

The relationship of cardiometabolic index with bowel movement frequency: an NHANES-based cross-sectional analysis



Qianyi Ren¹, Yanan Wang², Xinhui Han¹, Qingyi Wang¹ and Guoying Liang^{3*}

Abstract

Background Prior studies have indicated a notable link between gut health and metabolic syndrome (MetS). The cardiometabolic index (CMI), an innovative indicator of metabolic health, effectively predicts MetS. Bowel movement frequency (BMF) closely reflects gastrointestinal function and is a key sign of gut health. Nonetheless, the relationship between CMI and BMF is still unclear. Our research explores the possible association between these two variables.

Methods This study employed 2005 to 2010 National Health and Nutrition Examination Survey data. The CMI for each participant was determined by triglycerides, high-density lipoprotein cholesterol, and the waist-to-hip ratio. Multiple regression, smooth curve fitting, and threshold effect analyses were employed to investigate the association between CMI and BMF. The association's stability across populations was assessed through subgroup analyses and interaction tests.

Results The study included 9,678 participants in total. After controlling for potential confounding variables, those in the uppermost CMI quartile had a 0.69 more increase in BMF than the bottom quartile (β =0.69, 95% CI: 0.34, 1.03). The trend analyses showed that BMF increased steadily with the advancement of the CMI quartiles (*P* for trend < 0.0001). Associations between CMI and BMF were shown to be nonlinear through smooth curve fitting and threshold effect analyses. Specifically, when CMI ranged from 4.97 to 11.75, a negative connection was observed (β = -0.78, 95% CI: -1.33, -0.23), while positive associations were identified in other ranges. Subgroup analyses and interaction tests indicated significant CMI and BMF association variations when stratified by depression and age categories (*P* for interaction < 0.05).

Conclusions This research indicates that CMI is generally associated with an increase in BMF. However, when CMI ranges from 4.97 to 11.75, it is associated with a BMF decrease. Notably, the association of CMI and BMF is more potent in young, middle-aged, and depressed people.

Keywords Bowel movement frequency, Cardiometabolic index, Cross-sectional study, NHANES

*Correspondence: Guoying Liang Igy1976190606@sina.com ¹School of First Clinical Medicine, Heilongjiang University of Chinese Medicine, Harbin 150040, China



²Department of Intensive Care Rehabilitation 1, The Second Affiliated Hospital of Heilongjiang University of Chinese Medicine, Harbin 150001, China

³Department of Gastroenterology 1, The First Affiliated Hospital of Heilongjiang University of Chinese Medicine, Harbin 150040, China

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creative.commons.org/licenses/by-nc-nd/4.0/.

Introduction

Metabolic Syndrome (MetS) is a disorder marked by abdominal obesity, insulin resistance, dyslipidemia, and hypertension, which is closely linked to cardiovascular diseases, diabetes, and all-cause mortality [1]. Recent studies have revealed that the pathophysiological mechanisms of MetS extend beyond traditional cardiovascular and metabolic organ damage and may also be related to gut function [2]. For example, insulin resistance can affect the balance of gut microbiota [3]; dyslipidemia worsens intestinal inflammation and harms the mucosa [4]. These findings all imply an association between MetS and gut health.

The cardiometabolic index (CMI) has gained recognition as a promising biomarker with great potential in the prediction realm of MetS [5, 6]. Calculated as the product of the triglycerides (TG) to the high-density lipoprotein cholesterol (HDL-C) ratio and waist-to-height ratio (WHtR). In contrast to mass index (BMI), WHtR demonstrates greater accuracy as an indicator of metabolic and cardiovascular risk [7]. In addition, the TG/HDL-C ratio is significantly related to dysregulated lipid metabolism and MetS advancement [8, 9]. By combining these two indices, the CMI can provide a holistic evaluation of metabolic status. Nevertheless, the relationship between CMI and gut function has not been thoroughly investigated in any research.

The proper functioning of the gastrointestinal tract is crucial for overall health. Bowel movement frequency (BMF) serves as a critical indicator of gut health, closely reflecting gut function [10]. Beyond this, the maintenance of healthy bowel habits is essential in preventing and managing various pathologies, particularly cardiovascular disorders [11], chronic kidney disease [12], and anorectal disorders [13]. Recent studies have shown that BMF is strongly linked to overall health, further emphasizing its importance [14].

Although the regulatory mechanisms of BMF remain incompletely elucidated, it is clear that its regulatory network is highly complex [15]. This network involves multiple factors, including demographic characteristics [16], neural regulation [17], dietary habits [18], gut microbiota [19], physical activity [20], and psychological state [21], all of which can influence BMF. With advances in medical research, numerous studies have demonstrated that components of MetS, including obesity [22], type 2 diabetes [23], and hyperlipidemia [24], are correlated with abnormal bowel habits. Therefore, there is a complex association between gut function and MetS.

Therefore, conducting in-depth research on the association between MetS and gut function is significant. The association between CMI and BMF remains incompletely characterized in current research. To address this knowledge gap, we designed a cross-sectional study leveraging the National Health and Nutrition Examination Survey (NHANES) database to investigate the CMI-BMF association. By adopting this method, our objective is to offer new ideas for treatment and management strategies for patients with MetS and gastrointestinal dysfunction while promoting the development of interdisciplinary management approaches.

Methods

Data sources

This study utilized data from NHANES, a populationbased epidemiological program assessing health risks and nutritional profiles of non-institutionalized U.S. residents through standardized examinations. This database employed complicated, stratified, multi-stage probability cluster sampling to get a cross-section of United States citizens. This sampling method involves interviews, physical assessments, and laboratory analyses, all of which are carried out on a biennial basis. Consequently, the sample precisely mirrors the demographic traits of the U.S. population. After the ethics review board's approval, participants signed informed consent forms. Each process adhered to international research ethics guidelines and federal data protection laws.

Participants screening

Between 2005 and 2010, conducted NHANES cycles were the data employed in this study, as only these cycles included the bowel health questionnaire data. Initially, 31,034 participants were enrolled. Subsequently, the following exclusion criteria were used to evaluate participants: (1) absence of BMF and bowel movement type data; (2) missing data required for CMI calculation, including waist circumference (WC), height (H), TG, and HDL-C; (3) pregnancy during the survey; (4) history of cancer; (5) recent use of antidiarrheal or laxative medications; and (6) incomplete covariables data. After applying rigorous eligibility filters, 9,678 subjects met the study requirements and proceeded to subsequent analyses. Figure 1 illustrates the detailed overview of the participants' selection flowchart.

Exposure variable

In this study, CMI, the exposure variable, is a newly established index designed to evaluate metabolic health status. The calculation of CMI involves several physiological indicators, including WC, H, TG, and HDL-C. TG is measured using the Beckman Synchron LX20 with a timed endpoint method, and the unit is expressed in mmol/L. HDL-C is measured using the direct immunoassay method, with the unit also expressed in mmol/L. WC and H are measured by trained health technicians using standardized methods, with the units expressed in Exclude participants lacking CMI (N=1001)





Fig. 1 Participants screening flowchart

Abbreviations: NHANES: National Health and Nutrition Examination Survey; BMF: Bowel movement frequency; CMI: Cardiometabolic index

centimeters. The CMI calculation formula is as follows [5]:

$$CMI = \frac{TG}{HDL - C} \times \frac{WC}{H}$$

Outcome variable

BMF was evaluated through a bowel health questionnaire that included the inquiry, "How often do you usually have bowel movements?" The responses, initially reported in "times per day," were subsequently converted into "times per week" to standardize the data to a consistent weekly unit. At the same time, we also investigated the association between BMF and diarrhea or constipation. Employing the Bristol Stool Form Scale to categorize participants' bowel movements, we defined Type 1 and Type 2 stools as constipation, Types 3 to 5 as normal, and Types 6 or 7 as diarrhea.

Selection of covariables

To make the associated results more robust, we incorporated multiple confounding factors that might affect the results in this study, including sex, age, race, poverty-income ratio (PIR), education level, smoking [25], drinking [26], moderate activity [27], BMI [28], diabetes [23], gastrointestinal diseases, hypertension [29], depression [30], sleep disorders [31], and various dietary factors (e.g., energy, total fat, moisture, dietary fiber, protein, carbohydrate, and caffeine intake) [32], as guided by previous research and clinical experience.

Smoking and drinking were determined by standardized questionnaires, with thresholds defined as \geq 100 lifetime cigarettes smoked and \geq 12 alcoholic beverages consumed annually. The Patient Health Questionnaire-9 was utilized to assess depression, where scores \geq 10 met the diagnostic threshold [33]. The diagnoses of diabetes, hypertension, and sleep disorders were based on medical records. Gastrointestinal diseases and moderate activity were assessed through participant questionnaires. The intake of energy, total fat, moisture, dietary fiber, protein, carbohydrate, and caffeine was determined by calculating the mean consumption over a two-day period.

The study population was stratified by age into three cohorts: young (20–40 years), middle-aged (40–60 years), and elderly (\geq 60 years). Following the same stratification approach, PIR classified participants into lower-income (PIR < 1), intermediate-income ($1 \leq$ PIR < 4), and higher-income (PIR \geq 4) categories. BMI categorization included normal-range weight (25 kg/m²), overweight (25–30 kg/m²), and obese (\geq 30 kg/m²) classifications.

Statistical analysis

Statistical significance was determined in all statistical computations using a two-tailed P-value < 0.05. All

statistical analyses utilized the R Studio (version 4.4.2) and the EmpowerStats (version 4.2) analytical platforms. In the data analyses of this study, the data from three cycles of Full Sample 2 Year MEC Exam Weight (WTME-C2YR) were used for weighting to ensure nationally representative estimates. This study described continuous variables using the median with interquartile range or the mean with 95% confidence intervals (CI). It analyzed them for intergroup differences using the Kruskal-Wallis test or ANOVA. Categorical variables were reported as sample counts with weighted percentages. It analyzed them for intergroup evaluation through the survey-weighted Chi-square test.

Meanwhile, potential confounding covariables were considered to enhance the accuracy of the outcomes, and multiple covariables were adjusted in the statistical model. The non-adjusted model includes no covariable adjustments, and the minimally adjusted model controls for gender, age, and race. In addition to these adjustments, the fully adjusted model also accounts for education level, PIR, smoking, drinking, moderate activity, BMI, diabetes, gastrointestinal diseases, hypertension, depression, sleep disorders, and dietary factors such as energy, total fat, moisture, dietary fiber, protein, carbohydrate, and caffeine. All three models of multiple regression analyses were employed, and the fully adjusted model was utilized in other analyses.

The association between the two variables was evaluated through multiple regression analyses by Empower-Stats. CMI data were categorized into quartiles to analyze trends in the association with BMF. Results are presented as β coefficients or odds ratio (OR) followed by their corresponding 95% CI. Moreover, the nonlinear association between the two variables was explored by smooth curve fitting using the "gam" function in the mgcv package. Simultaneously, the inflection point was determined through threshold effect analysis. Interaction tests and subgroup analyses were implemented to assess potential heterogeneity in the research results.

Results

Baseline characteristics of participants

Table 1 and Table S1 present the essential characteristics of the study population categorized by CMI and BMF, respectively. Generally, this research had a total of 9,678 individuals. There were 49.25% males and 50.75% females among these participants. The median CMI for all participants was 0.62 (0.34, 1.16), with the quartile ranges as follows: first quartile < 0.34, second quartile 0.34 to 0.62, third quartile 0.62 to 1.16, and fourth quartile > 1.16.

In the quartile distribution of CMI, BMF growth corresponded with the ascent of the quartiles of the CMI (P < 0.0001). The distribution of bowel movement type across groups showed no statistically significant

Characteristics	Overall	Ouartiles of CMI				P-value
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	-
		< 0.34	(0.34-0.62)	(0.62-1.16)	>1.16	_
N	9678	2420	2419	2419	2420	
CMI	0.62 (0.34, 1.16)	0.23 (0.17, 0.28)	0.46 (0.40, 0.54)	0.84 (0.72, 0.99)	1 80 (1 39 2 58)	< 0.0001
BME	9 23 (9 10, 9 35)	8 48 (8 27 8 68)	8.91 (8.68, 9.13)	951 (922 981)	10.10 (9.81, 10.38)	< 0.0001
Gender	5.25 (5.10, 5.55)	0.10 (0.27, 0.00)	0.51 (0.00, 5.15)	5.51 (5.22, 5.01)	10.10 (9.01, 10.90)	< 0.0001
Male	4840 (49 25)	936 (35 62)	1109 (44 90)	1283 (54 43)	1512 (63 53)	< 0.0001
Fomalo	4838 (50 75)	1484 (64 38)	1310 (55 10)	1205 (54.45)	008 (36 47)	
	4030 (30.73)	1404 (04.30)	1310 (33.10)	51 00 (27 00 64 00)	900 (30.47) 40.00 (28.00, 63.00)	< 0.0001
Age (years)	46.00 (34.00, 02.00)	42.00 (29.00, 56.00)	47.00 (34.00, 03.00)	51.00 (57.00, 04.00)	49.00 (38.00, 02.00)	< 0.0001
Age gloup	2200 (27 40)	1060 (46 16)	047 (20 62)	700 (22 OF)	602 (20 07)	< 0.0001
roung	3308 (37.40)	1009 (40.10)	847 (38.02)	709 (32.95)	083 (30.97)	
Middle	3450 (41.94)	/83 (38.14)	825 (40.73)	855 (41.64)	987 (47.65)	
Elderly	2920 (20.67)	568 (15.70)	/4/ (20.64)	855 (25.41)	/50 (21.38)	0.0004
Race						< 0.0001
Mexican American	1769 (7.94)	275 (5.27)	390 (6.98)	503 (9.04)	601 (10.75)	
Non-Hispanic White	4842 (72.29)	1183 (71.16)	1185 (71.45)	1209 (72.34)	1265 (74.38)	
Non-Hispanic Black	1894 (10.38)	685 (14.48)	557 (12.26)	404 (8.67)	248 (5.61)	
Other Race	1173 (9.39)	277 (9.09)	287 (9.32)	303 (9.95)	306 (9.26)	
Education Level						< 0.0001
Less Than High School	2547 (16.97)	468 (12.28)	589 (16.35)	719 (18.88)	771 (20.85)	
High School Graduate	2306 (24.00)	531 (20.52)	569 (22.73)	565 (24.14)	641 (29.00)	
More Than High School	4825 (59.03)	1421 (67.20)	1261 (60.92)	1135 (56.98)	1008 (50.15)	
PIR group						0.0006
Low income	1840 (12.01)	418 (11.32)	416 (10.74)	470 (12.42)	536 (13.69)	
Middle income	5214 (49.91)	1252 (47.79)	1309 (50.54)	1308 (49.30)	1345 (52.20)	
High income	2624 (38.08)	750 (40.89)	694 (38.72)	641 (38.29)	539 (34.11)	
BMI group						< 0.0001
Normal	2710 (30.71)	1383 (62.37)	734 (32.23)	400 (17.22)	193 (7.96)	
Overweight	3349 (34.04)	702 (26.58)	933 (39.28)	921 (39.60)	793 (31.15)	
Obesity	3619 (35.25)	335 (11.05)	752 (28.49)	1098 (43.18)	1434 (60.88)	
Energy (kcal/d)	1932.50	1895.50	1905.00	1892.00	2051.00	< 0.0001
-)) ()	(1471.00, 2506.00)	(1468.88, 2473.50)	(1465.00, 2482.75)	(1423.75, 2411.00)	(1547.50, 2624.50)	
Protein (gm/d)	75.03	73.85	73.53	73.58	78.73	< 0.0001
	(56.25, 98.22)	(54.95, 96.87)	(55.45, 96.78)	(54.97, 95.09)	(59.45, 103.50)	
Carbohydrate (gm/d)	236.03	228.68	234.43	233.16	249.31	< 0.0001
	(178.19, 307.83)	(173.05, 297.63)	(177.06, 300.32)	(174.35, 300.88)	(186.96, 325.54)	
Dietary fiber (gm/d)	14.75	14.80	14.45	14.45	15.12	0.0113
	(10.40, 20.45)	(10.05, 20.56)	(10.38, 20.35)	(10.50, 20.05)	(10.69, 21.00)	
Total fat (gm/d)	70.52 (50.11, 96.69)	69.37 (50.07, 94.91)	70.02 (50.85, 96.13)	69.17 (48.11, 94.25)	73.34 (51.61, 101.75)	< 0.0001
Caffeine (mg/d)	103.50	92.00	102.00	104.00	116.00	< 0.0001
	(32.50, 215.50)	(23.50, 201.50)	(29.00, 209.50)	(34.75, 217.00)	(43.50, 235.62)	
Moisture (mg/d)	2556.24	2529.64	2496.97	2494.23	2690.74	< 0.0001
	(1930.92, 3382.56)	(1894.00, 3330.76)	(1897.31, 3312.94)	(1893.11, 3301.30)	(2062.11, 3536.35)	
Gastrointestinal diseases						0.4981
Yes	818 (8.34)	188 (7.73)	204 (9.04)	206 (8.01)	220 (8.60)	
No	8860 (91.66)	2243 (92.27)	2215 (90.96)	2213 (91.99)	2200 (91.40)	
Sleep disorders						< 0.0001
Yes	706 (7.19)	97 (4.03)	153 (5.99)	199 (7.94)	257 (11.14)	
No	8972 (92.81)	2323 (95.97)	2266 (94.01)	2220 (92.06)	2163 (88.86)	
Diabetes						< 0.0001
Yes	1039 (7.56)	128 (3.76)	218 (5.86)	306 (8.80)	387 (12.27)	
No	8639 (92.44)	2292 (96.24)	2201 (94.14)	2113 (91.20)	2033 (87.73)	
Hypertension						< 0.0001
Yes	3217 (29.08)	523 (16.84)	743 (25.97)	929 (34.69)	1022 (40.12)	

Table 1 Demographic profiles according to CMI quartile distribution

Characteristics	Overall	Quartiles of CM	P-value			
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	
		< 0.34	(0.34–0.62)	(0.62–1.16)	>1.16	
No	6461 (70.92)	1897 (83.16)	1676 (74.03)	1490 (65.31)	1398 (59.88)	
Depression						0.0011
Yes	810 (6.74)	164 (5.48)	170 (5.86)	225 (7.47)	251 (8.31)	
No	8868 (93.26)	2256 (94.52)	2249 (94.14)	2194 (92.53)	2169 (91.69)	
Smoking						< 0.0001
Yes	4552 (46.45)	1002 (41.45)	1083 (44.95)	1203 (49.04)	1264 (50.92)	
No	5126 (53.55)	1418 (58.55)	1336 (55.05)	1216 (50.96)	1156 (49.08)	
Drinking						0.4290
Yes	7012 (76.68)	1781 (78.38)	1736 (76.24)	1733 (75.89)	1762 (76.09)	
No	2666 (23.32)	639 (21.62)	683 (23.76)	686 (24.11)	658 (23.91)	
Moderate activity						0.0708
Yes	4241 (48.64)	1126 (51.10)	1050 (46.90)	1042 (48.95)	1023 (47.44)	
No	5437 (51.36)	1294 (48.90)	1369 (53.10)	1377 (51.05)	1397 (52.56)	
Bowel movement type						0.0663
Constipation	697 (6.52)	190 (7.33)	178 (6.84)	168 (5.75)	161 (6.05)	
Normal	8277 (87.18)	2093 (87.52)	2066 (86.38)	2063 (88.12)	2055 (86.73)	
Diarrhea	704 (6.30)	137 (5.15)	175 (6.78)	188 (6.13)	204 (7.22)	

Note: Categorical variables were presented as sample counts and weighted percentages, and continuous variables were presented as median and interquartile range or weighted mean and 95% confidence intervals; CMI: Cardiometabolic index; BMF: Bowel movement frequency; PIR: Poverty-income ratio; BMI: Body mass index

Table 2 Multiple regression analysis between CMI and BMF

	Non-adjusted model	Minimally adjusted model	Fully adjusted model β (95% CI)	
	β (95% Cl)	β (95% CI)		
CMI (quartile)				
Quartile 1	Reference	Reference	Reference	
Quartile 2	0.43 (0.14, 0.72)	0.25 (-0.04, 0.54)	0.12 (-0.18, 0.41)	
Quartile 3	1.04 (0.74, 1.33)	0.68 (0.38, 0.98)	0.47 (0.15, 0.79)	
Quartile 4	1.62 (1.32, 1.91)	1.10 (0.80, 1.41)	0.69 (0.34, 1.03)	
P for trend	< 0.0001	< 0.0001	0.0015	

Note: Non-adjusted model: Analysis without covariable adjustment; Minimally adjusted model: Adjusted for demographic covariables (gender, age, race); Fully adjusted model: Adjustments were made for age, sex, race, education level, poverty income ratio, smoking, drinking, moderate activity, body mass index, diabetes, gastrointestinal diseases, hypertension, depression, sleep disorders, and dietary factors such as energy, total fat, moisture, dietary fiber, protein, carbohydrate, and caffeine; CI: Confidence intervals; CMI: Cardiometabolic index

difference (P=0.0663). Participants categorized within the uppermost quartile of CMI exhibited a higher prevalence of middle-aged male predominance, smoking, and comorbid conditions, including diabetes, hypertension, depression, and sleep disorders, compared to individuals categorized within the lowest quartile group. Furthermore, participants from the top CMI quartile generally demonstrated higher BMI values and consumed more protein, fat, caffeine, and energy.

Within the BMF stratification, the proportion of females, younger individuals, those with low income, and those experiencing constipation were much greater with the lower BMF group than other groups. In the higher BMF group, the proportions of individuals with hypertension, diabetes, diarrhea, and obesity, as well as energy and macronutrient (protein, fat, carbohydrate) intake, were significantly higher than in other groups. Additionally, the abnormal BMF group has greater incidences of depression and gastrointestinal diseases than the normal group.

Association between CMI and BMF

The findings of the multiple regression analysis demonstrated that an association exists between CMI and BMF. In the fully adjusted model, upon classifying CMI into quartiles, the trend analysis showed that as the CMI quartiles increased, BMF exhibited a consistent upward trend (*P* for trend = 0.0015). Specifically, the greatest CMI quartile demonstrated an additional increase of 0.69 in BMF for each one-unit rise in CMI as contrasted with the lowest (β = 0.69, 95% CI: 0.349, 1.03). Table 2 displays the results of the multiple regression analysis.

Meanwhile, Table S2 and Table S3 present the outcomes of the multiple regression analysis between CMI and diarrhea or constipation, respectively. Neither constipation nor diarrhea was associated with CMI in the fully adjusted model (P > 0.05). Additionally, the P for trend among CMI quartiles exceeded 0.05 insignificance.

The smooth curve fitting test shows a nonlinear association between the CMI and BMF (P=0.0001). According to the fitted curve, CMI and BMF are often associated positively. Nonetheless, a declining trend is evident in specific regions, suggesting potential threshold effects. The outcomes of the smooth curve fitting are presented in Fig. 2.

Additionally, a threshold effect analysis identified two critical inflection points at 4.97 and 11.75, with both likelihood ratio test *P*-values below 0.05. When CMI is below 4.97, there is a positive association with BMF (β = 0.30, 95% CI: 0.17, 0.43). When CMI is between 4.97 and 11.75, a negative association with BMF is seen (β = -0.78, 95% CI: -1.33, -0.23). When CMI exceeds 11.75, a direct association is observed again (β =0.36, 95% CI: 0.03,



Fig. 2 Nonlinear association between CMI and BMF derived from smooth curve fitting

Note: Smooth curve fitting demonstrates the relationship between CMI and BMF. In the resulting graph, the y-axis represents BMF, and the x-axis represents CMI. The solid red line is the smoothing curve that models the link between CMI and BMF. The blue dotted lines represent the 95% confidence interval obtained from the fit; Model adjusted for age, sex, race, education level, poverty income ratio, smoking, drinking, moderate activity, body mass index, diabetes, gastrointestinal diseases, hypertension, depression, sleep disorders, and dietary factors such as energy, total fat, moisture, dietary fiber, protein, carbohydrate, and caffeine; CM: Cardiometabolic index; BMF: Bowel movement frequency

0.69). The comprehensive findings of the threshold effect analysis are shown in Table 3.

Subgroup analyses

The impact of stratified population heterogeneity was assessed by subgroup analyses and interaction tests. Significant interaction effects emerged in age and depression subgroups (P < 0.05). Each one-unit rise in CMI was associated in the age subgroup with a 0.31 increase in BMF in youth (β = 0.31, 95% CI: 0.17, 0.45) and a 0.11 increase in middle-aged ($\beta = 0.11$, 95% CI: 0.00, 0.22). Conversely, insignificant association was seen in the elderly participants (β = 0.09, 95% CI: -0.10, 0.28). Within the depression subgroup, a one-unit growth in CMI was associated with a 0.44 rise in BMF among participants with depression ($\beta = 0.44$, 95% CI: 0.16, 0.72), which was substantially higher than the 0.15 increase observed in non-depressed individuals ($\beta = 0.15$, 95% CI: 0.06, 0.23). Furthermore, our research revealed an absence of interaction related to another subgroup between CMI and BMF (*P* for interaction > 0.05). Figure 3 visually depicts differences across different subgroup strata through forest plot representations.

Discussion

By investigating the intricate association between CMI and BMF, this study advances understanding of the connections between MetS and gut health. The results show that, as the CMI quartile increases, BMF exhibits a consistent upward trend. Further threshold analysis and smoothing curve fitting revealed a nonlinear link between CMI and BMF. A negative association was observed when the CMI values ranged from 4.97 to 11.75, while a positive association was found in other ranges. Subgroup analyses and interaction tests indicated that age and depression significantly influenced this relationship. Furthermore, our analysis indicated that CMI was not significantly associated with either constipation or diarrhea.

Maintaining a proper BMF is essential for preserving a high quality of life. However, the mechanism of interaction between CMI and BMF remains unclear. Previous studies have shown that there is a connection between bowel habits and a number of indications of obesity. For example, a study conducted on the American population identified a notable association between chronic diarrhea and increased levels of the Visceral Adiposity Index (VAI) [34]. In a similar vein, Yang et al. [35] reported a strong positive association between an increased weightadjusted waist circumference index (WWI) and chronic diarrhea. These findings provide factual support for our claim that elevated CMI quartile association with heightened BMF. Firstly, the baseline data indicate that individuals with higher CMI values tend to have greater dietary intake, which may contribute to increased BMF. Secondly, compared with normal individuals, obese individuals, particularly those with abdominal obesity or insulin resistance, tend to have elevated plasma bile acid levels [36]. Excess bile acids can stimulate intestinal peristalsis, leading to increased BMF [37]. Moreover, decreased HDL-C and elevated TG values are linked to increased inflammation and oxidative stress [38-40]. These factors can damage intestinal epithelial cells, increase intestinal permeability, and impair barrier function, ultimately contributing to increased BMF [41]. Additionally, individuals with a higher BMF typically consume more carbohydrates and fats. This dietary pattern is closely linked to a heightened incidence of hypertension and diabetes. In turn, these conditions significantly elevate the risk of MetS, ultimately resulting in an increase in the CMI [42].

The association between MetS and BMF remains a subject of debate. Certain research has indicated that there is no substantial connection between obesity and BMF [43]. However, other research indicates that obese individuals tend to have longer colonic transit times, which may reduce BMF [44]. These findings contradict our results. Both of the previous studies used BMI to assess obesity. Compared to BMI, CMI more accurately reflects fat distribution, particularly abdominal and visceral fat accumulation, and offers advantages in predicting MetS [6]. Xiang et al. [45] found that BMI is not linearly correlated with BMF, and eliminating central adiposity lowers the likelihood of constipation.

Table 3 Threshold effect analysis between CMI and BMF

	Fully adjusted model	Log likelihood ratio	
	β (95% CI)		
Fitting by the two-piecewise linear model			
Inflection point I	4.97	0.012	
CMI < 4.97	0.30 (0.17, 0.43)		
Inflection point II	11.75	0.002	
CMI between 4.97 and 11.75	-0.78 (-1.33,-0.23)		
CMI>11.75	0.36 (0.03, 0.69)		

Note: Fully adjusted model: Adjustments were made for age, sex, race, education level, poverty income ratio, smoking, drinking, moderate activity, body mass index, diabetes, gastrointestinal diseases, hypertension, depression, sleep disorders, and dietary factors such as energy, total fat, moisture, dietary fiber, protein, carbohydrate, and caffeine; CI: Confidence intervals; CMI: Cardiometabolic index; BMF: Bowel movement frequency

Subgroup	β (95% CI)	P for interaction
Gender		0.1583
Male	0.21 (0.11, 0.31)	
Female	0.09 (-0.04, 0.23)	
Age		0.0456
Young	0.31 (0.17, 0.45)	
Middle	0.11 (0.00, 0.22)	
Elderly	0.09 (-0.10, 0.28)	
Race		0.3659
Mexican American	0.01 (-0.24, 0.25)	
Non–Hispanic White	0.19 (0.10, 0.29)	
Non–Hispanic Black	0.34 (-0.03, 0.71)	
Other Race	0.10 (-0.11, 0.32)	
Education Level		0.8290
Less Than High School	0.18 (0.04, 0.31)	
High School Graduate	0.21 (0.04, 0.38)	
More Than High School	0.15 (0.03, 0.26)	
PIR		0.4406
Low income	0.26 (0.08, 0.44)	
Middle income	0.16 (0.06, 0.26)	
High income	0.10 (-0.07, 0.28)	
Gastrointestinal diseases		0.2536
Yes	0.27 (0.08, 0.46)	
No	0.15 (0.06, 0.24)	
BMI		0.5378
Normal	0.39 (-0.01, 0.79)	
Overweight	0.17 (0.02, 0.32)	
Obesity	0.16 (0.06, 0.25)	
Sleep disorders		0.2504
Yes	0.26 (0.08, 0.44)	
No	0.15 (0.05, 0.24)	
Diabetes		0.3021
Yes	0.10 (-0.05, 0.25)	
No	0.20 (0.10, 0.29)	
Hypertension		0.8311
Yes	0.18 (0.06, 0.30)	
No	0.16 (0.06, 0.27)	
Depression		0.0436
Yes	0.44 (0.16, 0.72)	
No	0.15 (0.06, 0.23)	
Smoking		0.2093
Yes	0.12 (0.02, 0.23)	
No	0.22 (0.11, 0.34)	
Drinking		0.4482
Yes	0.18 (0.09, 0.27)	
No	0.10 (-0.08, 0.29)	
Moderate activity	(0.5090
Yes	0.19 (0.09, 0.30)	 1. Same and a second
	0.14 (0.02, 0.26)	

Fig. 3 (See legend on next page.)

(See figure on previous page.)

Fig. 3 Subgroup analyses for the association between CMI and BMF

Note: In the subgroup analyses, each subgroup was adjusted for age, sex, race, education level, poverty income ratio, smoking, drinking, moderate activity, body mass index, diabetes, gastrointestinal diseases, hypertension, depression, sleep disorders, and dietary factors such as energy, total fat, moisture, dietary fiber, protein, carbohydrate, and caffeine, except itself; CI: Confidence intervals; CMI: Cardiometabolic index; BMF: Bowel movement frequency; PIR: Poverty-income ratio

Additionally, this study's nonlinear association between CMI and BMF reasonably explains this discrepancy. When CMI is less than 4.97, metabolic disorders remain in their initial phases and may enhance intestinal motility via several pathways. Besides the mechanisms previously discussed, excess visceral fat may trigger cytokine release, including Tumor Necrosis Factor-α and Interleukin-6, which stimulate the enteric nervous system and increase intestinal permeability, thereby improving BMF [46, 47]. The negative association observed when CMI is in the range of 4.97 and 11.75 may be related to the following compensatory mechanisms. Under normal conditions, cortisol helps maintain the normal rhythm of gastrointestinal motility within a specific concentration range [48]. However, when fat mass and insulin resistance exceed a certain threshold, the inhibitory feedback signal of cortisol weakens, leading to an increase in cortisol levels [49]. Excessive cortisol suppresses the normal contraction of gastrointestinal smooth muscles, slowing motility and reducing BMF [50, 51]. Excessive visceral fat can elevate intra-abdominal pressure, impair intestinal motility, and decrease BMF [52]. Chronic metabolic disorders and a fatty diet can adversely affect intestinal neurons and extend intestinal transit time [53, 54]. When CMI > 11.75, additional pathogenic pathways may be activated. At this point, the increased frequency of defecation may lead to gut microbial dysbiosis, resulting in lower short-chain fatty acid production. This reduction, in turn, impairs PPARy-mediated lipid oxidation, raises the risk of MetS, and produces a vicious cycle, leading to the continual growth of both CMI and BMF [55, 56].

In addition, we found that there were important changes in the association between CMI and BMF among age and depression subgroups. Specifically, we observed that the association between CMI and BMF diminished with age across the different age subgroups. The possible reason for this is that the impact of age exceeds that of CMI and BMF. With advancing age, there is a corresponding prolongation of colon transit time, potentially linked to degenerative alterations within the enteric nervous system [57, 58]. Moreover, gut microbiota composition exhibits distinct variations in older individuals when contrasted with younger adults [59], and their dietary intake of most foods and nutrients often fails to meet recommended standards [60]. Moreover, the risk of MetS also rises as people age [61]. All these factors combined can have a significant impact on this association.

Furthermore, the subgroup analysis of depression revealed a more pronounced association between CMI and BMF in depressed patients. The possible reason for this is that studies have shown that depressed patients often exhibit reduced serotonin synthesis and abnormalities in their reuptake pathway [62]. Consequently, due to serotonin deficiency, the gut motility slows down, subsequently reducing BMF [63]. Typically, groups with higher CMI values tend to have greater fat intake, which can activate the serotonin pathway [64]. Additionally, depressed patients often have shorter activity periods [65], and certain antidepressant medications may cause abnormal blood lipids and reduced intestinal motility [66, 67]. All these factors interact with each other, thus resulting in a more pronounced association in the depression group.

Study strengths and limitations

The current study is the inaugural investigation into the relationship between CMI and BMF. By utilizing various methods to research the association between CMI and BMF, it has been found that there is a nonlinear association between the two, thereby enhancing our understanding of the relationship between them. Moreover, this study predominantly employs data derived from the NHANES database to ensure that the findings broadly apply to the general U.S. population. Additionally, all statistical analyses incorporated the appropriate NHANES sampling weights, and adjustments were implemented for possible confounding variables, augmenting the study findings' robustness and dependability.

However, considering the cross-sectional design of the NHANES, our analysis focuses on identifying associations between variables without inferring causality. Moreover, a significant portion of health-related conditions and lifestyle behaviors are derived from participant self-reports, which could lead to biased reports and make the data less accurate. Although various adjustments for possible confounding factors, there might still be other possible variables that could affect the research results. Furthermore, data collection is constrained by time limitations, and since health data can change rapidly, utilization of outdated data may not adequately capture contemporary health trends. At the same time, using CMI to represent MetS and BMF to represent gut health has certain limitations. Moreover, bowel movement types are also important to gut health; however, this

investigation did not identify any significant association between them and CMI. Therefore, further research is essential.

Conclusion

This study demonstrates that there is a nonlinear association between CMI and BMF. Generally, CMI is associated with an increase in BMF. However, within a specific range, where the CMI values fall between 4.97 and 11.75, there is an observed association between CMI and a decrease in BMF. Notably, the association of CMI with BMF is particularly significant among middle-aged and younger adult populations, as well as in individuals with depression. However, given the constraints of this study, additional prospective research is necessary to confirm these results.

Abbreviations

MetS	Metabolic Syndrome
BMF	Bowel movement frequency
CMI	Cardiometabolic index
NHANES	National Health and Nutrition Examination Survey
TG	Triglycerides
HDL-C	High-density lipoprotein cholesterol
WHtR	Waist-to-height ratio
BMI	Body mass index
WC	Waist circumference
Н	Height
PIR	Poverty-income ratio
WTMEC2YR	Full Sample 2 Year MEC Exam Weight
CI	Confidence intervals
OR	Odds ratio
VAI	Visceral Adiposity Index
WWI	Weight-adjusted waist circumference index

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12944-025-02567-w.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

QYR designed the research, collected the data, conducted the analysis, and wrote the manuscript. YNW performed the data analysis and conceived the manuscript. XWH was responsible for data collection and manuscript writing. QYW prepared the manuscript and generated the charts. GYL supervised the research design and overall process, including manuscript revision. The manuscript was reviewed and approved by all authors, who consented to its publication.

Funding

The study received funding from the Natural Science Foundation of Heilongjiang Province, China (Grant No. LH2022H072).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The National Center for Health Statistics Ethics Review Board approved this investigation. Informed consent was obtained from all subjects involved in the NHANES. As a secondary analysis of publicly available de-identified and anonymized data, the present study did not require additional ethical review.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 11 March 2025 / Accepted: 11 April 2025 Published online: 24 April 2025

References

- 1. Nilsson PM, Tuomilehto J, Ryden L. The metabolic syndrome What is it and how should it be managed? Eur J Prev Cardiol. 2019;26(2suppl):33–46.
- Busch C, Bergman J, Nieuwdorp M, van Baar A. Role of the intestine and its gut microbiota in metabolic syndrome and obesity. Am J Gastroenterol. 2024;119(6):1038–46.
- Saad MJ, Santos A, Prada PO. Linking gut microbiota and inflammation to obesity and insulin resistance. Physiology. 2016;31(4):283–93.
- Chen K, Guo J, Zhang T, Gu J, Li H, Wang J. The Role of Dyslipidemia in Colitis-Associated Colorectal Cancer. J Oncol 2021, 2021:6640384.
- Wakabayashi I, Daimon T. The cardiometabolic index as a new marker determined by adiposity and blood lipids for discrimination of diabetes mellitus. Clin Chim Acta. 2015;438:274–8.
- Lazzer S, D'Alleva M, Isola M, De Martino M, Caroli D, Bondesan A, Marra A, Sartorio A. Cardiometabolic index (CMI) and visceral adiposity index (VAI) highlight a higher risk of metabolic syndrome in women with severe obesity. J Clin Med 2023, 12(9).
- Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. Obes Rev. 2012;13(3):275–86.
- Kosmas CE, Rodriguez PS, Bousvarou MD, Papakonstantinou EJ, Pena GE, Guzman E, Kostara CE. The Triglyceride/High-Density lipoprotein cholesterol (TG/HDL-C) ratio as a risk marker for metabolic syndrome and cardiovascular disease. Diagnostics 2023, 13(5).
- 9. Wu L, Parhofer KG. Diabetic dyslipidemia. Metabolism. 2014;63(12):1469–79.
- 10. Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel Disorders. Gastroenterology 2016.
- Ahrens AP, Culpepper T, Saldivar B, Anton S, Stoll S, Handberg EM, Xu K, Pepine C, Triplett EW, Aggarwal M. A Six-Day, Lifestyle-Based Immersion Program Mitigates Cardiovascular Risk Factors and Induces Shifts in Gut Microbiota, Specifically Lachnospiraceae, Ruminococcaceae, Faecalibacterium prausnitzii: A Pilot Study. Nutrients 2021, 13(10).
- Sumida K, Yamagata K, Kovesdy CP. Constipation in CKD. Kidney Int Rep. 2020;5(2):121–34.
- Wald A, Bharucha AE, Limketkai B, Malcolm A, Remes-Troche JM, Whitehead WE, Zutshi M. ACG clinical guidelines: management of benign anorectal disorders. Am J Gastroenterol. 2021;116(10):1987–2008.
- Johnson-Martinez JP, Diener C, Levine AE, Wilmanski T, Suskind DL, Ralevski A, Hadlock J, Magis AT, Hood L, Rappaport N, et al. Aberrant bowel movement frequencies coincide with increased microbe-derived blood metabolites associated with reduced organ function. Cell Rep Med. 2024;5(7):101646.
- Heitmann PT, Vollebregt PF, Knowles CH, Lunniss PJ, Dinning PG, Scott SM. Understanding the physiology of human defaecation and disorders of continence and evacuation. Nat Rev Gastro Hepat. 2021;18(11):751–69.
- Panigrahi MK, Kar SK, Singh SP, Ghoshal UC. Defecation frequency and stool form in a coastal Eastern Indian population. J Neurogastroenterol. 2013;19(3):374–80.
- Servin-Vences MR, Lam RM, Koolen A, Wang Y, Saade DN, Loud M, Kacmaz H, Frausto S, Zhang Y, Beyder A, et al. PIEZO2 in somatosensory neurons controls Gastrointestinal transit. Cell. 2023;186(16):3386–99.
- Gill SK, Rossi M, Bajka B, Whelan K. Dietary fibre in Gastrointestinal health and disease. Nat Rev Gastro Hepat. 2021;18(2):101–16.

- Bianco A, Russo F, Prospero L, Riezzo G, Franco I, D'Attoma B, Ignazzi A, Verrelli N, Bagnato CB, Goscilo F et al. Beyond Nutritional Treatment: Effects of Fitwalking on Physical Capacity and Intestinal Barrier Integrity in BMI-Stratified IBS Patients. Nutrients: 2024, 16(23).
- Han L, Zhao L, Zhou Y, Yang C, Xiong T, Lu L, Deng Y, Luo W, Chen Y, Qiu Q, et al. Altered metabolome and Microbiome features provide clues in Understanding irritable bowel syndrome and depression comorbidity. ISME J. 2022;16(4):983–96.
- Camilleri M, Malhi H, Acosta A. Gastrointest Complications Obes Gastroenterol. 2017;152(7):1656–70.
- Sommers T, Mitsuhashi S, Singh P, Hirsch W, Katon J, Ballou S, Rangan V, Cheng V, Friedlander D, Iturrino J, et al. Prevalence of chronic constipation and chronic diarrhea in diabetic individuals in the united States. Am J Gastroenterol. 2019;114(1):135–42.
- 24. Abdul WP, Mohd YD, Abdul KA, Ali SH, Yeong YL. Prevalence, symptoms, and associated factors of chronic constipation among older adults in North-East of Peninsular Malaysia. Clin Nurs Res. 2022;31(2):348–55.
- Duan R, Zheng Y, Kong W, Wang Y, Zhou Y. Association of environmental tobacco smoke exposure with chronic constipation: a nationwide survey (NHANES 2005–2010). Environ Sci Pollut R. 2023;30(54):115776–87.
- Aberg F, Byrne CD, Pirola CJ, Mannisto V, Sookoian S. Alcohol consumption and metabolic syndrome: clinical and epidemiological impact on liver disease. J Hepatol. 2023;78(1):191–206.
- Liu Y, Wang Y, Ni Y, Cheung C, Lam K, Wang Y, Xia Z, Ye D, Guo J, Tse MA, et al. Gut Microbiome fermentation determines the efficacy of exercise for diabetes prevention. Cell Metab. 2020;31(1):77–91.
- Zhang X, Wang Y, Li Y, Gui J, Mei Y, Yang X, Liu H, Guo LL, Li J, Lei Y, et al. Fouryears change of BMI and waist circumference are associated with metabolic syndrome in middle-aged and elderly Chinese. Sci Rep-UK. 2024;14(1):10220.
- Li Y, Zeng L. Comparison of seven anthropometric indexes to predict hypertension plus hyperuricemia among U.S. Adults. Front Endocrinol. 2024;15:1301543.
- Ballou S, Katon J, Singh P, Rangan V, Lee HN, McMahon C, Iturrino J, Lembo A, Nee J. Chronic diarrhea and constipation are more common in depressed individuals. Clin Gastroenterol H. 2019;17(13):2696–703.
- Patel A, Hasak S, Cassell B, Ciorba MA, Vivio EE, Kumar M, Gyawali CP, Sayuk GS. Effects of disturbed sleep on Gastrointestinal and somatic pain symptoms in irritable bowel syndrome. Aliment Pharm Ther. 2016;44(3):246–58.
- 32. Kang Y, Yan J. Exploring the connection between caffeine intake and constipation: a cross-sectional study using National health and nutrition examination survey data. BMC Public Health. 2024;24(1):3.
- Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the patient health questionnaire (PHQ-9): a meta-analysis. Can Med Assoc J. 2012;184(3):E191–6.
- 34. Yang X, Wang M, Ren L, Shon K, Cui G, Cheng Y, Sun Z, Wang X. Association between visceral adiposity index and bowel habits and inflammatory bowel disease: a cross-sectional study. Sci Rep-UK. 2024;14(1):23923.
- 35. Yang X, Sun Z. Association between weight-adjusted-waist index and bowel habits. Sci Rep-UK. 2024;14(1):17658.
- Bishay RH, Tonks KT, George J, Samocha-Bonet D, Meyerowitz-Katz G, Chisholm DJ, James DE, Greenfield JR. Plasma bile acids more closely align with insulin resistance, visceral and hepatic adiposity than total adiposity. J Clin Endocr Metab. 2021;106(3):e1131–9.
- Di Vincenzo F, Puca P, Lopetuso LR, Petito V, Masi L, Bartocci B, Murgiano M, De Felice M, Petronio L, Gasbarrini A et al. Bile Acid-Related Regulation of Mucosal Inflammation and Intestinal Motility: From Pathogenesis to Therapeutic Application in IBD and Microscopic Colitis. Nutrients: 2022, 14(13).
- Mascarenhas-Melo F, Sereno J, Teixeira-Lemos E, Marado D, Palavra F, Pinto R, Rocha-Pereira P, Teixeira F, Reis F. Implication of low HDL-c levels in patients with average LDL-c levels: a focus on oxidized LDL, large HDL subpopulation, and adiponectin. Mediat Inflamm 2013, 2013:612038.
- Kochumon S, Hasan A, Al-Rashed F, Sindhu S, Thomas R, Jacob T, Al-Sayyar A, Arefanian H, Al MA, Al-Ozairi E et al. Increased Adipose Tissue Expression of IL-23 Associates with Inflammatory Markers in People with High LDL Cholesterol. Cells-Basel: 2022, 11(19).
- Collado A, Domingo E, Marques P, Perello E, Martinez-Hervas S, Piqueras L, Ascaso JF, Real JT, Sanz MJ. Oral unsaturated fat load impairs postprandial

systemic inflammation in primary hypercholesterolemia patients. Front Pharmacol. 2021;12:656244.

- 41. Hasegawa T, Mizugaki A, Inoue Y, Kato H, Murakami H. Cystine reduces tight junction permeability and intestinal inflammation induced by oxidative stress in Caco-2 cells. Amino Acids. 2021;53(7):1021–32.
- 42. Kwon YJ, Lee HS, Lee JW. Association of carbohydrate and fat intake with metabolic syndrome. Clin Nutr. 2018;37(2):746–51.
- Koppen IJ, Velasco-Benitez CA, Benninga MA, Di Lorenzo C, Saps M. Is there an association between functional constipation and excessive bodyweight in children?? J Pediatr-US. 2016;171:178–82.
- Bouchoucha M, Fysekidis M, Rompteaux P, Airinei G, Sabate JM, Benamouzig R. Influence of age and body mass index on total and segmental colonic transit times in constipated subjects. J Neurogastroenterol. 2019;25(2):258–66.
- Xiang N, Xu L, Qian H, Zhang D. Multiple obesity indices suggest a close relationship between obesity and constipation: evidence from NHANES. BMC Public Health. 2024;24(1):1273.
- 46. Castro-Barquero S, Casas R, Rimm EB, Tresserra-Rimbau A, Romaguera D, Martinez JA, Salas-Salvado J, Martinez-Gonzalez MA, Vidal J, Ruiz-Canela M, et al. Loss of visceral fat is associated with a reduction in inflammatory status in patients with metabolic syndrome. Volume 67. Mol Nutr Food Res; 2023. p. e2200264. 4.
- Xiao YT, Yan WH, Cao Y, Yan JK, Cai W. Neutralization of IL-6 and TNF-alpha ameliorates intestinal permeability in DSS-induced colitis. Cytokine. 2016;83:189–92.
- Lightman SL, Birnie MT, Conway-Campbell BL. Dynamics of ACTH and cortisol secretion and implications for disease. Endocr Rev 2020, 41(3).
- Aschbacher K, Rodriguez-Fernandez M, van Wietmarschen H, Tomiyama AJ, Jain S, Epel E, van der Doyle FR. The hypothalamic-pituitary-adrenal-leptin axis and metabolic health: a systems approach to resilience, robustness and control. Interface Focus. 2014;4(5):20140020.
- 50. Suzuki Y, Shimizu Y, Shiina T. ATP-Induced contractile response of esophageal smooth muscle in mice. Int J Mol Sci 2024, 25(4).
- Wong H, Qin HY, Tsang SW, Zuo X, Che S, Chow C, Li X, Xiao HT, Zhao L, Huang T, et al. Early life stress disrupts intestinal homeostasis via NGF-TrkA signaling. Nat Commun. 2019;10(1):1745.
- Lee CG, Lee JK, Kang YS, Shin S, Kim JH, Lim YJ, Koh MS, Lee JH, Kang HW. Visceral abdominal obesity is associated with an increased risk of irritable bowel syndrome. Am J Gastroenterol. 2015;110(2):310–9.
- 53. Farmer AD, Pedersen AG, Brock B, Jakobsen PE, Karmisholt J, Mohammed SD, Scott SM, Drewes AM, Brock C. Type 1 diabetic patients with peripheral neuropathy have pan-enteric prolongation of Gastrointestinal transit times and an altered caecal pH profile. Diabetologia. 2017;60(4):709–18.
- Nezami BG, Mwangi SM, Lee JE, Jeppsson S, Anitha M, Yarandi SS, Farris AR, Srinivasan S. MicroRNA 375 mediates palmitate-induced enteric neuronal damage and high-fat diet-induced delayed intestinal transit in mice. Gastroenterology. 2014;146(2):473–83.
- Parada VD, De la Fuente MK, Landskron G, Gonzalez MJ, Quera R, Dijkstra G, Harmsen H, Faber KN, Hermoso MA. Short chain fatty acids (SCFAs)-Mediated gut epithelial and immune regulation and its relevance for inflammatory bowel diseases. Front Immunol. 2019;10:277.
- den Besten G, Bleeker A, Gerding A, van Eunen K, Havinga R, van Dijk TH, Oosterveer MH, Jonker JW, Groen AK, Reijngoud DJ, et al. Short-Chain fatty acids protect against High-Fat Diet-Induced obesity via a PPARgamma-Dependent switch from lipogenesis to fat oxidation. Diabetes. 2015;64(7):2398–408.
- West CL, Amin JY, Farhin S, Stanisz AM, Mao YK, Kunze WA. Colonic motility and jejunal vagal afferent firing rates are decreased in aged adult male mice and can be restored by an aminosterol. Front Neurosci-Switz. 2019;13:955.
- 58. Britton E, McLaughlin JT. Ageing and the gut. P NUTR SOC. 2013;72(1):173–7.
- Lee SY, Lee DY, Kang HJ, Kang JH, Cho MG, Jang HW, Kim BK, Hur SJ. Differences in the gut microbiota between young and elderly persons in Korea. Nutr Res. 2021;87:31–40.
- Choi YJ, Crimmins EM, Kim JK, Ailshire JA. Food and nutrient intake and diet quality among older Americans. Public Health Nutr. 2021;24(7):1638–47.
- Kuk JL, Ardern CI. Age and sex differences in the clustering of metabolic syndrome factors: association with mortality risk. Diabetes Care. 2010;33(11):2457–61.
- 62. Yohn CN, Gergues MM, Samuels BA. The role of 5-HT receptors in depression. Mol Brain. 2017;10(1):28.
- 63. Israelyan N, Del CA, Li Z, Park Y, Xing A, Jacobsen J, Luna RA, Jensen DD, Madra M, Saurman V, et al. Effects of serotonin and Slow-Release

5-Hydroxytryptophan on Gastrointestinal motility in a mouse model of depression. Gastroenterology. 2019;157(2):507–21.

- 64. Hu S, Wang L, Yang D, Li L, Togo J, Wu Y, Liu Q, Li B, Li M, Wang G, et al. Dietary fat, but not protein or carbohydrate, regulates energy intake and causes adiposity in mice. Cell Metab. 2018;28(3):415–31.
- Burton C, McKinstry B, Szentagotai TA, Serrano-Blanco A, Pagliari C, Wolters M. Activity monitoring in patients with depression: a systematic review. J Affect Disorders. 2013;145(1):21–8.
- Uher R, Farmer A, Henigsberg N, Rietschel M, Mors O, Maier W, Kozel D, Hauser J, Souery D, Placentino A, et al. Adverse reactions to antidepressants. Brit J Psychiat. 2009;195(3):202–10.
- 67. Pan SJ, Tan YL, Yao SW, Xin Y, Yang X, Liu J, Xiong J. Fluoxetine induces lipid metabolism abnormalities by acting on the liver in patients and mice with depression. Acta Pharmacol Sin. 2018;39(9):1463–72.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.