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Dietary index for gut microbiota is associated with stroke among US adults†

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Aims: Emerging evidence underscores the diet–microbiota–gut–brain axis as vital to brain health. The dietary index for gut microbiota (DI-GM), quantifying diet quality linked to gut microbiota diversity, reflects healthier gut microbiota with higher scores. Therefore, this study was designed to explore the unclear association between DI-GM and stroke. *Methods*: A cross-sectional analysis was conducted using data from 48 677 participants aged ≥20 years in the National Health and Nutrition Examination Survey (NHANES). Demographic and dietary data were collected, and multivariable weighted logistic regression analysis was performed to evaluate the association between the DI-GM and stroke. Additionally, restricted cubic spline (RCS), subgroup analyses, and receiver operating characteristic (ROC) curve were conducted. *Results*: In participants aged ≥20 years, the odds ratio (OR) was 0.96 (95% CI: 0.92–1.00, $P = 0.075$) in the crude model, but after adjustment, the OR was 0.93 (95% CI: 0.89–0.98, $P = 0.003$), while higher beneficial to gut microbiota scores were consistently associated with lower stroke prevalence with ORs of 0.87 (95% CI: 0.83–0.90, $P < 0.001$) in the crude model and 0.88 (95% CI: 0.83–0.93, $P < 0.001$) after adjustment. Among participants aged 20–29 years, no significant association was observed. For those aged ≥30 years, higher DI-GM and beneficial to gut microbiota scores were associated with lower stroke prevalence, with DI-GM showing ORs of 0.93 (95% CI: 0.89–0.97, $P < 0.001$) in the crude model and 0.93 (95% CI: 0.89–0.98, $P = 0.003$) after adjustment, and beneficial to gut microbiota scores showing ORs of 0.82 (95% CI: 0.79–0.86, $P < 0.001$) in the crude model and 0.88 (95% CI: 0.83–0.93, $P < 0.001$) after adjustment. RCS indicated a linear relationship between DI-GM and stroke. *Conclusion*: The DI-GM was inversely and linearly associated with stroke prevalence, particularly in adults aged 30 years and above.

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Introduction

Stroke is a leading global cause of death and disability, with an age-standardized mortality rate of 87.4 per 100 000 population and 160.4 million disability-adjusted life years (DALYs) in 2021, according to the Global Burden of Disease (GBD) study.[1,2] Despite recent declines in age-standardized rates, stroke-related deaths and DALYs are projected to reach 9.7 million and 189.4 million, respectively, by 2050, primarily due to population growth, aging, and a rising incidence among young and middle-aged individuals.[3] This persistent burden poses a significant threat to public health, necessitating sustained focus on prevention and treatment strategies targeting modifiable risk factors to mitigate its global impact.

Diet, a key modifiable risk factor for stroke,[3] significantly determines gut microbiome composition.[4,5] The interplay between diet and gut microbiome profoundly shapes health consequences, with nutrient-microorganism interactions dictating microbiome stability or disruption, affecting glycemic sensitivity, cholesterol regulation, body weight, and other metabolic, inflammatory, and cardiovascular pathways.[6–10] Gut microbiota contributes to atherosclerosis through cholesterol and lipid metabolism.[11] Gut microbiota-derived metabolites and impaired gut barrier function promote vascular inflammation and thrombus formation.[12] These diet-microbiome interactions are increasingly recognized as key modulators of stroke risk, highlighting the potential of targeted dietary interventions to mitigate this risk.

The dietary index for gut microbiota (DI-GM), developed from an extensive review of 106 studies, quantifies the impact of diet on gut microbiota composition and diversity by scoring 14 foods or nutrients, with higher scores reflecting healthier gut microbiota.[13] Leveraging the diet-microbiome interplay, DI-GM serves as a practical and comprehensive tool to elucidate the effects of dietary modifications on gut microbiota and their downstream health impacts, supporting microbiome-targeted dietary recommendations and personalized nutrition strategies for disease prevention and management. Unlike other measures, such as direct microbiome diversity metrics

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requiring invasive sampling and advanced sequencing, or the sulfur-metabolizing diet score targeting only sulfur-metabolizing bacterium, DI-GM provides unique advantages by incorporating specific foods instead of generalized food groups, and capturing broad attributes of gut microbiota including diversity, short-chain fatty acid (SCFA) production, specific bacteria, and phyla-level changes.[13–15] These features make it a practical, diet-based surrogate particularly suited for large epidemiological datasets like the National Health and Nutrition Examination Survey (NHANES).

Recent findings have demonstrated that DI-GM is negatively correlated with depression prevalence and symptoms.[16] However, its association with stroke remains unexplored. We posit that DI-GM is an accessible and well-suited proxy to investigate the diet–microbiota–stroke connection in a study population. This cross-sectional study is the first to evaluate the association between DI-GM and stroke using data from the NHANES, providing actionable insights into personalized dietary strategies for stroke prevention.

Methods

Population under investigation

NHANES is a continuous cross-sectional study 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 noninstitutionalized US national population. NHANES data are publicly accessible at **https://wwwn.cdc.gov/nchs/nhanes/**. NHANES protocols were approved by the Institutional Review Board of the NCHS, and written informed consent was obtained from all participants. Data from participants in the 1999–2018 NHANES cycles were analyzed, as these cycles provided information on DI-GM and stroke. Exclusion criteria for the analysis included participants aged <20 years, absence of stroke data, and missing DI-GM components.

The DI-GM

The DI-GM consists of 14 foods or nutrients, with beneficial components including fermented dairy, chickpeas, soybean, whole grains, fiber, cranberries, avocados, broccoli, coffee, and green tea (not recorded in NHANES for specific tea types), and unfavorable components including red meat, processed meat, refined grains, and high-fat diet (≥40% energy from fat).[13] The DI-GM score was calculated using 24-hour dietary recall data from NHANES 1999–2018. For beneficial components, a score of 1 was assigned if consumption was ≥the sex-specific median, otherwise 0 score, with the scores summed to yield beneficial to gut microbiota score (BGMS, ranges from 0–9); for unfavorable components, a score of 0 was assigned if consumption was ≥the sex-specific median or 40% (for high-fat diet), otherwise 1 score, resulting in unfavorable to gut microbiota score (UGMS, ranges from 0–4). The DI-GM score (ranges from 0–13) was the sum of these component scores and categorized into four groups: 0–3, 4, 5, and ≥6.[16]

Stroke

Stroke data were collected from the NHANES using self-reported information. Participants were asked whether a doctor or other health professional had ever told them that they had a stroke. This question was part of the Medical Conditions Questionnaire (MCQ), and responses were categorized as 'yes' or 'no'. Only participants with complete responses to this question were included in the analysis to ensure accuracy in identifying stroke cases within the dataset.

Covariates

Based on previous studies, the potential covariates included age, gender, race/ethnicity, education level, marital status, poverty income ratio (PIR), smoking status, alcohol drinking status, physical activity, body mass index (BMI), hypertension, diabetes mellitus (DM), and energy intake.[17–21] Race/ethnicity were classified into 5 categories: non-hispanic white, non-hispanic black, Mexican American, other hispanic, and other race (including multiracial participants). Education level was divided into 3 categories: less than high school, high school or equivalent, and college or above. Marital status was classified into 4 categories: married, never married, living with a partner, and other (*e.g.*, widowed, divorced, or separated). Smoking status can be grouped into 3 categories: never (less than 100 cigarettes), former (more than 100 cigarettes but quit), and now (more than 100 cigarettes and currently smoke).[22] Alcohol drinking status was divided into 5 categories: never (<12 drinks in lifetime), former (≥12 drinks in 1 year and did not drink last year, or did not drink last year but drank ≥12 drinks in lifetime), current mild (≤1 drinks per day for females, ≤2 drinks per day for males), current moderate (≥2 drinks per day for females, ≥3 drinks per day for males, or binge drinking ≥2 days per month), current heavy (≥3 drinks per day for females, ≥4 drinks per day for males, or binge drinking [≥4 drinks on same occasion for females, ≥5 drinks on same occasion for males] on 5 or more days per month).[23] Physical activity refers to the amount of time individuals report spending during the week on activities such as walk or bicycle, task around home or in the yard, work activities, and recreational activities.[22] Average blood pressure was calculated by the following protocol: the diastolic reading with zero is not used to calculate the diastolic average; if all diastolic readings were zero, then the average would be zero; if only one blood pressure reading was obtained, that reading is the average; if there is more than one blood pressure reading, the first reading is always excluded from the average.[22] Hypertension was diagnosed when systolic ≥140 mmHg or diastolic ≥90 mmHg. The diagnostic criteria for DM include a diagnosis from a doctor, glycohemoglobin (HbA1c) levels >6.5%, fasting glucose levels ≥7.0 mmol L^{-1}, random/2-hour oral glucose tolerance test (OGTT) blood glucose levels ≥11.1 mmol L^{-1}, or use of diabetes medication/insulin.[22] In addition, energy intake was derived from the 24-hour dietary recall data.

Statistical analysis

Following NHANES analytic guidelines,[24–26] we applied the complex sampling design and mobile examination center

(MEC) sample weights to ensure representative, unbiased, and precise estimates. The sampling weights were calculated as follows: for 1999–2002, weights were 2/10 × 4-year MEC weight, and for 2003–2018, weights were 1/10 × 2-year MEC weight. Categorical variables were represented by proportions (%), while continuous variables were described by the mean (standard deviation, SD) or median (interquartile range, IQR), as appropriate. To compare the differences across groups, we employed the Wilcoxon rank-sum test for continuous variables and the Rao-Scott chi-squared test for categorical variables.

Multivariable weighted logistic regression models were used to determine the odds ratio (OR) and 95% confidence interval (CI) for the association between DI-GM and stroke. Model 1 was adjusted for age, sex, and race/ethnicity. Model 2 was adjusted for the factors included in model 1 and education level, marital status, and PIR. Model 3 was adjusted for factors included in model 2 and smoking status, alcohol drinking status, physical activity, and BMI. Model 4 was adjusted for factors included in model 3 and hypertension, DM, and energy intake.

Missing covariate values (9534 with unavailable adjusted factors information) were imputed using multiple imputation by chained equations, resulting in 5 imputed datasets based on variables in the final statistical model. Furthermore, weighted restricted cubic spline (RCS) curves were performed to investigate the potentially nonlinear association between exposure and outcome. Subgroup analyses were analyzed based on age, sex, race/ethnicity, marital status, education level, smoking status, alcohol drinking status, physical activity, hypertension, and DM. Receiver operating characteristic (ROC) curves were used to evaluate the predictive efficacy of DI-GM on stroke. 1-Specificity is the *X* axis in the ROC curve plot, and the *Y* axis represents the sensitivity. The accuracy of prediction was evaluated by area under the curve (AUC).

Since large databases inherently involve large sample sizes, such studies rarely describe sample size determination, as exemplified by Teng *et al.*[27] and Chen *et al.*[28] However, to estimate statistical power, we performed a *post hoc* calculation using PASS 2021, based on secondary NHANES data to analyze associations. A minimum sample size of 19 333 was required to achieve a two-sided 95% CI with a width of 0.004 for a stroke prevalence of 0.02 among US adults aged ≥20 years, as reported in the Global Burden of Disease (GBD) study (**https://vizhub.healthdata.org/gbd-results/**). This statistical analysis was conducted using R version 4.3.3, and multiple imputation was conducted using mice package (version 3.17.0) in R. $P < 0.05$ (two-tailed) was considered statistically significant.

Results

Study population

Of the 101 316 participants, 48 677 were included in the final analyses (Fig. 1), exceeding the calculated minimum sample size. The baseline characteristics of the study population are presented in Table 1. Statistically significant differences were observed across several variables, including age, sex, race/ethnicity, education level, marital status, PIR, smoking status, alcohol drinking status, physical activity, BMI, and energy intake (all $P < 0.0001$), with notable variation among different DI-GM categories.

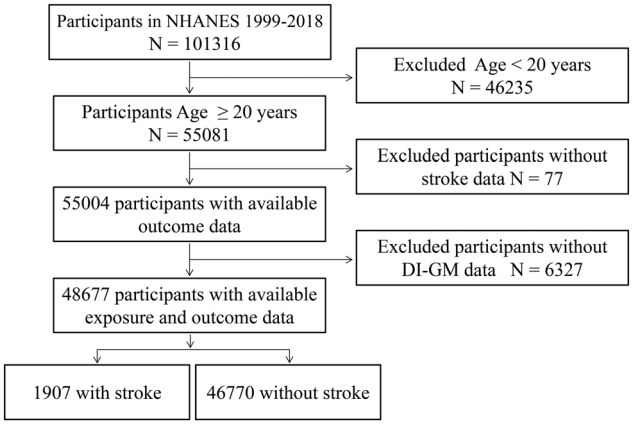

Fig. 1 Study flow chart. Abbreviations: DI-GM, dietary index for gut microbiota; NHANES, National Health and Nutrition Examination Survey.

Association between DI-GM and stroke

As shown in Table 2, no significant association was observed between DI-GM and stroke in the unadjusted model (OR: 0.96; 95% CI: 0.92–1.00; $P = 0.075$). After adjusting for demographic factors, including age, sex, and race/ethnicity (model 1), a significant inverse association emerged (OR: 0.87; 95% CI: 0.83–0.91; $P < 0.001$). This association remained significant after further adjustments for socioeconomic factors, including education level, marital status, and PIR (model 2: OR: 0.90; 95% CI: 0.86–0.95; $P < 0.001$), behavioral factors, such as smoking status, alcohol drinking status, physical activity, and BMI (model 3: OR: 0.92; 95% CI: 0.88–0.97; $P < 0.001$), and additional factors, including hypertension, DM, and energy intake (model 4: OR: 0.93; 95% CI: 0.89–0.98; $P = 0.003$). When DI-GM scores were grouped, no significant associations were observed in the unadjusted model, but in the fully adjusted model, the DI-GM = 5 group (OR: 0.80; 95% CI: 0.65–0.98; $P = 0.035$) and the DI-GM ≥6 group (OR: 0.77; 95% CI: 0.63–0.93; $P = 0.007$) were both significantly associated with reduced stroke prevalence (Table 2). Notably, each 1-point increase in BGMS was associated with a 13% reduction in stroke prevalence in the unadjusted model (OR: 0.87; 95% CI: 0.83–0.90; $P < 0.001$) and a 12% reduction in the fully adjusted model (OR: 0.88; 95% CI: 0.83–0.93; $P < 0.001$), while no significant association was observed between UGMS and stroke after adjustments (Table 2).

Separate analyses for participants aged 20–29 years and those aged ≥30 years revealed differing results. Among individuals aged 20–29 years ($n = 8513$), no significant association was observed between DI-GM and stroke (Table 3). Conversely, among participants aged ≥30 years ($n = 40\,164$), DI-GM was inversely associated with stroke, with each 1-point increase

Table 1 Participants' characteristics

Characteristics	Overall, N = 204 326 645; n = 48 677	DI-GM				P value
		0–3 N = 51 165 742; n = 12 650 (25%)	4 N = 51 728 459; n = 12 643 (25%)	5 N = 48 523 025; n = 11 625 (24%)	6–11 N = 52 909 418; n = 11 759 (26%)	
Age, mean (SD), years	47.04 (16.95)	43.17 (16.36)	45.74 (16.82)	48.13 (16.90)	51.04 (16.71)	<0.001
Sex, n (%)						<0.001
Male	23 471 (48.13)	6312 (50.55)	6322 (50.08)	5617 (48.32)	5220 (43.73)	
Female	25 206 (51.87)	6338 (49.45)	6321 (49.92)	6008 (51.68)	6539 (56.27)	
Race, n (%)						<0.001
Non-hispanic white	21 829 (68.80)	4964 (62.33)	5436 (66.77)	5284 (69.84)	6145 (76.10)	
Non-hispanic black	10 189 (11.03)	3679 (16.50)	2835 (12.29)	2095 (9.24)	1580 (6.18)	
Mexican American	8547 (8.04)	2127 (8.60)	2395 (9.12)	2236 (8.58)	1789 (5.96)	
Other hispanic	3954 (5.55)	944 (5.99)	1002 (5.66)	994 (5.77)	1014 (4.81)	
Other race	4158 (6.57)	936 (6.58)	975 (6.16)	1016 (6.57)	1231 (6.95)	
Education level, n (%)						<0.001
Less than high school	13 049 (17.11)	3752 (20.71)	3671 (19.16)	3129 (16.64)	2497 (12.05)	
High school or equivalent	11 320 (24.17)	3416 (29.39)	3131 (26.39)	2565 (22.45)	2208 (18.54)	
College or above	24 308 (58.72)	5482 (49.90)	5841 (54.45)	5931 (60.91)	7054 (69.42)	
Marital status, n (%)						<0.001
Married	25 757 (56.39)	6011 (51.05)	6556 (55.17)	6383 (58.28)	6807 (61.01)	
Never married	8481 (17.66)	2844 (22.29)	2362 (18.96)	1807 (16.25)	1468 (13.19)	
Living with partner	3640 (7.52)	1151 (8.96)	996 (7.77)	807 (6.90)	686 (6.45)	
Other	10 799 (18.44)	2644 (17.70)	2729 (18.10)	2628 (18.57)	2798 (19.36)	
PIR, mean (SD)	2.99 (1.64)	2.70 (1.62)	2.84 (1.63)	3.05 (1.63)	3.38 (1.59)	<0.001
BMI, mean (SD), kg m^{-2}	28.79 (6.76)	29.73 (7.34)	29.02 (6.90)	28.66 (6.54)	27.79 (6.05)	<0.001
Smoking status, n (%)						<0.001
Never	26 391 (53.78)	6683 (52.98)	6717 (52.38)	6289 (53.37)	6702 (56.29)	
Former	12 141 (24.91)	2700 (20.89)	2953 (23.03)	2988 (25.64)	3500 (29.97)	
Now	10 145 (21.31)	3267 (26.14)	2973 (24.59)	2348 (21.00)	1557 (13.74)	
Alcohol drinking status, n (%)						<0.001
Never	7205 (11.62)	1801 (11.99)	1884 (12.04)	1757 (11.64)	1763 (10.83)	
Former	8501 (14.33)	2229 (14.69)	2224 (14.77)	2114 (14.89)	1934 (13.03)	
Mild	16 201 (35.98)	3595 (29.54)	3952 (34.17)	3940 (36.39)	4714 (43.60)	
Moderate	7161 (16.91)	1881 (16.99)	1836 (16.08)	1674 (16.84)	1770 (17.72)	
Heavy	9609 (21.16)	3144 (26.79)	2747 (22.94)	2140 (20.24)	1578 (14.82)	
Physical activity, median [IQR], minutes per week	160.00 [7.88, 640.00]	126.00 [0.00, 600.00]	141.75 [0.00, 660.00]	160.00 [10.50, 640.00]	210.00 [31.50, 660.00]	<0.001
Hypertension, n (%)	20 498 (37.02)	5134 (36.40)	5133 (36.14)	5084 (38.37)	5147 (37.24)	0.046
DM, n (%)	8353 (12.73)	2153 (13.20)	2115 (12.59)	2047 (13.14)	2038 (12.04)	0.060
Energy intake, mean (SD), kcal	2130.66 (897.84)	2189.39 (913.28)	2146.53 (966.67)	2128.52 (915.78)	2060.31 (784.47)	<0.001
DI-GM score, mean (SD)	4.54 (1.52)	2.60 (0.61)	4.00 (0.00)	5.00 (0.00)	6.52 (0.75)	<0.001
BGMS, mean (SD)	2.14 (1.21)	1.07 (0.81)	1.77 (0.91)	2.43 (0.86)	3.40 (0.87)	<0.001
UGMS, mean (SD)	2.34 (1.02)	1.53 (0.85)	2.23 (0.91)	2.57 (0.86)	3.10 (0.76)	<0.001

Continuous variables are presented as weighted mean (SD) or median [IQR], whereas categorical variables are presented as actual frequency (weighted percentage [%]). The DI-GM score comprises BGMS and UGMS, categorized into four groups: 0–3, 4, 5, and ≥6. N represents weighted counts to reflect the population distribution, while n represents unweighted counts from the actual sample size. Abbreviations: BGMS, beneficial to gut microbiota score; BMI, body mass index; DI-GM, dietary index for gut microbiota; DM, diabetes mellitus; IQR, interquartile range; PIR, poverty income ratio; SD, standard deviation; UGMS, unfavorable to gut microbiota score.

linked to a 7% reduction in prevalence in the unadjusted model (OR: 0.93; 95% CI: 0.89–0.97; $P < 0.001$), and this association remained significant after adjusting for demographic factors (model 1: OR: 0.87; 95% CI: 0.83–0.91; $P < 0.001$), socioeconomic factors (model 2: OR: 0.90; 95% CI: 0.86–0.94; $P < 0.001$), behavioral factors (model 3: OR: 0.92; 95% CI: 0.88–0.97; $P < 0.001$), and additional factors (model 4: OR: 0.93; 95% CI: 0.89–0.98; $P = 0.003$) (Table 4). When DI-GM scores were grouped, among participants aged ≥30 years, the DI-GM = 5 group (OR: 0.80; 95% CI: 0.65–0.98; $P = 0.033$) and DI-GM ≥6 group (OR: 0.76; 95% CI: 0.63–0.92; $P = 0.006$) were significantly associated with reduced stroke prevalence in the fully adjusted model, with the DI-GM ≥6 group also significant in the unadjusted model (OR: 0.76; 95% CI: 0.63–0.91; $P = 0.003$) (Table 4). Furthermore, an inverse association was observed between BGMS and stroke prevalence across all models, with each 1-point increase linked to an 18% reduction in the unadjusted model (OR: 0.82; 95% CI: 0.79–0.86; $P < 0.001$) and a 12% reduction in the fully adjusted model (OR: 0.88; 95% CI: 0.83–0.93; $P < 0.001$), whereas UGMS showed no significant association with stroke after adjustments (Table 4).

Table 2 Association between DI-GM and stroke among the NHANES 1999–2018 participants (N = 204 326 645; n = 48 677)

	Crude model		Model 1		Model 2		Model 3		Model 4	
Characteristics	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
DI-GM score	0.96 (0.92–1.00)	0.075	0.87 (0.83–0.91)	<0.001	0.90 (0.86–0.95)	<0.001	0.92 (0.88–0.97)	<0.001	0.93 (0.89–0.98)	0.003
DI-GM group										
0–3	1(reference)		1(reference)		1(reference)		1(reference)		1(reference)	
4	0.98 (0.82–1.17)	0.818	0.84 (0.70–1.02)	0.073	0.88 (0.72–1.06)	0.175	0.89 (0.74–1.08)	0.243	0.91 (0.74–1.10)	0.323
5	0.92 (0.76–1.11)	0.404	0.69 (0.57–0.85)	<0.001	0.76 (0.62–0.94)	0.010	0.79 (0.64–0.97)	0.026	0.80 (0.65–0.98)	0.035
≥6	0.89 (0.74–1.06)	0.177	0.57 (0.48–0.69)	<0.001	0.67 (0.56–0.82)	<0.001	0.74 (0.61–0.89)	0.002	0.77 (0.63–0.93)	0.007
Trend test		0.135		<0.001		<0.001		0.001		0.003
BGMS	0.87 (0.83–0.90)	<0.001	0.80 (0.76–0.84)	<0.001	0.85 (0.81–0.89)	<0.001	0.87 (0.82–0.91)	<0.001	0.88 (0.83–0.93)	<0.001
UGMS	1.13 (1.06–1.20)	<0.001	1.00 (0.94–1.06)	0.997	1.00 (0.94–1.07)	0.969	1.02 (0.96–1.08)	0.493	1.01 (0.94–1.08)	0.826

The crude model was not adjusted for any covariates. Model 1 = age, sex, and race/ethnicity. Model 2 = model 1 + (education level, marital status, and PIR). Model 3 = model 2 + (smoking status, alcohol drinking status, physical activity, and BMI). Model 4 = model 3 + (hypertension, DM, and energy intake). The DI-GM score comprises BGMS and UGMS, categorized into four groups: 0–3, 4, 5, and ≥6. N represents weighted counts to reflect the population distribution, while n represents unweighted counts from the actual sample size. Abbreviations: BGMS, beneficial to gut microbiota score; BMI, body mass index; CI, confidence interval; DI-GM, dietary index for gut microbiota; DM, diabetes mellitus; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; PIR, poverty income ratio; UGMS, unfavorable to gut microbiota score.

Table 3 Association between DI-GM and stroke among the NHANES 1999–2018 participants aged 20–29 years (N = 38 301 799; n = 8513)

	Crude model		Model 1		Model 2		Model 3		Model 4	
Characteristics	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
DI-GM score	0.94 (0.68–1.30)	0.699	0.94 (0.68–1.29)	0.687	0.97 (0.68–1.38)	0.871	1.00 (0.71–1.41)	0.993	1.00 (0.71–1.41)	0.999
DI-GM group										
0–3	1(reference)		1(reference)		1(reference)		1(reference)		1(reference)	
4	1.07 (0.40–2.85)	0.886	1.08 (0.41–2.84)	0.879	1.10 (0.41–2.93)	0.855	1.14 (0.44–2.99)	0.781	1.15 (0.43–3.06)	0.775
5	0.64 (0.18–2.28)	0.486	0.64 (0.18–2.31)	0.490	0.69 (0.18–2.62)	0.578	0.73 (0.19–2.75)	0.633	0.73 (0.19–2.75)	0.634
≥6	0.81 (0.20–3.22)	0.759	0.79 (0.20–3.12)	0.734	0.92 (0.96–1.37)	0.905	1.02 (0.26–4.03)	0.976	1.03 (0.26–4.06)	0.968
Trend test		0.598		0.578		0.757		0.861		0.865
BGMS	0.85 (0.54–1.36)	0.507	0.85 (0.53–1.37)	0.503	0.89 (0.53–1.49)	0.660	0.92 (0.55–1.53)	0.751	0.90 (0.52–1.55)	0.705
UGMS	1.09 (0.74–1.61)	0.672	1.08 (0.73–1.61)	0.686	1.09 (0.74–1.61)	0.645	1.11 (0.75–1.63)	0.613	1.14 (0.75–1.74)	0.525

The crude model was not adjusted for any covariates. Model 1 = age, sex, and race/ethnicity. Model 2 = model 1 + (education level, marital status, and PIR). Model 3 = model 2 + (smoking status, alcohol drinking status, physical activity, and BMI). Model 4 = model 3 + (hypertension, DM, and energy intake). The DI-GM score comprises BGMS and UGMS, categorized into four groups: 0–3, 4, 5, and ≥6. N represents weighted counts to reflect the population distribution, while n represents unweighted counts from the actual sample size. Abbreviations: BGMS, beneficial to gut microbiota score; BMI, body mass index; CI, confidence interval; DI-GM, dietary index for gut microbiota; DM, diabetes mellitus; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; PIR, poverty income ratio; UGMS, unfavorable to gut microbiota score.

For the entire adult participants, the RCS analysis indicated a linear association between DI-GM and stroke (P for non-linearity = 0.715), as well as between BGMS and stroke (P for non-linearity = 0.532) (Fig. 2). Similarly, among participants aged ≥30 years, DI-GM was linearly associated with stroke (P for non-linearity = 0.791), along with BGMS (P for non-linearity = 0.449) (Fig. 3).

Subgroup analyses

Fig. 4 illustrates consistent associations between DI-GM and stroke prevalence among the NHANES 1999–2018 participants aged ≥30 years across various subgroups. Higher DI-GM scores were significantly associated with reduced stroke prevalence in participants aged <60 years, females, non-hispanic white indi-

Table 4 Association between DI-GM and stroke among the NHANES 1999–2018 participants aged ≥30 years (N = 166 024 846; n = 40 164)

	Crude model		Model 1		Model 2		Model 3		Model 4	
Characteristics	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
DI-GM score	0.93 (0.89–0.97)	<0.001	0.87 (0.83–0.91)	<0.001	0.90 (0.86–0.94)	<0.001	0.92 (0.88–0.97)	<0.001	0.93 (0.89–0.98)	0.003
DI-GM group										
0–3	1 (reference)		1 (reference)		1 (reference)		1 (reference)		1 (reference)	
4	0.93 (0.77–1.11)	0.398	0.83 (0.69–1.01)	0.061	0.87 (0.72–1.05)	0.150	0.88 (0.73–1.07)	0.212	0.90 (0.74–1.09)	0.281
5	0.84 (0.70–1.02)	0.076	0.69 (0.57–0.85)	<0.001	0.76 (0.62–0.93)	0.009	0.79 (0.64–0.97)	0.025	0.80 (0.65–0.98)	0.033
≥6	0.76 (0.63–0.91)	0.003	0.57 (0.47–0.69)	<0.001	0.67 (0.55–0.81)	<0.001	0.73 (0.60–0.89)	0.002	0.76 (0.63–0.92)	0.006
Trend test		0.002		<0.001		<0.001		<0.001		0.003
BGMS	0.82 (0.79–0.86)	<0.001	0.79 (0.76–0.83)	<0.001	0.85 (0.80–0.89)	<0.001	0.86 (0.82–0.91)	<0.001	0.88 (0.83–0.93)	<0.001
UGMS	1.12 (1.05–1.19)	<0.001	1.00 (0.94–1.06)	0.967	1.00 (0.94–1.07)	0.994	1.02 (0.96–1.08)	0.542	1.00 (0.94–1.07)	0.917

The crude model was not adjusted for any covariates. Model 1 = age, sex, and race/ethnicity. Model 2 = model 1 + (education level, marital status, and PIR). Model 3 = model 2 + (smoking status, alcohol drinking status, physical activity, and BMI). Model 4 = model 3 + (hypertension, DM, and energy intake). The DI-GM score comprises BGMS and UGMS, categorized into four groups: 0–3, 4, 5, and ≥6. N represents weighted counts to reflect the population distribution, while n represents unweighted counts from the actual sample size. Abbreviations: BGMS, beneficial to gut microbiota score; BMI, body mass index; CI, confidence interval; DI-GM, dietary index for gut microbiota; DM, diabetes mellitus; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; PIR, poverty income ratio; UGMS, unfavorable to gut microbiota score.

viduals, those with college or above, other marital statuses, all smoking statuses, current alcohol drinkers, those with varying levels of physical activity and BMI, individuals with hypertension, those with or without DM, and individuals with energy intake ≤1865.5 kcal.

Establishment of the predictive nomogram

Based on model 4 (the fully adjusted model), the nomogram was constructed for participants aged ≥30 years. Each predictor was calculated as a specific score on a rating scale, the total points of each variable were summed, and a vertical line was drawn downward at the total points to correspond to the probability of stroke. A higher score indicated a higher probability of stroke (Fig. 5A). The predictive accuracy of this nomogram was assessed using the receiver operating characteristic (ROC) curve, yielding an area under the curve (AUC) of 0.795 (95% CI: 0.787–0.804) (Fig. 5B).

Discussion

This cross-sectional study is the first to reveal a significantly inverse association between the DI-GM with stroke prevalence in the US population. Among adults aged ≥20 years, DI-GM showed no significant association in the unadjusted model, but after adjustments for demographic, socioeconomic, behavioral, and health factors, higher DI-GM scores correlated with reduced stroke prevalence, as well as higher BGMS across all models. Among participants aged ≥30 years, DI-GM and BGMS were significantly and negatively associated with stroke prevalence across all models, with each 1-point increase corresponding to 7% and 12% reductions, respectively. RCS analysis indicated linear relationships between DI-GM, BGMS, and stroke prevalence. Subgroup analyses demonstrated consistent protective effects across participants aged <60 years, females, non-hispanic white individuals, those with college or above, other marital statuses, all smoking statuses, current alcohol drinkers, those with varying levels of physical activity and BMI, individuals with hypertension, those with or without DM, and individuals with energy intake ≤1865.5 kcal. These findings underscore the potential of personalized dietary interventions focused on DI-GM for stroke prevention, particularly in middle-aged and older populations.

The lack of significance in the crude model likely reflects the influence of confounding factors, particularly age, a key determinant of stroke risk. Stroke incidence rises substantially with age, as younger populations exhibit lower stroke rates and weaker dependence on modifiable risk factors like diet.[29–34] Age is also an independent risk factor for cardiovascular disease (CVD), with older individuals facing higher risks of adverse outcomes, including ischemic and bleeding events.[35] To address this, age-stratified analyses were conducted, revealing no significant association between DI-GM and stroke in participants aged 20–29 years. Conversely, in those aged ≥30 years, a significant inverse association was observed even in the crude model, highlighting age-related variations in stroke risk and DI-GM associations. These findings suggest younger age groups dilute the overall effect, reinforcing the importance of focusing on middle-aged and older populations where the relationship is stronger. Adjusted models across all age groups consistently showed significant inverse associations, emphasizing the need to control for confounders when exploring

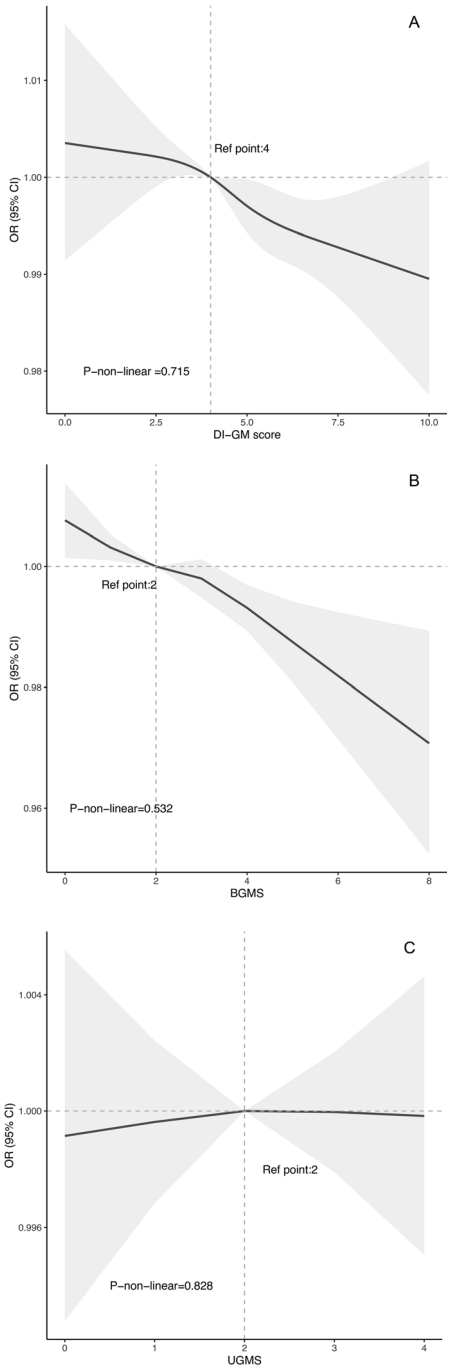

Fig. 2 Association between DI-GM and stroke among the NHANES 1999–2018 participants by RCS (N = 204 326 645; n = 48 677). (A) Linear association between DI-GM score and stroke prevalence. (B) Linear association between BGMS and stroke prevalence. (C) Linear association between UGMS and stroke prevalence. The model was adjusted for age, sex, race, education level, marital status, PIR, smoking status, alcohol drinking status, physical activity, BMI, hypertension, DM, and energy intake. The DI-GM score comprises BGMS and UGMS. N represents weighted counts to reflect the population distribution, while n represents unweighted counts from the actual sample size. Abbreviations: BGMS, beneficial to gut microbiota score; BMI, body mass index; CI, confidence interval; DI-GM, dietary index for gut microbiota; DM, diabetes mellitus; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; PIR, poverty income ratio; RCS, restricted cubic spline; UGMS, unfavorable to gut microbiota score.

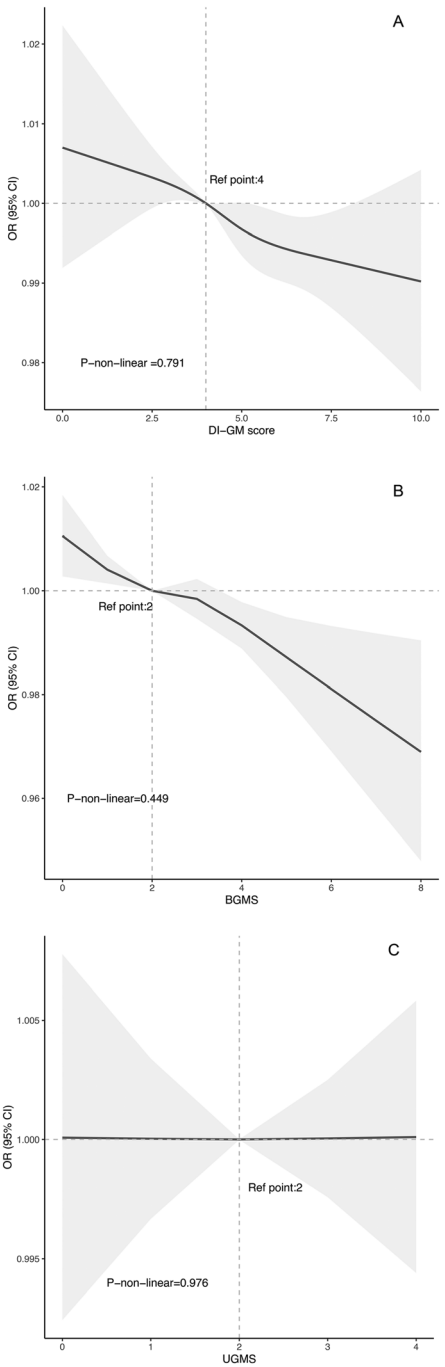

Fig. 3 Association between DI-GM and stroke among the NHANES 1999–2018 participants aged ≥30 years by RCS (N = 166 024 846; n = 40 164). (A) Linear association between DI-GM score and stroke prevalence. (B) Linear association between BGMS and stroke prevalence. (C) Linear association between UGMS and stroke prevalence. The model was adjusted for age, sex, race, education level, marital status, PIR, smoking status, alcohol drinking status, physical activity, BMI, hypertension, DM, and energy intake. The DI-GM score comprises BGMS and UGMS. N represents weighted counts to reflect the population distribution, while n represents unweighted counts from the actual sample size. Abbreviations: BGMS, beneficial to gut microbiota score; BMI, body mass index; CI, confidence interval; DI-GM, dietary index for gut microbiota; DM, diabetes mellitus; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; PIR, poverty income ratio; RCS, restricted cubic spline; UGMS, unfavorable to gut microbiota score.

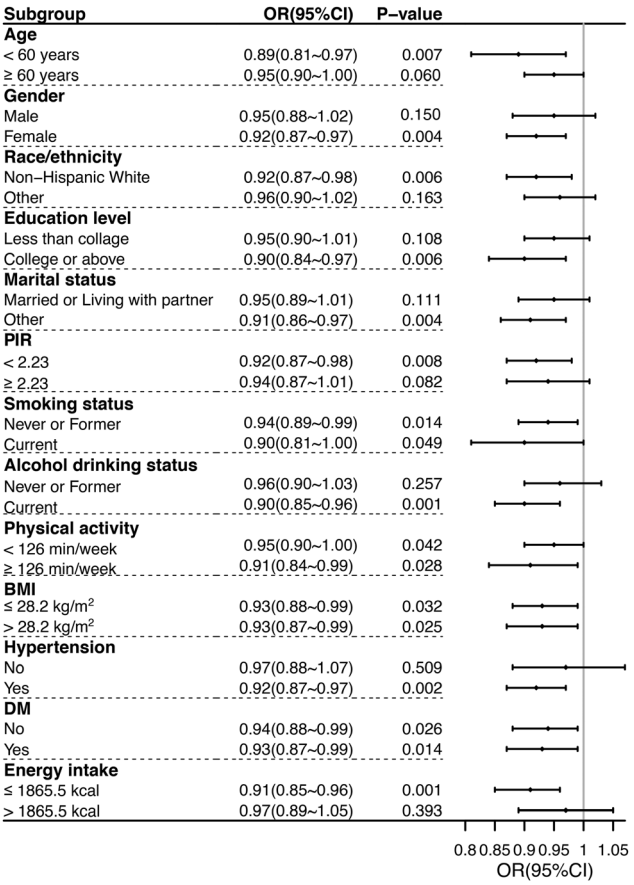

Fig. 4 Subgroup analyses of the association between DI-GM and stroke among the NHANES 1999–2018 participants aged ≥30 years (*N* = 166 024 846; *n* = 40 164). *N* represents weighted counts to reflect the population distribution, while *n* represents unweighted counts from the actual sample size. Abbreviations: CI, confidence interval; DI-GM, dietary index for gut microbiota; DM, diabetes mellitus; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; PIR, poverty income ratio. This forest plot presents ORs and 95% CIs for the association between DI-GM and stroke across various subgroups. Significant associations were observed among participants aged <60 years, females, non-hispanic white individuals, those with college or above, other marital statuses, PIR < 2.23, all smoking statuses, current alcohol drinkers, those with varying levels of physical activity and BMI, individuals with hypertension, those with or without DM, and individuals with energy intake ≤1865.5 kcal.

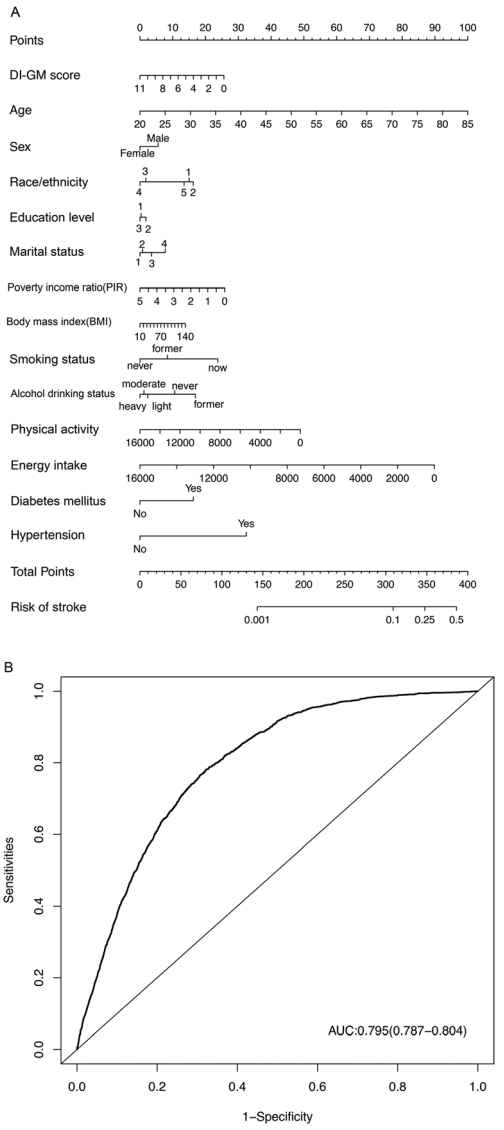

Fig. 5 Establishment of a risk prediction model for stroke among the NHANES 1999–2018 participants aged ≥30 years (*N* = 166 024 846; *n* = 40 164). (A) The nomogram model based on model 4. Numbers in the figure represent the following values: race/ethnicity: 1 = non-hispanic white, 2 = non-hispanic black, 3 = Mexican American, 4 = other hispanic, 5 = other race. Education level: 1 = less than high school, 2 = high school or equivalent, 3 = college or above. Marital status: 1 = married, 2 = never married, 3 = living with partner, 4 = other. (B) ROC curve based on model 4, evaluating the predictive power for stroke of the nomogram model. Model 4 is the fully adjusted model, including adjustments for age, sex, race/ethnicity, marital status, PIR, education level, smoking status, alcohol drinking status, physical activity, BMI, energy intake, hypertension, and DM. Abbreviations: AUC, area under curve; BMI, body mass index; DM, diabetes mellitus; DI-GM, dietary index for gut microbiota; NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio; ROC, receiver operating characteristic. Based on model 4, the nomogram was constructed for participants aged above 30 years. Each predictor was calculated as a specific score on a rating scale, the total points of each variable were summed, and a vertical line was drawn downward at the total points to correspond to the probability of stroke. A higher score indicated a higher probability of stroke (A). The predictive accuracy of this nomogram was assessed using the receiver operating characteristic (ROC) curve, yielding an area under the curve (AUC) of 0.795 (95% CI: 0.787–0.804) (B).

diet–microbiota–stroke relationships. This aligns with evidence from prior studies where crude models often fail to capture complex associations until adjusted.[36,37] These results underscore the potential of DI-GM in stroke prevention, particularly among middle-aged and older populations.

The protective association between DI-GM and stroke is rooted in the diet–gut microbiota interplay, which plays a central role in stroke pathophysiology. Gut microbiota contribute to the pathophysiology of stroke through the microbiota–gut–brain axis (MGBA), influencing inflammation, and immune regulation, mediated by gut microbes and microbiota-derived metabolites such as SCFAs, secondary bile acids, trimethylamine-*N*-oxide (TMAO), and phenylacetylglutamine.[38–40] In addition, Schneider

et al.[41] proposed the diet–microbiota–gut–brain axis as a framework linking diet to brain health, highlighting how dietary factors shape gut microbiota to influence brain function and overall well-being. Fermented dairy, a unique beneficial component of the DI-GM, contains beneficial microbes, microbial metabolites, and bioactives that shape composition of the gut microbiota, and, ultimately, modulate the microbiota–gut–brain axis.[42] A meta-analysis by Zhang *et al.*[43] indicated that fermented dairy intake was associated with decreased CVD risk. Our findings are also consistent with previous research highlighting the role of gut microbiota in stroke risk, with dietary fiber, a beneficial component of DI-GM, improving stroke outcomes by fostering SCFA production, while choline- and L-carnitine-rich foods, unfavorable components of DI-GM, increasing stroke risk *via* TMAO production.[44] Furthermore, poor diet is strongly associated with first stroke risk, whereas adherence to a Mediterranean diet, emphasizing whole-plant foods, olive oil, moderate poultry and fish, and minimal red meat, has been shown to reduce this risk.[45] The DI-GM, with a correlation of 0.42 with the Mediterranean diet score (MDS; $P < 0.0001$),[13] similarly highlights the dual focus on diet and gut microbiota in stroke prevention. In addition, the microbiome regulates gut inflammation *via* diet-driven microbial mechanisms,[46] and the inverse association between DI-GM and stroke aligns with dietary inflammatory index (DII)-linked stroke risk.[47] DI-GM provides a comprehensive framework for understanding diet-stroke connections, complementing indices like DII, with potential to mitigate stroke risk pending further research to confirm causal links.

Our study has several limitations. First, its cross-sectional design precludes establishing temporal or causal relationships between DI-GM and stroke, necessitating longitudinal or prospective studies. Second, the DI-GM reflects dietary habits at the time of data collection rather than long-term patterns. However, most adults maintain relatively stable diets unless influenced by major health concerns, suggesting that the DI-GM reasonably represents habitual diets in the general population. Third, residual confounding due to measurement error cannot be fully excluded. Fourth, the NHANES 24-hour dietary recalls lacked information on specific types of tea consumption, limiting the comprehensiveness of the DI-GM. Fifth, reliance on self-reported dietary data and covariates introduces potential recall bias. Finally, generalizability is limited, as significant associations were observed primarily among Caucasians, likely due to their larger sample size in this study, which provided greater statistical power, whereas other racial subgroup did not achieve statistical significance, possibly due to smaller sample sizes. Further studies with more balanced representation of diverse populations are needed to validate these findings and deepen understanding of the diet–gut microbiota–stroke risk relationship.

Conclusions

The DI-GM, an innovative dietary quality index reflecting gut microbiota diversity, was significantly and inversely associated with stroke prevalence, particularly in individuals aged ≥30 years. Notably, beneficial to gut microbiota scores showed a strong linear inverse relationship with stroke prevalence. These findings highlight the potential of gut–microbiota-focused dietary interventions as a promising strategy for stroke prevention.

Author contributions

Jingjing Liu: conceptualization, methodology, investigation, data curation, formal analysis, writing – original draft, writing – review & editing. Shaoqiang Huang: conceptualization, methodology, resources, supervision, validation, visualization, writing – review & editing. All authors have read and agreed to the published version of the manuscript.

Data availability

These survey data are free and publicly available, and can be downloaded directly from the NHANES website (**https://www.cdc.gov/nchs/nhanes.htm**) by users and researchers worldwide.

Conflicts of interest

There are no conflicts of interest to declare.

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