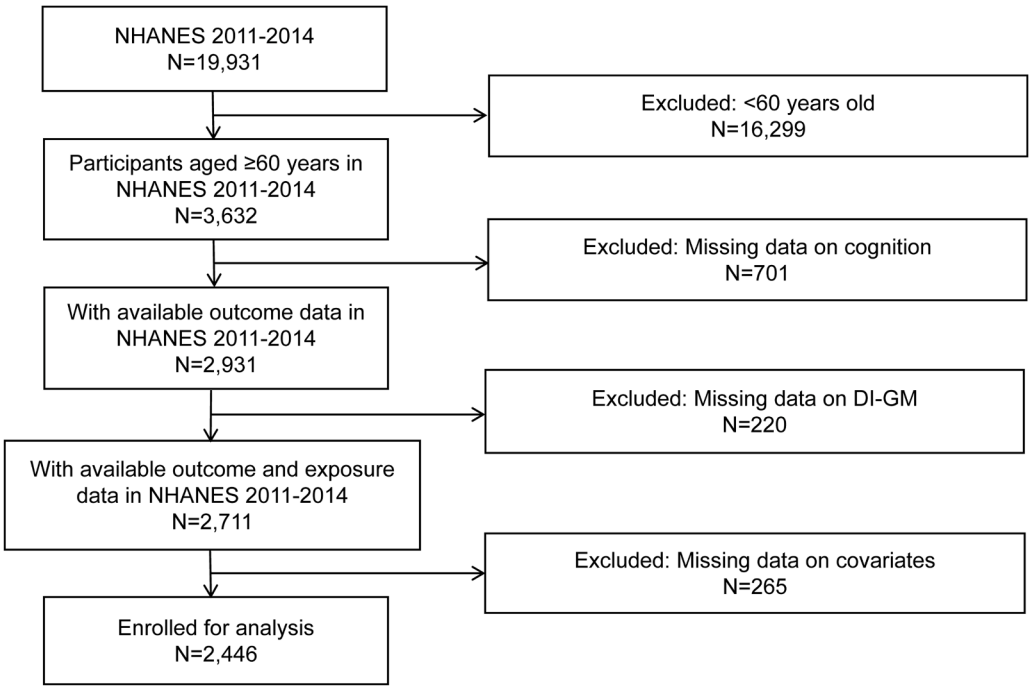

Fig. 1. Study flow chart. Abbreviations: DI-GM, dietary index for gut microbiota; NHANES, National Health and Nutrition Examination Survey.

1.29, $p = 0.036$). No significant associations were observed between UGMS and poor performance on AFT, DSST, or Cognition-total (Table 2).

3.3. RCS analysis of the associations of DI-GM, BGMS, and UGMS with p-MCI risk

RCS analysis was applied to assess potential dose-response relationships between DI-GM, BGMS, and UGMS and the risk of p-MCI, adjusting for covariates included in Model 3. For the DI-GM score, neither the overall association (P-overall=0.437) nor the test for non-linearity (P-non-linear=0.280) reached statistical significance. In contrast, both BGMS (P-overall=0.014; P-non-linear=0.149) and UGMS (P-overall=0.015; P-non-linear=0.962) demonstrated significant linear associations with p-MCI (Fig. 2).

3.4. Subgroup analysis

After adjusting for all covariates included in Model 3, higher DI-GM scores were significantly associated with a lower incidence of p-MCI among participants with a PIR ≤1.30. Higher BGMS was significantly associated with reduced p-MCI prevalence in females, individuals with a college education or higher, non-Hispanic Black individuals, married participants, never smokers, and those with a PIR >3.50. Elevated UGMS was significantly associated with increased p-MCI prevalence in non-Hispanic Black individuals, participants with BMI <25 kg/m^2, heavy drinkers, those with a PIR >3.50, individuals with hypertension, and those with or without diabetes (Fig. 3).

3.5. *Individual DI-GM components were significantly associated with cognitive function*

As shown in Fig. 4A-F, several individual components of the DI-GM were significantly associated with cognitive function in the NHANES cohort. These associations were assessed using logistic regression analysis. In the fully adjusted model (Model 3), higher fiber intake was significantly associated with better performance on CERAD-IR (OR=0.72; 95 % CI:0.55, 0.96; $p = 0.029$), CERAD (OR=0.74; 95 % CI: 0.57, 0.97; $p = 0.031$), and DSST (OR=0.64; 95 % CI: 0.51, 0.80; $p = 0.002$). In contrast, refined grains intake was positively associated with higher odds of p-MCI and poorer performance on AFT and DSST across all three models. In Model 3, refined grains consumption was significantly associated with higher odds of p-MCI (OR=1.83; 95 % CI: 1.26, 2.67; $p = 0.007$), poorer AFT performance (OR=1.33; 95 % CI: 1.11, 1.59; $p = 0.007$), and poorer DSST performance (OR=1.60; 95 % CI: 1.08, 2.37; $p = 0.025$). In addition, higher soybean intake was significantly associated with better AFT performance (OR=0.75; 95 % CI: 0.57, 0.99; $p = 0.048$), while higher intake of avocado (OR=0.31; 95 % CI: 0.11, 0.87; $p = 0.031$) and fermented dairy products (OR=0.60; 95 % CI: 0.39, 0.92; $p = 0.026$) were significantly linked to better DSST performance.

Given the significant associations between dietary fiber and refined grains and cognitive function observed in the NHANES cohort, we further validated their associations in the OS cohort using linear regression analysis (Fig. 5A-B). Model 1 was unadjusted, whereas Model 2 adjusted for age and sex. After adjusting for covariates, dietary fiber intake was significantly positively associated with overall HK-MoCA score and four individual cognitive domains: visuospatial/executive, language, memory, and orientation (all $p < 0.05$). In contrast, refined grains intake was inversely associated with both the HK-MoCA score and the orientation domain, as indicated by negative beta coefficients (all $p < 0.05$). Age-stratified analyses within the OS cohort revealed that the positive association between dietary fiber intake and HK-MoCA scores was statistically significant in the 71–84 and 87–89 age groups. Similarly, a significant negative association between refined grains intake and HK-MoCA scores was observed in the 71–84 age group (Supplementary Table S5 and S6).

3.6. Gut microbiota mediated the association between dietary fiber and cognition in the OS cohort

A network analysis revealed the interconnections among dietary fiber, gut microbiota characteristics, and HK-MoCA, based on Spearman correlation analysis (Fig. 6). Firstly, the results indicated a significant positive correlation between dietary fiber and HK-MoCA, as well as its individual domains: visuospatial/executive, language, delayed recall,

Table 1
Participant's characteristics.

Variables	Total	DI-GM category				p-value
		≤3	4	5	≥6	
Weighted/Population	N = 46,640,954	N = 5831,252	N = 8142,729	N = 10,429,353	N = 22,237,621	/
Unweighted/Sample	n = 2446	n = 366	n = 494	n = 539	n = 1047	/
Age, mean (SE), years	68.99 (0.21)	68.76 (0.41)	69.24 (0.34)	68.20 (0.36)	69.32 (0.32)	**0.023**
Age group, n (%)						0.296
60–69	1344 (57.32)	222 (60.28)	275 (57.62)	309 (61.65)	538 (54.41)	
70–79	723 (29.23)	92 (25.33)	150 (29.94)	150 (26.15)	331 (31.43)	
≥80	379 (13.45)	52 (14.40)	69 (12.44)	80 (12.19)	178 (14.16)	
Sex, n (%)						0.110
Male	1197 (46.33)	187 (50.20)	254 (48.33)	285 (49.56)	471 (43.07)	
Female	1249 (53.67)	179 (49.80)	240 (51.67)	254 (50.44)	576 (56.93)	
Education level, n (%)						**0.001**
Less than high school	248 (5.14)	50 (7.74)	52 (6.40)	50 (4.78)	96 (4.17)	
High school or equivalent	897 (31.16)	171 (42.44)	209 (35.64)	197 (29.80)	320 (27.20)	
College or above	1301 (63.70)	145 (49.82)	233 (57.96)	292 (65.43)	631 (68.63)	
Race, n (%)						**<0.001**
Mexican American	210 (3.17)	30 (3.73)	43 (3.75)	51 (3.46)	86 (2.67)	
Non-Hispanic Black	568 (7.82)	123 (13.88)	131 (10.27)	131 (7.78)	183 (5.36)	
Non-Hispanic White	1229 (81.14)	150 (74.58)	226 (76.53)	270 (81.41)	583 (84.42)	
Other Hispanic	239 (3.37)	37 (4.10)	63 (5.12)	41 (2.31)	98 (3.05)	
Other race	200 (4.50)	26 (3.71)	31 (4.32)	46 (5.04)	97 (4.51)	
Marital, n (%)						**0.033**
Married	1359 (63.19)	204 (63.84)	237 (52.79)	327 (68.15)	591 (64.51)	
Never married	136 (4.13)	27 (5.63)	22 (3.61)	27 (3.30)	60 (4.33)	
Living with partner	65 (2.57)	11 (1.87)	20 (4.64)	9 (2.38)	25 (2.09)	
Other	886 (30.10)	124 (28.67)	215 (38.96)	176 (26.18)	371 (29.07)	
Smoking status, n (%)						**0.011**
Never	1190 (49.09)	159 (42.93)	226 (47.63)	265 (47.99)	540 (51.75)	
Former	954 (40.19)	148 (42.57)	185 (37.95)	206 (38.72)	415 (41.07)	
Current	302 (10.72)	59 (14.50)	83 (14.41)	68 (13.29)	92 (7.17)	
Drinking status, n (%)						0.443
Never	356 (12.30)	47 (13.76)	74 (12.75)	81 (13.20)	154 (11.33)	
Former	699 (23.36)	126 (25.95)	142 (24.72)	158 (24.23)	273 (21.77)	
Mild	972 (46.46)	126 (43.45)	180 (42.40)	203 (42.14)	463 (50.77)	
Moderate	240 (11.91)	29 (9.39)	56 (13.47)	58 (13.26)	97 (11.37)	
Heavy	179 (5.97)	38 (7.45)	42 (6.66)	39 (7.18)	60 (4.76)	
PIR, mean (SE)	3.15 (0.08)	2.70 (0.12)	2.83 (0.12)	3.26 (0.12)	3.34 (0.10)	**<0.001**
PIR category, n (%)						**<0.001**
≤1.30	713 (17.03)	132 (24.71)	172 (22.95)	165 (15.74)	244 (13.44)	
1.31–3.50	940 (38.35)	150 (42.76)	197 (41.73)	192 (35.36)	401 (37.36)	
>3.50	793 (44.62)	84 (32.53)	125 (35.31)	182 (48.90)	402 (49.20)	
Hypertension, n (%)						**0.017**
No	717 (33.60)	93 (27.87)	124 (29.47)	158 (30.81)	342 (37.92)	
Yes	1729 (66.40)	273 (72.13)	370 (70.53)	381 (69.19)	705 (62.08)	
Diabetes, n (%)						**0.023**
No	1388 (61.77)	189 (54.70)	259 (57.79)	309 (62.91)	631 (64.54)	
IFG	104 (4.67)	19 (4.58)	27 (6.46)	16 (2.67)	42 (4.98)	
IGT	141 (6.52)	19 (7.51)	24 (4.00)	31 (6.64)	67 (7.13)	
DM	813 (27.04)	139 (33.21)	184 (31.75)	183 (27.79)	307 (23.35)	
Hyperlipidemia, n (%)						0.835
No	444 (17.11)	65 (15.03)	88 (17.55)	101 (17.96)	190 (17.10)	
Yes	2002 (82.89)	301 (84.97)	406 (82.45)	438 (82.04)	857 (82.90)	
BMI, Mean (SE), kg/m^2	29.20 (0.24)	31.01 (0.84)	29.38 (0.40)	29.65 (0.35)	28.44 (0.27)	**0.009**
BMI category, n (%)						0.069
Underweight (<18.5)	32 (1.21)	5 (1.63)	6 (0.69)	5 (0.90)	16 (1.43)	
Normal (18.5 to <25)	609 (24.58)	72 (18.66)	114 (23.12)	127 (22.43)	296 (27.69)	
Overweight (25 to <30)	856 (35.96)	138 (34.22)	177 (39.16)	176 (33.23)	365 (36.53)	
Obese (30 or greater)	949 (38.25)	151 (45.49)	197 (37.02)	231 (43.44)	370 (34.36)	
CERAD-IR, mean (SE)	19.84 (0.23)	19.48 (0.41)	19.47 (0.27)	19.75 (0.26)	20.11 (0.28)	0.092
CERAD-DR, mean (SE)	6.29 (0.10)	6.18 (0.19)	6.12 (0.12)	6.25 (0.12)	6.40 (0.12)	0.232
CERAD, mean (SE)	26.13 (0.32)	25.66 (0.60)	25.59 (0.38)	26.00 (0.35)	26.51 (0.39)	0.109
AFT, mean (SE)	18.37 (0.20)	17.33 (0.40)	18.08 (0.24)	18.44 (0.36)	18.71 (0.29)	**0.006**
DSST, mean (SE)	52.74 (0.56)	49.31 (1.45)	50.67 (1.06)	52.84 (1.05)	54.35 (0.66)	**0.005**
Cognition-total, mean (SE)	97.24 (0.86)	92.30 (1.84)	94.34 (1.33)	97.28 (1.42)	99.57 (1.16)	**0.003**
Cognition-total-Z, mean (SE)	0.23 (0.03)	0.10 (0.06)	0.15 (0.04)	0.23 (0.04)	0.30 (0.04)	**0.008**
p-MCI, n (%)						0.741
No	2053 (88.83)	299 (87.34)	405 (88.25)	450 (88.54)	899 (89.56)	
Yes	393 (11.17)	67 (12.66)	89 (11.75)	89 (11.46)	148 (10.44)	

Abbreviations: SE, standard error; p-MCI, psychometric mild cognitive impairment; PIR, ratio of family income to poverty; IFG, impaired fasting glycaemia; IGT, impaired glucose tolerance; DM, diabetes mellitus; BMI, body mass index; DI-GM, dietary index for gut microbiota; CERAD-IR, Consortium to Establish a Registry for Alzheimer's Disease Immediate Recall; CERAD-DR, Consortium to Establish a Registry for Alzheimer's Disease Delayed Recall; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; AFT, Animal Fluency Test; DSST, Digit Symbol Substitution Test.
Categorical variables were presented as unweighted frequencies and weighted percentages. The DI-GM was categorized into four groups: ≤3, 4, 5, and ≥6. N represented weighted counts to reflect the population distribution, while n represented unweighted counts from the actual sample size.

Table 2
Multivariate logistic regression analysis of the association between DI-GM and its subcomponents with different cognitive outcomes among the NHANES 2011–2014 participants.

Variable	Model 1 [a]		Model 2 [b]		Model 3 [c]	
	OR (95 % CI)	p-value	OR (95 % CI)	p-value	OR (95 % CI)	p-value
p-MCI						
DI-GM	0.93 (0.87, 1.00)	**0.041**	0.93 (0.87, 0.99)	**0.021**	0.98 (0.89, 1.08)	0.620
BGMS	0.81 (0.75, 0.88)	**<0.001**	0.82 (0.76, 0.89)	**<0.001**	0.88 (0.80, 0.98)	**0.022**
UGMS	1.27 (1.06, 1.52)	**0.010**	1.23 (1.03, 1.46)	**0.022**	1.22 (1.01, 1.48)	**0.045**
CERAD-IR-Low-Performance						
DI-GM	0.93 (0.87, 0.98)	**0.013**	0.92 (0.87, 0.97)	**0.002**	0.98 (0.91, 1.06)	0.584
BGMS	0.82 (0.76, 0.87)	**<0.001**	0.82 (0.76, 0.87)	**<0.001**	0.90 (0.82, 0.99)	**0.039**
UGMS	1.24 (1.10, 1.40)	**0.001**	1.18 (1.06, 1.33)	**0.005**	1.17 (1.03, 1.33)	**0.023**
CERAD-DR-Low-Performance						
DI-GM	0.93 (0.88, 0.98)	**0.007**	0.92 (0.87, 0.97)	**0.002**	0.97 (0.91, 1.03)	0.239
BGMS	0.84 (0.78, 0.90)	**<0.001**	0.84 (0.79, 0.90)	**<0.001**	0.89 (0.83, 0.97)	**0.011**
UGMS	1.16 (1.04, 1.30)	**0.009**	1.13 (1.02, 1.25)	**0.025**	1.14 (1.01, 1.29)	**0.036**
CERAD-Low-Performance						
DI-GM	0.92 (0.85, 0.99)	**0.030**	0.91 (0.84, 0.98)	**0.010**	0.97 (0.88, 1.06)	0.441
BGMS	0.81 (0.73, 0.89)	**<0.001**	0.82 (0.74, 0.90)	**<0.001**	0.89 (0.79, 1.01)	0.061
UGMS	1.22 (1.06, 1.40)	**0.006**	1.17 (1.01, 1.34)	**0.032**	1.16 (0.00, 1.34)	0.053
AFT-Low-Performance						
DI-GM	0.92 (0.85, 0.98)	**0.012**	0.90 (0.84, 0.96)	**0.004**	0.98 (0.92, 1.05)	0.508
BGMS	0.82 (0.77, 0.87)	**<0.001**	0.83 (0.78, 0.88)	**<0.001**	0.93 (0.86, 1.00)	0.059
UGMS	1.17 (1.04, 1.33)	**0.014**	1.11 (0.98, 1.26)	0.091	1.10 (0.95, 1.26)	0.177
DSST-Low-Performance						
DI-GM	0.82 (0.76, 0.89)	**<0.001**	0.80 (0.75, 0.86)	**<0.001**	0.90 (0.82, 0.99)	**0.033**
BGMS	0.69 (0.65, 0.74)	**<0.001**	0.70 (0.66, 0.74)	**<0.001**	0.82 (0.74, 0.90)	**0.002**
UGMS	1.21 (1.04, 1.40)	**0.016**	1.13 (0.99, 1.30)	0.073	1.12 (0.95, 1.31)	0.158
Cognition-total-Low-Performance						
DI-GM	0.86 (0.78, 0.94)	**0.002**	0.83 (0.76, 0.91)	**<0.001**	0.93 (0.83, 1.03)	0.138
BGMS	0.72 (0.67, 0.79)	**<0.001**	0.73 (0.67, 0.79)	**<0.001**	0.84 (0.75, 0.94)	**0.008**
UGMS	1.26 (1.08, 1.46)	**0.004**	1.16 (1.01, 1.33)	**0.034**	1.15 (0.96, 1.37)	0.108

Abbreviations: DI-GM, dietary index for gut microbiota; BGMS, beneficial to gut microbiota score; UGMS, unfavorable to gut microbiota score; CERAD-IR, Consortium to Establish a Registry for Alzheimer's Disease Immediate Recall; CERAD-DR, Consortium to Establish a Registry for Alzheimer's Disease Delayed Recall; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; AFT, Animal Fluency Test; DSST, Digit Symbol Substitution Test; OR, odds ratio; CI, confidence interval.

[a] Model 1: Non-adjusted model adjusted for none.

[b] Model 2: Minimally-adjusted model adjusted for age, sex.

[c] Model 3: Fully-adjusted model adjusted for age, sex, race, educational level, marital status, PIR, smoking status, drinking status, BMI, hypertension, DM, and hyperlipidemia.

and orientation. Additionally, dietary fiber showed positive correlations with four specific gut microbiota species: *Coprococcus eutactus, Eubacterium siraeum, Eubacterium ventriosum*, and *Bacteroides congonensis*. These species were then selected for inclusion in the network to focus on microbes most strongly associated with dietary fiber intake. These species were also positively correlated with microbial diversity indices including Richness, Shannon, and Simpson. Notably, *Eubacterium siraeum* and *Eubacterium ventriosum* were also significantly positively associated with cognitive function, including HK-MoCA and its individual domains: language and delayed recall. Furthermore, Bayesian causal mediation analysis was conducted to explore the potential mediating effects of gut microbiota in the relationship between dietary fiber intake and dementia risk. The results indicated that dietary fiber was associated with a reduced risk of dementia, both through a direct effect (average direct effect (ADE)=−0.098, 95 % Credible Interval (CrI): −0.181, −0.022) and an indirect effect mediated by *Eubacterium ventriosum* (average causal mediation effect (ACME)=−0.014, 95 % CrI: −0.040, −0.001), accounting for approximately 12.7 % of the total effect (Fig. 7).

Using Spearman correlation analysis, refined grains intake was not significantly associated with HK-MoCA score (Supplementary Table S7). However, refined grains were found to be negatively correlated with seven specific gut microbiota species: *Lachnospira pectinoschiza, Ruminococcus bromii, Bacteroides xylanisolvens, Oxalobacter formigenes, Acidaminococcus intestini, Bacteroides congonensis*, and *Bifidobacterium animalis*. These species were then selected for inclusion in the network to focus on microbes most strongly associated with refined grains intake. Among these, *Lachnospira pectinoschiza* and *Ruminococcus bromii* also suggested positive correlations with HK-MoCA (Supplementary Figure S1). Due to the absence of a consistent and significant association between refined grains intake and cognitive outcomes (Fig. 5, Supplementary Table S7), mediation analysis was not conducted for refined grains. Correlation results are provided in Supplementary File 2.

4. Discussion

This study provides novel insights into the diet-gut-microbiota-brain axis by introducing the DI-GM, a gut-microbiota-oriented dietary metric linked to cognitive function. To our knowledge, this is the first cross-sectional study to comprehensively assess associations between the DI-GM, its components, and multiple cognitive domains using a battery of cognitive tests. Our findings indicated that higher DI-GM scores were significantly associated with better performance on the DSST. Similarly, higher BGMS were significantly associated with reduced incidence of p-MCI and poor performance on the CERAD-IR, CERAD-DR, and DSST. Additionally, higher intake of dietary fiber was associated with better cognitive function, while greater consumption of refined grains was linked to poorer cognition. These results were further validated in an independent cohort, where higher dietary fiber intake was correlated with higher HK-MoCA scores and greater abundance of fermenting gut bacterial species. Among these species, *Eubacterium ventriosum* emerged as a mediator linking dietary fiber intake to reduced dementia risk.

Diet plays a crucial role in cognitive health, with various dietary

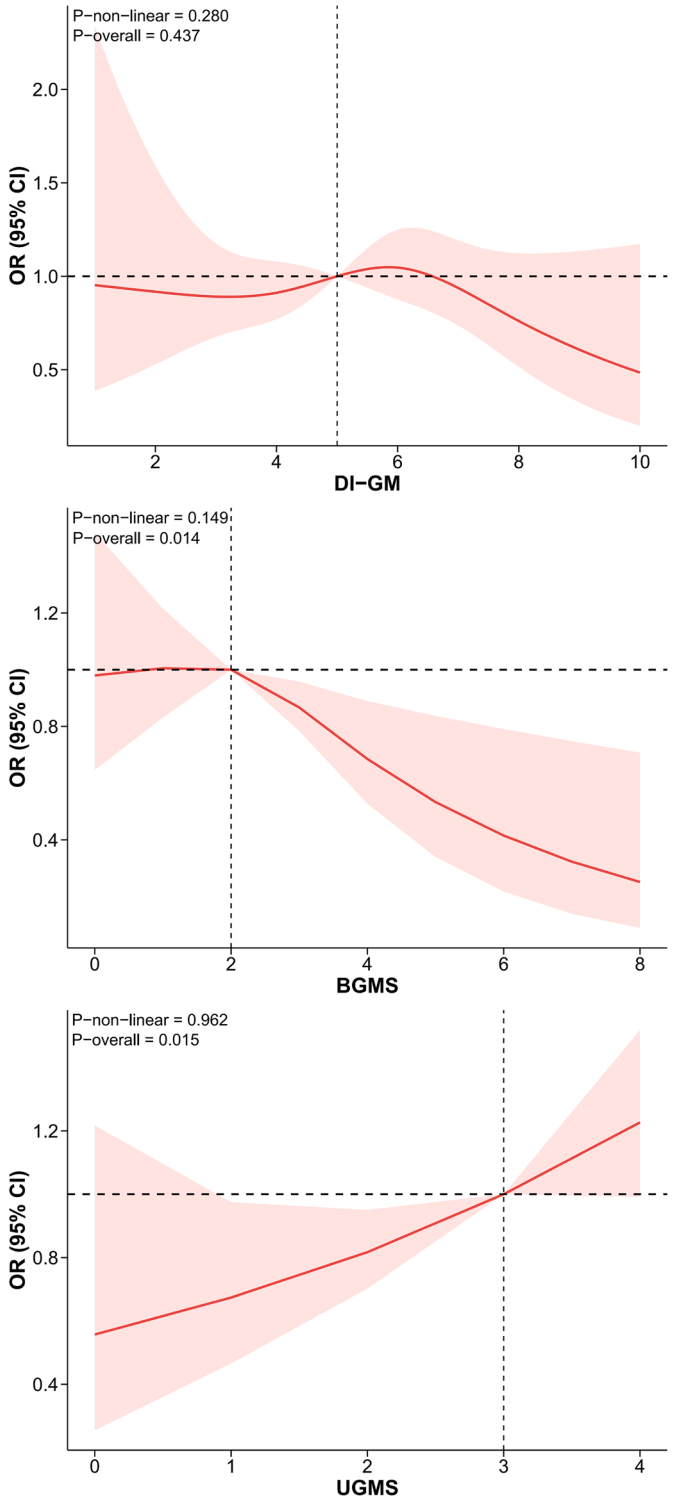

Fig. 2. RCS analyses of the association between DI-GM and its subcomponents with p-MCI among the NHANES 2011–2014 participants. Abbreviations: DI-GM, dietary index for gut microbiota; BGMS, beneficial to gut microbiota score; UGMS, unfavorable to gut microbiota score; OR, odds ratio; CI, confidence interval; p-MCI, psychometric mild cognitive impairment.

patterns and components impacting brain function. A meta-analysis found that higher adherence to the Mediterranean diet, characterized by high intake of vegetables, fruits, legumes, nuts, whole grains, olive oil, and moderate consumption of fish, dairy products, and eggs, had a lower risk of AD (risk ratio=0.71, 95 % CI: 0.56, 0.89) and MCI (risk ratio=0.75, 95 % CI: 0.66, 0.86) [26]. Similar benefits were observed with the DASH diet [27] and the MIND diet, which combines elements of both and emphasizes brain-supportive nutrients [28,29]. Moreover, adherence to the MIND diet is associated with lower postmortem AD pathology, particularly reduced β-amyloid burden (β=−0.022, p = 0.034) [30], suggesting a neurobiological pathway for its protective effect on cognition. In contrast, the Western dietary pattern, characterized by high intakes of saturated fats, refined sugars, and processed foods, has been consistently associated with poorer cognitive outcomes [31,32]. Beyond overall dietary patterns, the diet's inflammatory potential, as measured by the Dietary Inflammatory Index (DII), has also been associated with cognitive function (risk ratio=1.34; 95 % CI: 1.15, 1.55) [33]. Researchers have also explored specific dietary components for their effects on cognitive health. Dietary fiber has gained attention for its anti-inflammatory and gut-brain benefits. In older U.S. adults, higher fiber intake correlated with better cognitive function [34]. Refined grains are a staple of the Western diet. A study in aged rats showed that a refined grain-rich diet induced inflammation in the hippocampus and amygdala, along with memory deficits [35]. The findings above collectively underscored that dietary factors played a pivotal role in modulating cognitive health. Our study aligned with and extended these observations, demonstrating that higher adherence to beneficial-to-gut-microbiota dietary pattern, as reflected by the DI-GM, was significantly associated with better cognitive function in older adults, particularly in DSST performance, which reflected processing speed, attention, and working memory function. Our study also found that the BGMS was significantly associated with better cognitive function, which was consistent with the benefits seen in other healthy dietary patterns such as the Mediterranean, DASH, and MIND diets, which emphasized foods like fruits, vegetables, whole grains, and fiber. However, the composite DI-GM showed no significant association likely due to a dilution effect from combining components with varying directions and strengths of association with cognition. Some individual components, like dietary fiber, have clear protective effects, while others are weaker or inconsistent, which may weaken the overall signal. This underscores the complexity of interpreting composite dietary scores and suggests that focusing on key individual nutrients may better clarify diet-cognition relationships. Notably, in the NHANES dataset, higher intake of dietary fiber, a beneficial-to-gut-microbiota component, was significantly associated with better cognitive function, particularly in domains assessed by the DSST (processing speed, attention, and working memory) and CERAD (memory). This finding was further validated in the OS cohort, where fiber intake positively correlated with HK-MoCA total score and its memory domain, reinforcing the potential protective role of dietary fiber in cognitive health. Given the substantial age difference between the two cohorts, age-stratified analyses within the OS cohort confirmed that the positive associations with dietary fiber were significant in younger subgroups, though attenuated in the oldest groups, likely influenced by higher prevalence of comorbidities and neurodegenerative processes common in very old adults [36], suggesting age-related modification of these effects. To account for other cross-cohort differences, we noted that NHANES and OS participants differed substantially in ethnic composition, dietary culture, and regional environment. For example, the average intake of dietary fiber and refined grains varied considerably between cohorts, reflecting distinct cultural backgrounds and dietary preferences. These differences may potentially modify the exposure-outcome relationship. However, the scientific value of cross-cohort validation lies in this heterogeneity. Despite these marked differences, we observed a consistent positive association between dietary fiber intake and cognitive performance across both populations. This reproducibility under different conditions strengthens the reliability of a possible causal relationship and supports the generalizability of our findings. The fact that similar associations were found despite the differences lowers the chance that results were driven by factors specific to one cohort. Although residual confounding cannot be fully ruled out, the consistency of this association across

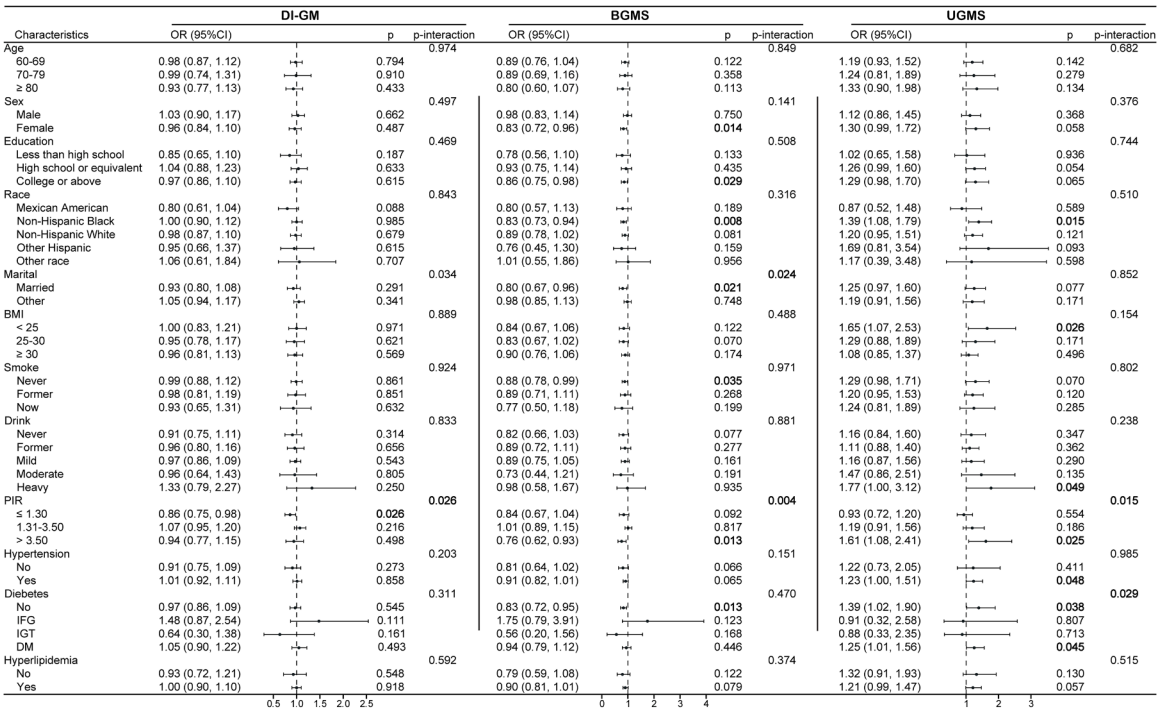

Fig. 3. Subgroup analyses of the association between DI-GM and its subcomponents with p-MCI among the NHANES 2011–2014 participants. Abbreviations: PIR, ratio of family income to poverty; BMI, body mass index; OR, odds ratio; CI, confidence interval.

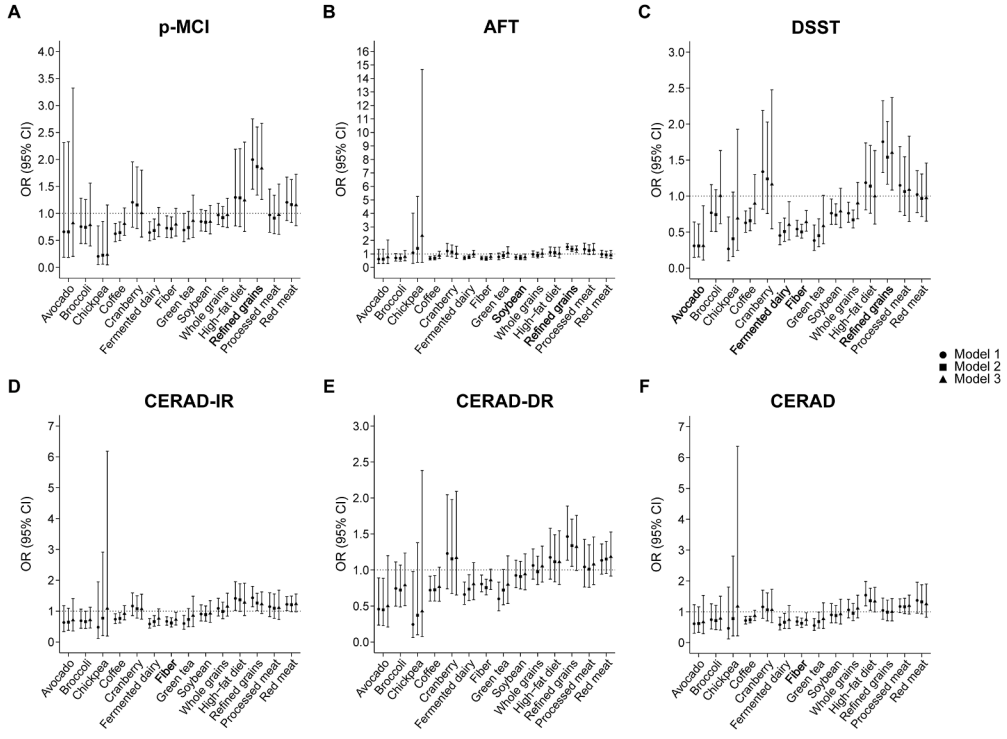

Fig. 4. Association between the components of DI-GM and cognitive performance among the NHANES 2011–2014 participants. Abbreviations: CERAD-IR, Consortium to Establish a Registry for Alzheimer's Disease Immediate Recall; CERAD-DR, Consortium to Establish a Registry for Alzheimer's Disease Delayed Recall; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; AFT, Animal Fluency Test; DSST, Digit Symbol Substitution Test; p-MCI, psychometric mild cognitive impairment; OR, odds ratio; CI, confidence interval.

cohorts supports the protective role of dietary fiber. These results warranted further validation through large-scale prospective studies to elucidate the long-term impact of fiber-rich diets on cognitive function.

The type, quality, and origin of our food influenced the composition and function of gut microbiota, consequently modulating host-microbiota dynamics [8,9]. The DI-GM reflects diet-driven changes in gut microbiota, indicating patterns beneficial or harmful to gut health. Changes in DI-GM may affect gut microbiota composition and be

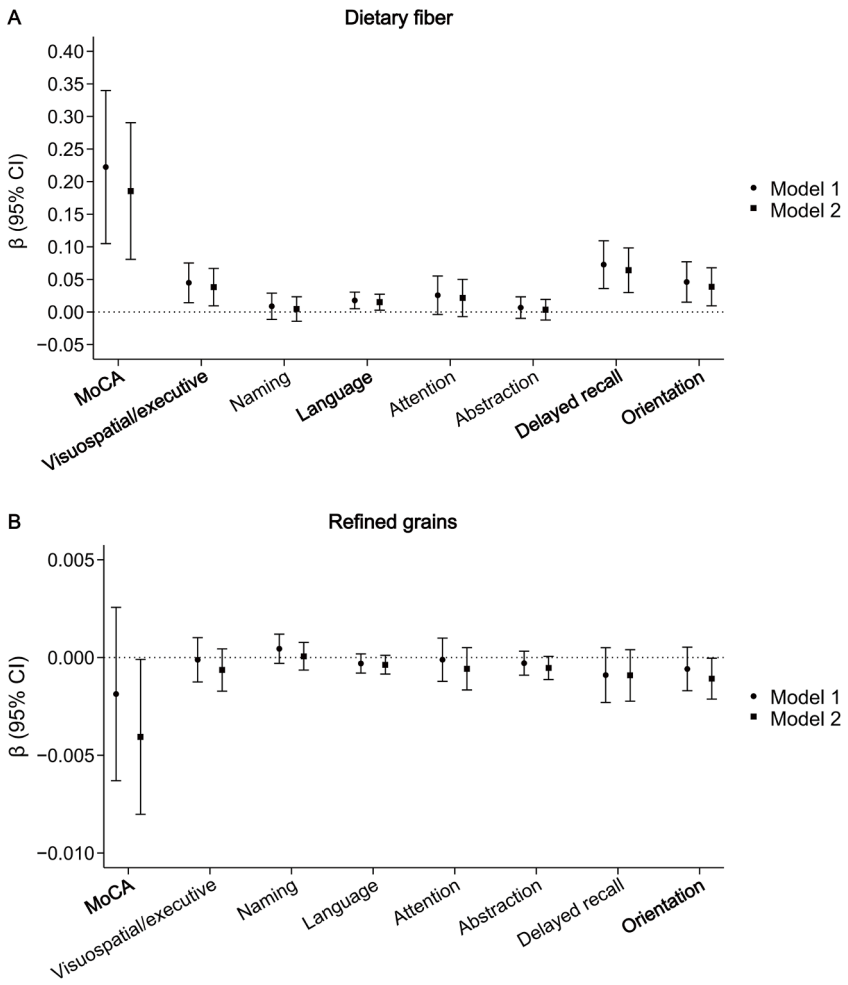

Fig. 5. Association of DI-GM components (dietary fiber and refined grains) with MoCA in OS cohort. Abbreviations: CI, confidence interval; MoCA, Montreal Cognitive Assessment.

associated with cognitive function. A high-fiber diet is linked to greater gut microbial diversity, which helps maintain gut balance and suppress harmful bacteria [8]. Dietary fiber serves as a substrate for beneficial bacteria, promoting production of short-chain fatty acid (SCFA) that support health [37]. Fiber fermentation also lowers gut pH, creating a favorable environment for anaerobic beneficial bacteria while inhibiting inflammatory microbes [38]. In contrast, diets low in fiber and high in refined grains may reduce these benefits, encourage growth of pro-inflammatory bacteria such as *Enterobacteriaceae*, and increase lipopolysaccharide (LPS) levels [39], which can cause systemic and brain inflammation, contributing to cognitive decline. Evidence shows gut microbiota diversity and composition differ between cognitively impaired individuals and healthy controls, with the former having lower diversity, more pro-inflammatory bacteria (e.g., *Escherichia, Desulfovibrio*) and fewer anti-inflammatory bacteria (*Faecalibacterium, Bifidobacterium, Lactobacillus*, and *Eubacterium*) [40–45]. Gut microbiota dysbiosis and its metabolites were thought to affect cognitive function through pathways such as immune modulation, endocrine signaling, and neural communication via the vagus nerve [46,47]. Moreover, diet influences cognition partly through this axis, as certain microbes ferment dietary fiber into beneficial compounds like SCFA. Though mechanisms remain unclear, fiber-metabolizing bacteria promote metabolites that affect neurochemical pathways, neurotransmitter synthesis, and neuronal function [48]. Furthermore, gut microbiota and their metabolites might regulate neuroactive hormones like ghrelin [49]. Dietary fiber might also affect brain function through immune-mediated pathways, such as modulation of the kynurenine pathway or vagus nerve signaling [50].

Eubacterium spp. are commonly associated with high dietary fiber intake. Multiple studies have shown that a Western diet-characterized by high levels of animal protein and fat but low in fiber-can significantly reduce the abundance of beneficial gut bacteria, including *Eubacterium* and *Bifidobacterium* [51,52]. Besides, the positive role of *Eubacterium spp*. was emphasized in a large-scale study by Ghosh et al., which examined a cohort of 612 older adults to explore how the Mediterranean diet influences gut microbiota. The findings revealed that species like *Eubacterium rectale* and *Eubacterium eligens* were positively linked to reduced frailty, better cognitive function, and higher production of SCFA [53], which are known to exert protective effects in various health conditions, including inflammatory bowel disease [54], colorectal cancer [55], and AD [56,57]. Our findings were consistent with these results, as we also observed a positive correlation between *Eubacterium spp*. and cognitive function, which was further associated with dietary fiber intake and microbiota diversity metrics. These findings revealed significant correlations among dietary fiber intake, gut microbiota features (including the abundance of fermenting bacterial species, microbial diversity, and levels of microbial metabolites like SCFA), and cognitive function (HK-MoCA). This correlative pattern raised the possibility that dietary fiber might influence cognitive function by modulating the gut microbiota. Specifically, given the significant correlations observed between dietary fiber, HK-MoCA, and specific bacteria such as *Eubacterium siraeum* and *Eubacterium ventriosum*, we hypothesized that these bacteria might mediate the relationship between dietary fiber intake and cognitive function. To test this

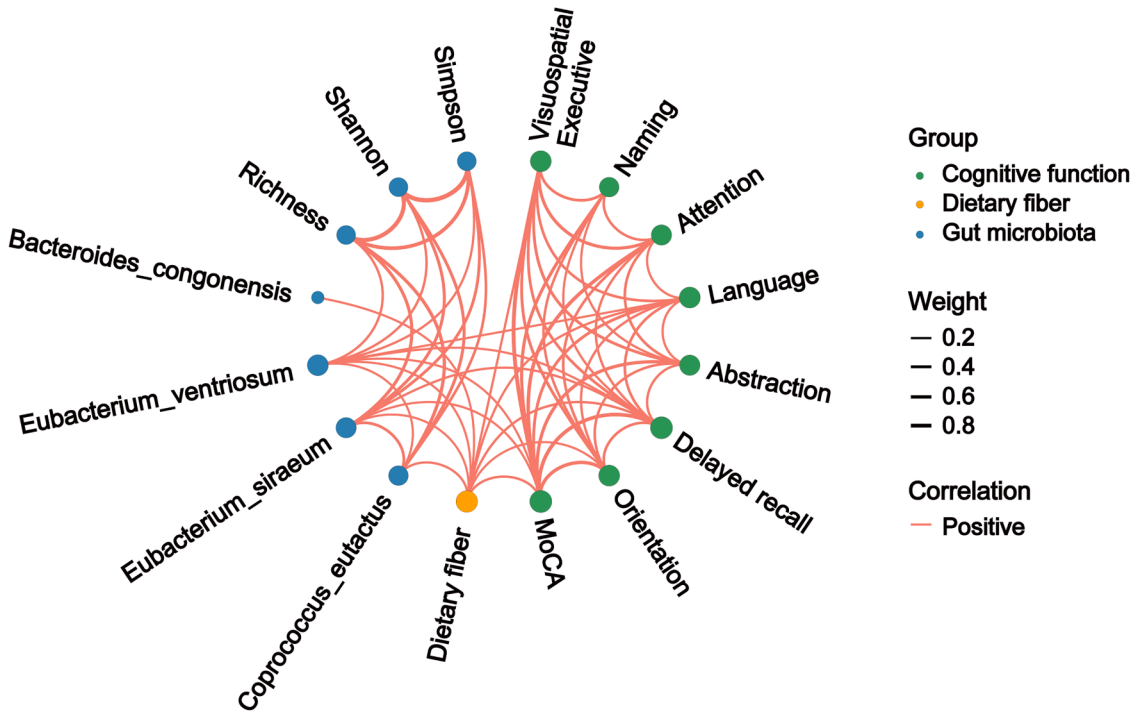

Fig. 6. Network analysis of dietary fiber, MoCA scores, and gut microbiota in the OS cohort. Abbreviations: MoCA, Montreal Cognitive Assessment.

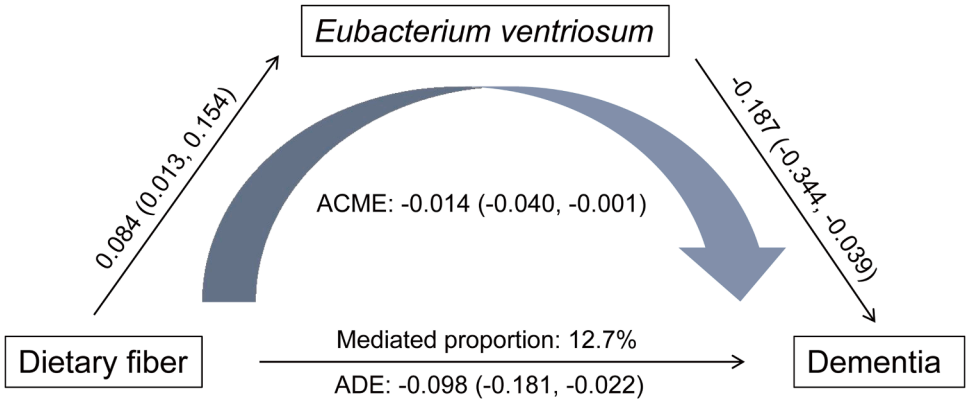

Fig. 7. Mediation analysis of the association between dietary fiber and dementia risk in the OS cohort. Abbreviations: ADE, average direct effect; ACME, average causal mediation effect.

hypothesis, we conducted mediation analysis. Our mediation analysis showed that *Eubacterium ventriosum* accounted for approximately 12.7 % of the total effect of dietary fiber on dementia risk. Although this is a partial mediation, it holds biological significance. Mediation proportions in this range (10–15 %) are commonly reported in studies on microbiota and health-related outcomes [58–60], suggesting that this level of effect is meaningful. The fact that a single species contributes to more than 10 % of the total effect also points to its potential as a target for dietary interventions. For instance, prebiotics designed to promote the growth of *Eubacterium ventriosum* may help enhance the cognitive benefits of dietary fiber, or certain metabolites produced by this bacterium might also have beneficial effects on cognition. Drawing on existing literature, *Eubacterium* spp. are known to produce butyrate, a SCFA that may promote brain health by activating the vagus nerve and increasing hippocampal brain-derived neurotrophic factor (BDNF) [61], reducing inflammation through inhibition of nuclear factor kappa B (NF-κB) [62], and modulating bile acid metabolism via the farnesoid X receptor (FXR) to decrease brain β-amyloid [63]. Additionally, these bacteria participate in tryptophan metabolism, produce neurotransmitters such as gamma-aminobutyric acid (GABA) [64], and help maintain gut barrier integrity. Together, these findings suggest that *Eubacterium* spp. could play a protective role in cognitive function through the gut-brain axis. While our findings did not establish a consistent direct relationship between refined grains intake and cognitive function in the OS cohort, we observed that refined grains were negatively associated with several gut microbiota species, including *Lachnospira pectinoschiza* and *Ruminococcus bromii*, both of which have been linked to better cognitive function, as reported by other studies [65,66]. This observation generates the hypothesis that refined grains might indirectly influence cognition by reducing beneficial bacteria, although formal mediation analysis was precluded due to the lack of a significant total effect between refined grains and cognition. Given the well-established role of diet in shaping gut microbiota and its connection to cognitive outcomes (Fig. 8), further research is warranted to clarify how these bacteria contribute to cognition, including their dietary determinants and biological mechanisms.

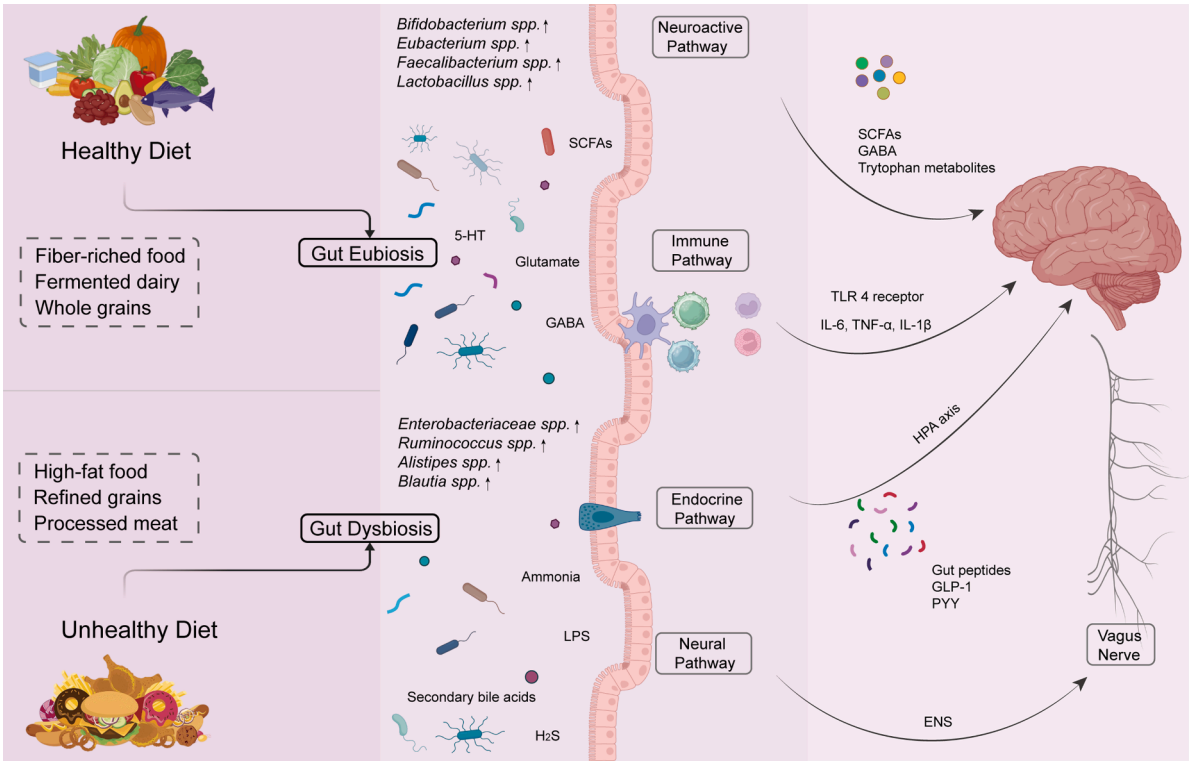

Fig. 8. Mechanistic pathways linking Diet, Gut Microbiota, and Brain. Abbreviations: SCFAs, Short-Chain Fatty Acids; 5-HT, 5-Hydroxytryptamine (Serotonin); GABA, Gamma-Aminobutyric Acid; LPS, Lipopolysaccharide; TLR 4, Toll-Like Receptor 4; IL-6, Interleukin-6; TNF-α, Tumor Necrosis Factor-alpha; IL-1β, Interleukin-1 beta; HPA, Hypothalamic-Pituitary-Adrenal; GLP-1, Glucagon-Like Peptide-1; PYY, Peptide YY; ENS, Enteric Nervous System.

These findings suggest that diet may influence cognitive health through gut microbiota-related pathways. Promoting dietary patterns that support gut microbial balance, particularly those high in fiber, may help preserve cognitive function in aging populations. This has important implications for public health strategies and clinical practices aimed at preventing cognitive decline through feasible and non-invasive dietary interventions. The current study also has several limitations. First, its cross-sectional design limits our ability to understand the causal relationships between the DI-GM, its components, and cognitive outcomes. Longitudinal studies are needed to clarify these associations. Second, the DI-GM reflects dietary intake at a single time point, which may not fully capture long-term habits; however, in the absence of major health events, dietary patterns tend to be stable, suggesting that the DI-GM reasonably reflects habitual intake. Third, OS participants were very old, and gut microbiota may differ in young-old adults, warranting further validation. Fourth, there remains a possibility of residual confounding arising from measurement inaccuracies. Fifth, the relatively small sample size of the OS cohort may have limited the statistical power to detect subtle associations and increased the risk of statistical errors, particularly in mediation analyses involving complex gut microbiota data. Also, using cognitive screening tools like HK-MoCA may cause measurement bias by missing subtle cognitive impairments, leading to possible misclassification. Additionally, limited availability of covariate information in the validation OS cohort may have resulted in residual confounding, which warrants further investigation in future studies with more comprehensive covariate data. Finally, researchers' reliance on self-reported 24-hour dietary questionnaires may lead to bias, and several covariates were also based on self-reported data.

5. Conclusion

In conclusion, this study investigated the associations between the gut-microbiota-oriented dietary index (DI-GM), its components, and cognitive function in older adults, with partial validation in an independent Hong Kong cohort. Higher DI-GM and BGMS scores were linked to better cognition and lower p-MCI prevalence. Dietary fiber was linked to improved cognition and greater abundance of fermenting gut bacterial species. Among these species, *Eubacterium ventriosum* emerged as a mediator linking dietary fiber intake to reduced dementia risk. These findings support the potential of gut-microbiota-targeted dietary strategies for cognitive health and warrant further prospective investigation.

Data availability

NHANES data are free and publicly available, and can be downloaded directly from the NHANES website (https://www.cdc.gov/nchs/nhanes.htm) by researchers worldwide. The data analyzed in the OS cohort are available from the corresponding author upon reasonable request.

Funding

This study was supported by the National Institutes of Health R01 Grant AR049439-01A1, the Chinese University of Hong Kong Research Grants Council Earmarked Grant CUHK4101/02M, and partially supported by InnoHK, the Government of Hong Kong, Special Administrative Region of the People's Republic of China.

CRediT authorship contribution statement

Hui Jiang: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis. **Jiashuo Zhang:** Software, Formal analysis. **Shuyi Li:** Resources, Data curation. **Timothy Kwok:** Resources, Funding acquisition. **Siew C Ng:** Supervision, Funding acquisition, Conceptualization. **Allen Ting Chun Lee:** Writing – review & editing, Supervision, Conceptualization. **Zhilu Xu:** Writing – review & editing, Supervision, Methodology,

Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Zhilu Xu is Scientist (Diagnostics) of GenieBiome Ltd. Siew C Ng has served as an advisory board member for Pfizer, Ferring, Janssen and Abbvie and received honoraria as a speaker for Ferring, Tillotts, Menarini, Janssen, Abbvie and Takeda; has received research grants through her affiliated institutions from Olympus, Ferring and Abbvie; is a founder member, non-executive director, non-executive scientific advisor and shareholder of GenieBiome Ltd which is non-remunerative; is a shareholder of MicroSigX Diagnostic Holding Limited; is a founder member, non-executive Board Director, and non-executive scientific advisor of MicroSigX Biotech Diagnostic Limited, which is non-remunerative; and receives patent royalties through her affiliated institutions; is a named inventor of patent applications held by CUHK and MagIC that cover the therapeutic and diagnostic use of the microbiome. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We sincerely thank the NHANES database and the OS cohort from Hong Kong.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.tjpad.2025.100319.

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