Nutrition Journal

RESEARCH

Open Access

Dietary index for gut microbiota and risk of gastrointestinal cancer: a prospective gene-diet study

Dong-Run Li[1,2†], Bang-Quan Liu[1,2†], Ming-Hui Li[1,2,3], Ying Qin[1,2,3], Jia-Cheng Liu[4], Wen-Rui Zheng[1,2], Ting-Ting Gong[4*], Shan-Yan Gao[1,2,6*] and Qi-Jun Wu[1,2,3,4,5*]

Abstract

Background The dietary index for gut microbiota (DI-GM) is a newly proposed index that evaluates dietary intake patterns associated with gut microbial health. Limited studies have examined whether DI-GM influences gastrointestinal (GI) cancer risk. We aimed to investigate the association between DI-GM and GI cancer risk and evaluate its combined effect with genetic risk.

Methods We included 178,148 UK Biobank participants who completed at least one 24-hour dietary recall. DI-GM was constructed from 13 dietary components known to influence gut microbial health and was divided into three groups. The GI cancer polygenic risk score was calculated from 205 significant single-nucleotide polymorphisms related to esophageal cancer (EC), gastric cancer (GC), and colorectal cancer (CRC). Cox proportional hazards models with hazard ratios (HRs) and 95% confidence intervals (CIs) were used to estimate the associations between DI-GM, genetic risk, and GI cancer.

Results During a median follow-up of 13.47 years, 2,682 participants developed GI cancer. In fully adjusted models, higher DI-GM was associated with a lower GI cancer risk (HR for GI cancer: 0.83; 95% CI: 0.75–0.92; HR for EC: 0.62, 95% CI: 0.45–0.86; HR for GC: 0.99, 95% CI: 0.71–1.39; HR for CRC: 0.84, 95% CI: 0.75–0.95), compared with participants in the lowest DI-GM category. In joint analysis, individuals with higher DI-GM and lower genetic risk had lower GI cancer risk, with HRs (95% CI) of 0.28 (0.21, 0.36), 0.50 (0.42, 0.58) for low and intermediate genetic risk, respectively, compared with those with low DI-GM and high genetic risk. And a significant interaction between DI-GM and genetic risk was observed.

Conclusion Higher DI-GM was associated with a lower risk of GI cancer including EC and CRC. These findings highlight the importance of considering a gut microbiota-friendly diet and genetic risk in GI cancer prevention.

†Dong-Run Li and Bang-Quan Liu contributed equally to this work.

*Correspondence:
Ting-Ting Gong
gongtt@sj-hospital.org
Shan-Yan Gao
gaosy@sj-hospital.org
Qi-Jun Wu
wuqj@sj-hospital.org

Full list of author information is available at the end of the article

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, 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 changes were made. 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://creativecommons.org/licenses/by/4.0/.

Keywords Dietary index for gut microbiota, Genetic risk, Gastrointestinal cancer

Introduction

Gastrointestinal (GI) cancer, including colorectal cancer (CRC), gastric cancer (GC), and esophageal cancer (EC), is among the most frequently diagnosed malignancies worldwide, with high incidence and mortality rates [1]. According to the Global Burden of Disease Study, GI cancers account for 26% of the global cancer incidence and 35% of all cancer-related deaths [2]. Established risk factors include age, sex, genetic predisposition, smoking, alcohol consumption, and unhealthy dietary habits [3].

In recent years, the gut microbiota has received growing attention in cancer research. It is critical in immune regulation, nutrient metabolism and inflammatory control. Emerging evidence also connects it to a range of chronic diseases, such as obesity, diabetes, cardiovascular disease, neurological disorders, and cancer [4, 5]. In particular, an imbalanced gut microbiota has been associated with tumor initiation, progression and prognosis in GI cancers [6–8]. Diet is a major determinant of the gut microbiota composition, and it is estimated that 21.5% of GI cancer cases worldwide can be attributed to suboptimal dietary practices [9]. Numerous studies have shown that certain dietary patterns (e.g., Healthy Eating diet, Mediterranean diet, Western diet, and high-fat diet) can alter the diversity and functionality of gut microbiota, thereby influencing GI cancer risk [10–12]. The dietary index for gut microbiota (DI-GM), developed by Kase et al., is a novel integrative index that captures dietary patterns conducive to a healthy gut microbiota. It has been validated by markers of gut microbiota health [13]. The development of DI-GM provides a new quantitative approach to investigate the relationships between diet, gut microbiota, and diseases. However, its role in GI cancer remains relatively underexplored.

Gene-lifestyle interaction theory suggests that the impact of modifiable lifestyle factors on disease risk may differ depending on an individual's genetic predisposition [14]. Advances in genome-wide association studies have identified genetic variants associated with GI cancer [15–17], laying a foundation for cancer polygenic risk scores (CPRS) that reflect the cumulative influence of multiple risk alleles [18, 19]. Previous studies have shown that dietary patterns and genetic risk can jointly affect both the occurrence and progression of GI cancers [20, 21].

In this study, based on the UK Biobank database, we aimed to investigate the associations of DI-GM with GI cancer risk and further assess the joint effects of DI-GM and genetic risk on the risk of GI cancer.

Method

Study design and population

Data were derived from the UK Biobank, a large-scale cohort study that recruited over 500,000 adults from the United Kingdom during 2006–2010 [22]. We included 201,131 participants who completed 24-hour food recall questionnaires. We excluded participants who had been diagnosed with cancer at baseline ($n = 17{,}502$), had implausible total energy intake (< 800 or > 5000 kcal/day for males and < 500 or > 4000 kcal/day for females; $n = 1{,}795$) [23], withdrew from the study ($n = 65$), or had incomplete genetic data for constructing CPRS at baseline ($n = 3{,}621$). The final analytic sample comprised 178,148 participants (Supplementary Fig. 1). This study was conducted under UK Biobank application number 211,772.

Definition of dietary index for gut microbiota

The UK Biobank employed a validated online tool for 24-hour dietary assessments (Oxford WebQ) to collect comprehensive data on the quantity and types of food consumed [24]. It has been confirmed for accuracy through comparison with an interviewer-administered 24-hour dietary recall and biomarkers [25, 26]. To estimate nutrient intake, the Oxford WebQ automatically computes total nutrient consumption by multiplying the number of portions consumed by each food's predetermined portion size and its corresponding nutrient composition. The nutrient composition data used for these calculations were derived from the UK Nutrient Databank food composition Table (24). Initial dietary assessment took place at the assessment centers between April 2009 and September 2010, followed by four additional online questionnaires after recruitment ended. If participants completed dietary assessments multiple times, we used the means of all available measurements to calculate dietary intake.

Based on the scoring criteria of the article by Kase et al. [13], 14 food items or nutrients were identified as components of DI-GM, including avocado, broccoli, chickpeas, coffee, cranberries, fermented dairy, fiber, green tea, soybean, and whole grains as beneficial components, while high-fat diet (≥ 40% energy from fat), red meat, processed meat, and refined grains were considered adverse components. For beneficial to gut microbiota items, a score of 1 was assigned when consumption ≥ sex-specific median, otherwise 0 score; for unfavorable to gut microbiota items, a score of 0 was assigned when consumption ≥ sex specific median, otherwise 1 score. Scores were summed to obtain the overall DI-GM, ranging from 0 to 13 (chickpeas unavailable due to the UK Biobank not

recording the consumption). The higher the index, the greater adherence to the beneficial gut microbiota diet. The details of scoring criteria, coding information and portion size for each component used in this study can be seen in Supplementary Tables 1–3.

Cancer polygenic risk score for GI cancer

The genetic data from the UK Biobank have undergone extensive quality control and imputation as described previously [27]. Briefly, genotyping was performed using the UK BiLEVE array and the UK Biobank Axiom array, followed by QC measures including variant and sample-level filtering, population structure adjustment, and imputation using the Haplotype Reference Consortium panel. To evaluate the genetic predisposition of EC, GC, and CRC, we constructed a PRS based on 205 single-nucleotide polymorphisms (SNPs) that reached the genome-wide significance threshold ($P < 5 \times 10^{-8}$) in populations of European ancestry [28–30]. Detailed information on the SNPs is provided in Supplementary Table 4. The calculation of PRS was performed by using the PRSice-2 algorithm with the following formula:

$$PRS_i = \sum_{k=1}^{k} \beta_k SNP_{i,k}$$

Where β_k value is the summary statistic for the effective allele and $SNP_{i,k}$ is the number of the effective allele observed.

Then the CPRS was built to serve as an indicator of genetic risk for overall GI cancer, following this process:

$$CPRS_i = \sum_{k=1}^{k} h_k PRS_{i,k}$$

The cancer polygenic risk score for the i^{th} individual is denoted as $PRS_{i,k}$, where h_k represents the age-standardized incidence of cancer type k in the UK population.

Based on their CPRS, participants were categorized into three genetic risk groups: low risk (lowest quintile), moderate risk (quintiles 2 to 4), and high risk (highest quintile). The details of construction of CPRS for GI cancer are provided in Supplementary Method.

Outcome assessment

The primary outcome of interest was incident GI cancer, identified from the UK Biobank-linked national cancer registries as a first-ever diagnosis coded according to the International Classification of Diseases, 10th Revision, as esophagus (C15), stomach (C16), colorectum (C18-20). Follow-up commenced at the date of baseline assessment and ended at the earliest occurrence of any of the following events: the first recorded GI cancer diagnosis, death from any cause, or the end of follow-up on May 31, 2022. Detailed codes are provided in Supplementary Table 3.

Covariates

Covariates were obtained from baseline data, and potential confounders were selected based on prior literature and biologically plausible associations [20, 21]. The following covariates were included: age at recruitment (continuous), sex, annual household income (categorized as <£31,000, ≥£31,000, or unknown/missing), education level (high qualifications, middle qualifications, no qualifications, or unknown/missing), and the Townsend deprivation index (continuous), a widely used measure of socioeconomic deprivation derived from participants' residential postcodes, with lower values indicating higher socioeconomic status. Anthropometric measures, including height and weight, were collected by trained staff at baseline, and body mass index (BMI) was calculated as weight (kg)/ [height (m)] ^{2} (continuous). Family history of cancer (yes, no, or unknown) was self-reported at baseline. Lifestyle and behavioral factors included total energy intake (continuous), smoking status (never, previous, current, or unknown/missing), alcohol consumption (never, previous, current, or unknown/missing), and physical activity (high, moderate, low). Missing data for continuous covariates were imputed using mean values, while missing categorical covariates were assigned to an unknown/missing indicator category. Detailed coding information is shown in Supplementary Table 3.

Statistical analysis

Based on our population characteristics and previous references [31], DI-GM were classified into three groups: low (0–4), moderate [5, 6], and high (≥7). Baseline characteristics were described as mean with standard deviation (SD) or median with interquartile range (IQR) for continuous variables, and as counts with percentages for categorical variables, stratified by DI-GM groups. To assess differences, the Student's t-test or Kruskal-Wallis test was applied for continuous variables, and chi-square tests for categorical variables.

The proportional hazards assumption was tested using the Schoenfeld residual test, with no violations observed ($P > 0.05$). Multivariable Cox proportional hazards regression models were conducted to assess associations between DI-GM, CPRS, and the risks of GI cancer, with results expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). The models were adjusted for age, sex, BMI, total energy intake, income, education level, the Townsend deprivation index, smoking status, alcohol consumption, physical activity, and family history of cancer. The DI-GM and CPRS were analyzed by both

categorical variable (low group as reference) and continuous variable (per 1-SD). Additionally, we examined the potential nonlinear relation between DI-GM, CPRS and GI cancer risk with restricted cubic splines, and the model was conducted with 4 knots at the 5th, 35th, 65th, and 95th percentiles.

To evaluate the combined effects of DI-GM and genetic factors on GI cancer risk, participants were categorized into nine groups based on DI-GM and CPRS categories. We assessed both additive and multiplicative interaction models, as they provide complementary information about the joint effects of risk factors. Additive interaction measures whether the combined effect of two risk factors is greater than the sum of their individual effects (important for public health implications and prevention strategies), while multiplicative interaction assesses whether the combined effect exceeds the product of individual effects (important for understanding biological mechanisms). Using participants with low DI-GM and high genetic risk as the reference group, additive interaction was evaluated by calculating the Relative Excess Risk due to Interaction (RERI) and Attributable Proportion (AP) using the delta method to determine significance. Multiplicative interaction was measured using likelihood ratio tests.

In subgroup analyses, the models were reanalyzed stratified by age, sex, BMI, education level, the Townsend deprivation index, smoking status, alcohol consumption, physical activity, and family cancer history. We conducted a series of sensitivity analyses to assess the robustness of our primary findings: (1) reconstructing the DI-GM by substituting broader pulses intake for the chickpea component; (2) excluding cranberries due to UK Biobank not recording the specific type of dried fruit consumption [32]; (3) excluding participants diagnosed with GI cancer within the first two years of follow-up to minimize the risk of reverse causality; (4) excluding individuals who completed the 24-hour online dietary recall questionnaire only once, to ensure that the average intake of all dietary components accurately reflected habitual intake; and (5) excluding individuals with unknown or missing covariates. All statistical analyses were performed using R software version 4.3.1, with a two-tailed *P*-value of < 0.05 considered statistically significant.

Result

Baseline characteristics of participants

Among the 178,148 participants enrolled in the study, 2,682 individuals (1.51%) were diagnosed with GI cancer during a median follow-up period of 13.47 years (IQR: 12.87–14.27 years). Baseline characteristics classified according to the DI-GM are shown in Table 1 and Supplementary Table 5. Individuals ranked in the highest group of DI-GM tended to be older, female, exhibit lower BMI, possess higher education levels, have a lower Townsend deprivation index, never smoke, have no alcohol consumption and have higher physical activity. Furthermore, they reported higher consumption of avocado, broccoli, coffee, cranberries, fermented dairy, fiber, green tea, soybean, and whole grains.

Association of DI-GM with the risk of GI cancer

The DI-GM was significantly associated with a decreased risk of GI cancer in all models. In model 2, after adjustment for potential confounders, each additional SD of DI-GM was linked to a 5% decrease in GI cancer risk (HR: 0.95, 95% CI: 0.93–0.97; Supplementary Table 6). Participants with the highest DI-GM category had a 17% lower risk of GI cancer compared with those in the lowest DI-GM group (HR: 0.83, 95% CI: 0.75–0.92; *P* for trend < 0.001; Fig. 1). Additionally, restricted cubic spline analysis showed that the DI-GM associated, in a linear dose–response manner, with GI cancer risk (*P* for non-linearity > 0.05; Fig. 2). Further analysis of site-specific GI cancer revealed that each SD increase of DI-GM was associated with a 16% decreased risk of EC (95% CI: 0.75–0.94) and an 8% decreased risk of CRC (95% CI: 0.88–0.96). Compared with the lowest DI-GM group, the highest category was linked with a reduced risk of EC (HR: 0.62, 95% CI: 0.45–0.86), and CRC (HR: 0.84, 95% CI: 0.75–0.95), with all *P* for trend < 0.05. Linear association and dose–response manner were also observed (all *P* for non-linearity > 0.05; Fig. 2). For GC, association was significant in the middle DI-GM category (HR: 0.67, 95% CI: 0.49–0.91), but not in the highest group (HR: 0.99, 95% CI: 0.71–1.39; Supplementary Table 7). Analysis of individual food items showed that fermented dairy, fiber, whole grains, and meat had significant associations with GI cancer (all $P < 0.05$; Supplementary Table 8).

In subgroup analysis, we observed significant associations between DI-GM and GI cancer risk in participants who were older, male, overweight, non-smokers, drinkers, had high education level and low Townsend deprivation index, and maintained physical activity. Additionally, significant interactions were observed between DI-GM and age, sex, the Townsend deprivation index, and smoking status on GI cancer risk (*P* for interaction < 0.05; Supplementary Table 9). The significant associations between DI-GM and GI cancer risk remained robust after recalculating the DI-GM, excluding participants diagnosed with GI cancer during the first two years of follow-up, as well as those who completed the online 24-hour dietary recall questionnaire only once and had unknown or missing covariates (Supplementary Tables 10–14).

Association of genetic risk with the risk of GI cancer

In the fully adjusted model, a per SD increase in genetic risk was associated with a 48% higher risk of developing

Table 1 Baseline characteristics of 178,148 UK biobank participants across levels of DI-GM

Characteristics	DI-GM			Total (*N* = 178,148)
	Low (*N* = 67,109)	Moderate (*N* = 68,711)	High (*N* = 42,328)	
Age, year	55.03 ± 8.00	56.24 ± 7.86	57.03 ± 7.68	55.97 ± 7.91
BMI, kg/m^2	27.59 ± 4.82	26.90 ± 4.51	25.93 ± 4.23	26.93 ± 4.61
Total energy intake, kJ/d	8,608.17 ± 2,406.20	8,636.34 ± 2,458.56	8,759.94 ± 2,212.25	8,655.09 ± 2,383.01
Townsend deprivation index	-1.58 ± 2.86	-1.75 ± 2.78	-1.73 ± 2.78	-1.68 ± 2.81
Sex				
Female	33,896 (50.51)	37,341 (54.35)	24,995 (59.05)	96,232 (54.02)
male	33,213 (49.49)	31,370 (45.65)	17,333 (40.95)	81,916 (45.98)
Annual household Income, Pound				
< 31,000	23,297 (34.72)	24,003 (34.93)	15,173 (35.85)	62,473 (35.01)
≥ 31,000	37,160 (55.37)	37,808 (55.02)	23,063 (54.49)	98,031 (55.03)
Unknown/missing	6,652 (9.91)	6,900 (10.05)	4,092 (9.66)	17,644 (9.96)
Education level				
No above	6,538 (9.74)	5,857 (8.52)	2,687 (6.35)	15,082 (8.47)
Medium	35,609 (53.06)	33,044 (48.09)	18,211 (43.02)	86,864 (48.76)
High	24,665 (36.75)	29,556 (43.01)	21,296 (50.31)	75,517 (42.39)
Unknown/missing	297 (0.45)	254 (0.47)	134 (0.32)	685 (0.38)
Smoking status				
Never	36,740 (54.75)	38,850 (56.54)	24,762 (58.50)	100,352 (56.33)
Previous	23,390 (34.85)	24,848 (36.16)	15,335 (36.23)	63,573 (35.65)
Current	6,837 (10.19)	4,855 (7.07)	2,160 (5.10)	13,852 (7.78)
Unknown/missing	142 (0.21)	158 (0.23)	71 (0.17)	371 (0.24)
Alcohol consumption				
Never	1,767 (2.63)	1,709 (2.49)	1,083 (2.56)	4,559 (2.56)
Previous	1,874 (2.79)	1,935 (2.82)	1,358 (3.21)	5,167 (2.90)
Current	63,433 (95.52)	65,046 (94.67)	39,873 (94.20)	168,352 (94.50)
Unknown/missing	35 (0.06)	21 (0.02)	14 (0.03)	70 (0.04)
Family history of cancer				
No	43,233 (64.42)	44,183 (64.30)	27,005 (63.80)	114,421 (64.23)
Yes	23,438 (34.93)	24,228 (35.26)	15,144 (35.78)	62,810 (35.26)
Unknown/missing	438 (0.65)	300 (0.44)	179 (0.42)	917 (0.51)
Physical activity level				
Low	11,848 (17.65)	9,830 (14.31)	4,677 (11.05)	26,355 (14.80)
Medium	40,774 (60.76)	42,446 (61.77)	26,115 (61.70)	109,335 (61.37)
High	14,487 (21.59)	16,435 (23.92)	11,536 (27.25)	42,458 (23.83)

Data are presented as mean ± (standard deviation) for continuous variables and n (%) for categorical variables

Low: DI-GM ≤ 4; moderate: 5 ≤ DI-GM ≤ 6; high: DI-GM ≥ 7

Abbreviations: BMI, body mass index; DI-GM, dietary index for gut microbiota

GI cancer (95% CI: 1.42–1.54; Supplementary Table 15). Compared with participants with low genetic risk, those with moderate and high genetic risk had a significantly higher risk of GI cancer, with HRs (95% CIs) of 1.65 (1.46–1.87) and 2.89 (2.53–3.29), respectively (Supplementary Table 15). Restricted cubic spline analysis showed a nonlinear association between genetic risk and GI cancer (*P* for non-linearity = 0.012; Fig. 3), which indicated a rapid increase in risk among populations with extremely high genetic risk.

Joint association and interaction of DI-GM and genetic risk on GI cancer risk

Joint analysis showed that GI cancer risk decreased with both elevation of DI-GM and reduction of genetic risk in a dose-response manner. When compared with participants in the low DI-GM and high genetic risk group, those with high DI-GM and low genetic risk showed the lowest risk of GI cancer (HR: 0.28, 95% CI: 0.21–0.36; Fig. 4, Supplementary Table 16). Similar association was also observed in EC and CRC risk, with HR (95% CI) of 0.27 (0.11–0.63) and 0.21 (0.16–0.30), respectively (Supplementary Tables 17–18). Significant additive interactions between DI-GM and genetic risk on the risk of

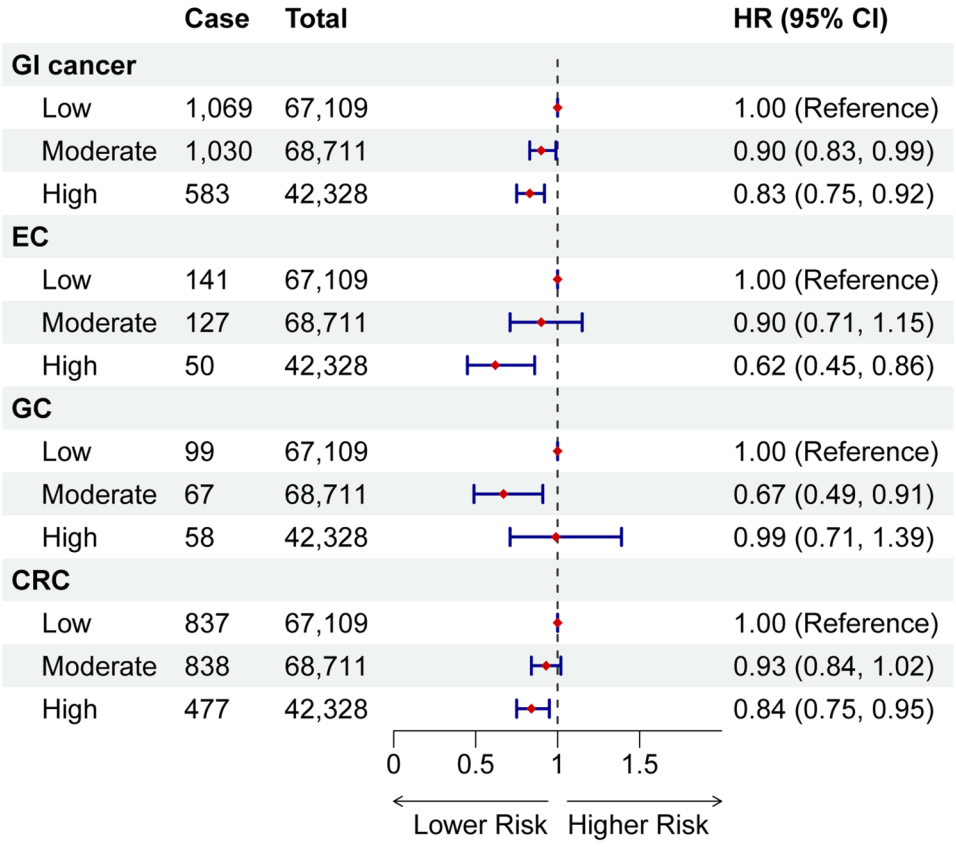


Fig. 1 Associations of DI-GM with risk of gastrointestinal cancer. Low: DI-GM ≤ 4; moderate: 5 ≤ DI-GM ≤ 6; high: DI-GM ≥ 7. The models adjusted for age, sex, body mass index, total energy intake, annual household income, education level, Townsend deprivation index, smoking status, alcohol consumption, family history of cancer, and physical activity level. Abbreviations: CI, confidence interval; CRC, colorectal cancer; DI-GM: dietary index for gut microbiota; EC, esophageal cancer; GC, gastric cancer; GI: gastrointestinal; HR, hazard ratio

GI cancer were observed. Taking participants with low DI-GM and high genetic risk as a reference, the RERI (95% CI) for those with high DI-GM and low genetic risk was -0.09 (-0.16, -0.01) for the risk of GI cancer. This negative RERI value indicates that the protective effect of having both high DI-GM and low genetic risk is greater than would be expected from simply adding their individual protective effects. The AP value of 0.17 indicated that if both low DI-GM and high genetic risk did not exist, the incidence of GI cancer would decrease by approximately 17%. However, no significant multiplicative interaction was observed (Supplementary Table 19).

Discussion

In this large-scale prospective cohort study based on the UK Biobank, we found a significant association between adherence to the high DI-GM diet and the reduced risk of GI cancers, with a significant linear dose-response relationship. Additionally, higher genetic risk, as quantified by the CPRS, was strongly associated with increased GI cancer risk. Importantly, we observed a significant additive interaction between DI-GM and genetic risk. These findings underscore the importance of considering both dietary factors that influence gut microbiota and genetic risk in GI cancer prevention strategies.

Our findings regarding the protective association of DI-GM with GI cancer risk align with previous research on dietary patterns and cancer risk, while providing novel insights specific to gut microbiota-related dietary components. Traditional dietary patterns such as the Healthy Eating diet, Mediterranean diet and healthful plant-based diet have been associated with reduced GI cancer risk [20, 33], whereas Western dietary patterns have shown positive associations with these cancers [34, 35]. However, the DI-GM offers a more targeted approach by specifically focusing on dietary components that influence gut microbiota composition and function, providing a potential mechanistic link between diet and cancer development.

The differential associations observed across GI cancer sites in our study are consistent with site-specific etiological factors identified in previous research, and may reflect differences in local microbiota composition and the varying influence of diet-microbiota interactions [6, 7]. The inconsistent association for gastric cancer, where a significant protective association was observed in the

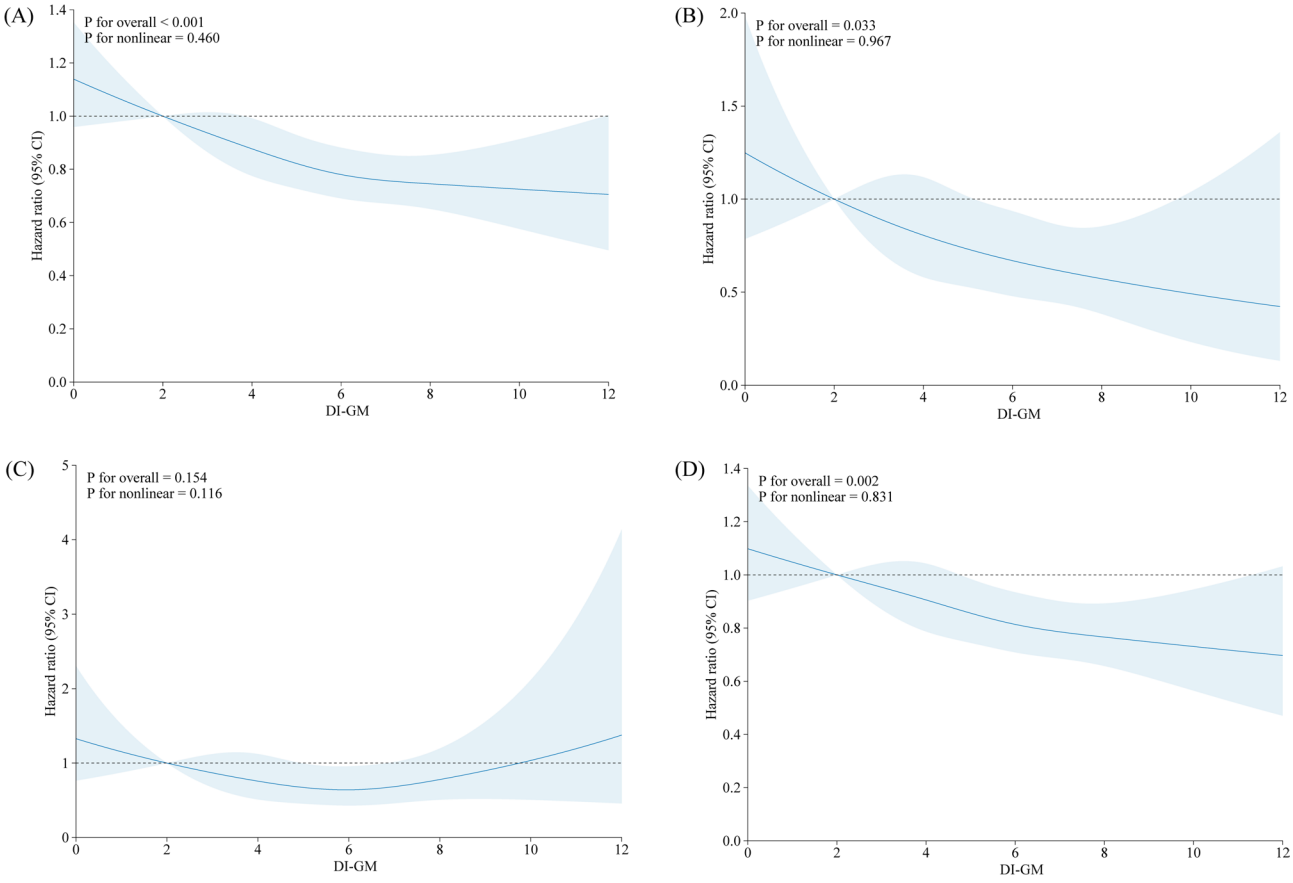


Fig. 2 Restricted cubic splines for DI-GM and risk of (**A**) gastrointestinal cancer, (**B**) esophageal cancer, (**C**) gastric cancer, and (**D**) colorectal cancer. The models adjusted for age, sex, body mass index, total energy intake, annual household income, education level, Townsend deprivation index, smoking status, alcohol consumption, family history of cancer, and physical activity level. Abbreviations: CI, confidence interval; DI-GM: dietary index for gut microbiota

middle DI-GM category but not in the highest, warrants further discussion. This pattern may be primarily attributed to the dominant role of Helicobacter pylori infection in gastric carcinogenesis [36], which is estimated to account for 60–90% of gastric cancers worldwide. Unlike colorectal cancer, where dietary factors play a more central etiological role, the relative contribution of dietary factors to gastric cancer risk may be more limited or complex in the context of H. pylori infection. Additionally, gastric cancer is notably heterogeneous, with distinct subtypes (intestinal and diffuse) and anatomical locations (cardia and non-cardia) that may respond differently to dietary influences [37]. Our inability to stratify by these subtypes represents a limitation in fully characterizing the relationship between DI-GM and gastric cancer risk.

Our analysis of individual dietary components revealed significant associations between fermented dairy, fiber, whole grains, and meat consumption with GI cancer risk, corroborating previous findings. Meta-analyses have consistently shown inverse associations between dietary fiber and whole grains intake and colorectal cancer risk [38], while processed meat consumption has been classified as a Group 1 carcinogen for colorectal cancer by the International Agency for Research on Cancer [39]. The protective association of fermented dairy products observed in our study adds to the growing evidence suggesting beneficial effects of these foods on gut microbiota and cancer prevention [40, 41].

The DI-GM includes key dietary components that promote a healthy gut microbiome, such as dietary fiber, legumes, fermented dairy products, and whole grains [42–46], while limiting foods associated with gut imbalances, such as high-fat diets, red meat, and refined grains [12, 47, 48]. This approach is consistent with previous findings on how diet influences gut microbiota health, emphasizing dietary patterns that can either benefit or impair gut health. High DI-GM pattern helps maintain the health of gut microbiome and promotes the growth of beneficial bacteria, which intervene in cancer development through multiple pathways. For instance, soy foods can increase the levels of bifidobacteria and lactobacilli [49], while broccoli provides sulfur compounds that may prevent the excessive growth of certain sulfur metabolizing bacteria [50]. Sufficient dietary fiber intake boosts the

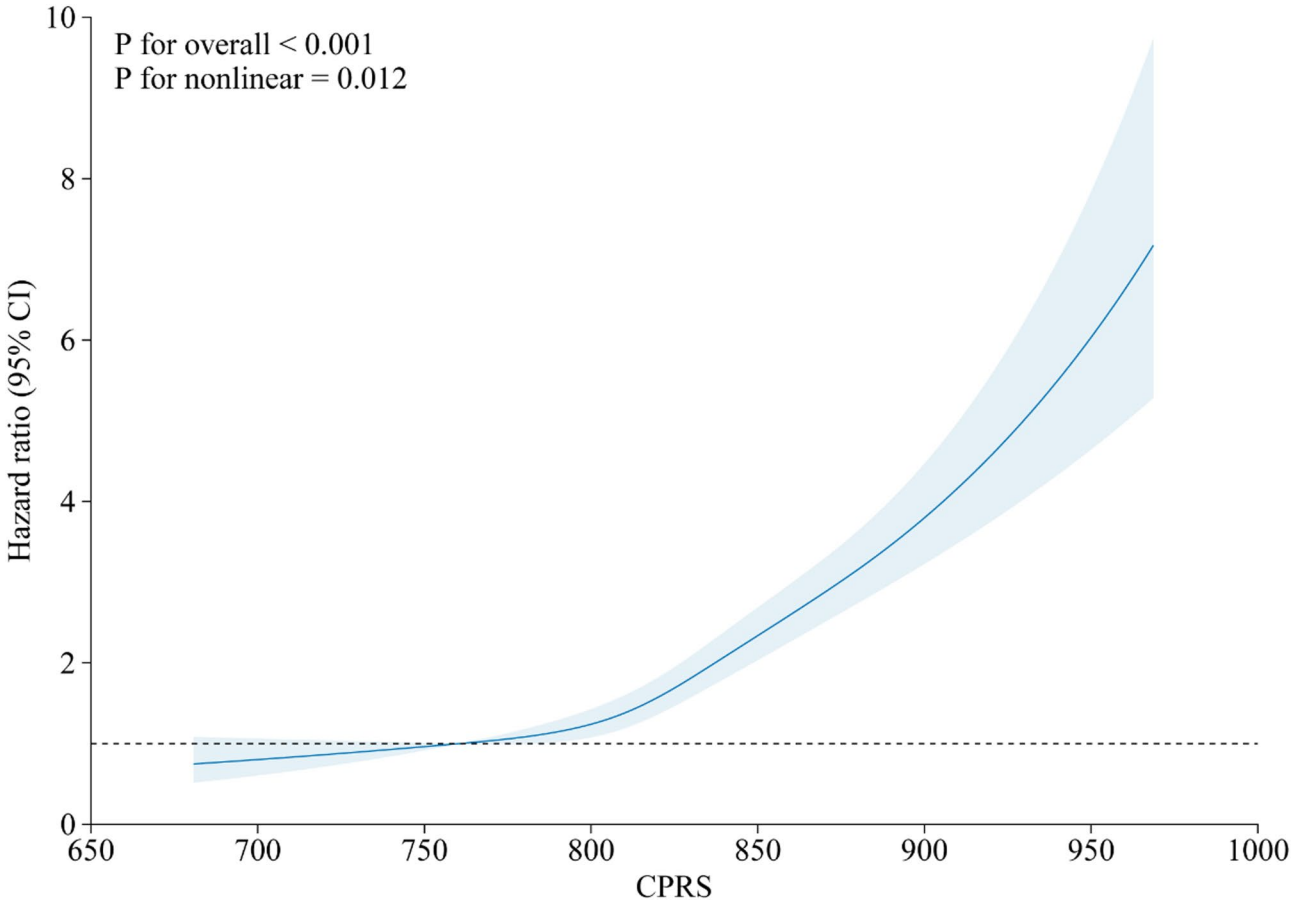


Fig. 3 Restricted cubic splines for CPRS and risk of gastrointestinal cancer. The models adjusted for age, sex, body mass index, total energy intake, annual household income, education level, Townsend deprivation index, smoking status, alcohol consumption, family history of cancer, and physical activity level. Abbreviations: CI, confidence interval; CPRS, cancer polygenic risk score. Abbreviations: CI, confidence interval; HR, hazard ratio

production of short-chain fatty acids, particularly butyrate, which supports colonic mucosal barrier function and reduces inflammation [51]. Additionally, fermented dairy products rich in probiotics [52], along with polyphenol-rich foods like coffee, green tea, and cranberries, help inhibit the overgrowth of harmful bacteria [53–55]. These protective mechanisms likely contribute to the observed inverse relationship between higher DI-GM and the risk of GI cancer.

In addition to microbial factors, genetic risk plays a critical role in the development of GI cancer. Emerging evidence indicates that individuals with higher polygenic risk scores are more likely to undergo malignant transformation when exposed to adverse lifestyle factors [56, 57]. Our study confirmed that a higher GI-CPRS corresponds to an elevated risk of GI cancer, aligning with results from other large-scale studies [15, 58]. The additive interaction observed between DI-GM and genetic risk suggests that dietary factors may partially mitigate genetic risk to GI cancer. The observed interaction pattern is consistent with several previous gene-diet studies [59, 60]. From a mechanistic perspective, this pattern may reflect parallel biological pathways through which diet-influenced gut microbiota composition and genetic factors affect GI cancer risk. While genetic variants may influence cellular processes such as proliferation, DNA repair, and inflammation, dietary components may modify the gut microbiome in ways that partially counteract these genetic effects without necessarily operating through the same molecular pathways [61–63]. Additionally, certain dietary components such as phytonutrients may attenuate the effects of genetic variants by influencing pathways, DNA repair mechanisms, or inflammatory processes [64, 65].

Our findings have significant implications for clinical practice and public health strategies. The DI-GM offers a novel tool for assessing gut microbiota-related dietary patterns, with evidence suggesting even modest improvements could associate with reduced GI cancer risk through a linear dose-response relationship. The additive interaction between DI-GM and genetic risk highlights the value of personalized dietary interventions based on genetic risk stratification. Practical dietary recommendations can be derived from our findings on individual components: increasing consumption of fermented dairy,

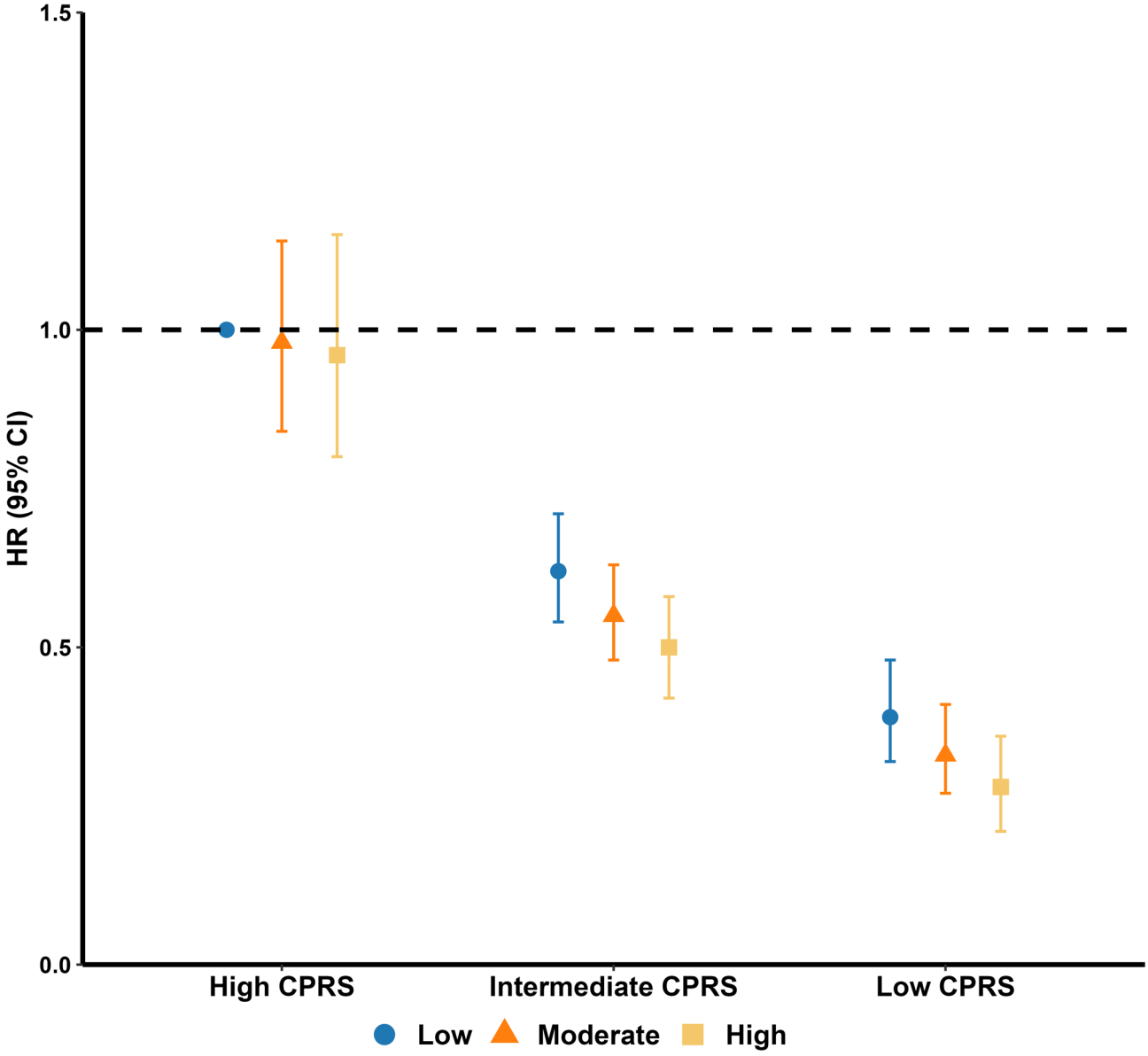


Fig. 4 Joint effect of DI-GM and genetic risk on gastrointestinal cancer incidence. Low: DI-GM ≤ 4; moderate: 5 ≤ DI-GM ≤ 6; high: DI-GM ≥ 7. The models adjusted for age, sex, body mass index, energy intake, annual household income, education level, Townsend deprivation index, smoking status, alcohol consumption, family history of cancer, and physical activity level. Abbreviations: CI, confidence interval; CPRS, cancer polygenic risk score; HR, hazard ratio

fiber-rich foods, and whole grains while limiting red and processed meat intake consistent with established guidelines for overall health [66]. Additionally, the varying associations across GI cancer sites suggest the need for targeted prevention strategies, particularly for EC and CRC, where dietary interventions appear more effective.

Our study has several key strengths. First, it is the first to use the UK Biobank to examine the relationship between the DI-GM, a dietary quality index associated with gut microbiota health, and the risk of GI cancer across different genetic risk levels. Second, the large sample size of the UK Biobank cohort provides sufficient statistical power, and the comprehensive data available allows for adjustment of a wide range of covariates, thereby enhancing the reliability of our findings. Additionally, the inclusion of genetic data allowed us to construct the specific PRS to predict GI cancer risk and incorporate genetic risk into our analyses. Third, the prospective study design and long median follow-up period enhance the temporal inference between DI-GM and GI cancer.

Despite these strengths, several limitations merit consideration. As an observational study, we cannot definitively establish causality, although the observed dose-response relationship supports a possible causal link. Dietary intake was self-reported, potentially

introducing recall bias, but the use of repeated measures helps to mitigate this concern. Additionally, a notable limitation of our study is the incomplete adaptation of the DI-GM to the UK Biobank dietary data. Specifically, the original DI-GM developed by Kase et al. consists of 14 dietary components, but our adaptation includes only 13 components due to the absence of chickpea-specific intake data in the Oxford WebQ dietary assessment tool. To address this limitation, we conducted sensitivity analyses with results remaining consistent. Finally, the cohort primarily comprised White British individuals, potentially limiting the generalizability of our findings to other ethnicities. The DI-GM components were validated predominantly in Western populations, and their impact could differ in other ethnic groups with different baseline gut microbiota profiles. Future research should validate the DI-GM and its association with GI cancer risk in more ethnically diverse populations, potentially adapting the index to incorporate culturally relevant foods for different ethnic groups. This would improve the global applicability of microbiota-based dietary recommendations for cancer prevention.

Conclusions

Higher DI-GM was associated with a lower risk of GI cancer, including EC and CRC. Individuals with both high DI-GM and low genetic risk had the lowest risk of GI cancer with a significant interaction. These findings suggest the importance of promoting a healthy gut microbiome through dietary interventions, and considering genetic risk in GI cancer prevention.

Abbreviations

AP	Attributable Proportion
BMI	Body Mass Index
CI	Confidence Interval
CRC	Colorectal Cancer
CPRS	Cancer Polygenic Risk Scores
DI-GM	Dietary Index for Gut Microbiota
EC	Esophageal Cancer
GC	Gastric Cancer
HR	Hazard Ratio
IQR	Interquartile Range
RERI	Relative Excess Risk due to Interaction
SD	Standard Deviation
SNPs	Single Nucleotide Polymorphisms

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12937-025-01151-3.

Supplementary Material 1

Acknowledgements

The authors are grateful to all participants in the UK Biobank project for their contributions.

Author contributions

D-RL, T-TG, S-YG, and Q-JW contributed to the study design. D-RL, B-QL, J-CL, W-RZ, and S-YG analysis of data. D-RL, B-QL, J-CL, M-HL, YQ, W-RZ, T-TG, S-YG, and Q-JW wrote the first draft of the manuscript and edited the manuscript. All authors read and approved the final manuscript. D-RL and B-QL contributed equally to this work.

Funding

This study is funded by the Scientific Research Project of the Liaoning Province Education Department (grant number JYTMS20230092) and Joint Fund Project General Support Program Project of Liaoning Provincial Department of Science and Technology (grant number 2024-MSLH-591).

Data availability

Data used in this study are available on application to the UK Biobank (www.ukbiobank.ac.uk). Analytical methods and study materials will be available to other researchers from the corresponding authors upon reasonable request for the purposes of reproducing the results or replicating the procedure.

Declarations

Ethics approval and consent to participate

The UK Biobank received approval from the North West Multicenter Research Ethics Committee, and all participants provided written informed consent. As the dataset is publicly accessible and free of identifiable information, additional ethical approval and informed consent were not required.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

Author details

[1]Department of Clinical Epidemiology, Shengjing Hospital of China Medical University, Shenyang, China
[2]Key Laboratory of Precision Medical Research on Major Chronic Disease, Shengjing Hospital of China Medical University, Shenyang, China
[3]Department of Epidemiology, School of Public Health, China Medical University, Shenyang, China
[4]Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang, China
[5]NHC Key Laboratory of Advanced Reproductive Medicine and Fertility (China Medical University), National Health Commission, Shenyang, China
[6]Clinical Trials and Translation Center, Shengjing Hospital of China Medical University, Shenyang, China

Received: 10 April 2025 / Accepted: 6 May 2025
Published online: 17 May 2025

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229–63. https://doi.org/10.3322/caac.21834
2. Arnold M, Abnet CC, Neale RE, Vignat J, Giovannucci EL, McGlynn KA, Bray F. Global burden of 5 major types of gastrointestinal cancer. Gastroenterology. 2020;159(1). https://doi.org/10.1053/j.gastro.2020.02.068
3. Lu L, Mullins CS, Schafmayer C, Zeißig S, Linnebacher M. A global assessment of recent trends in gastrointestinal cancer and lifestyle-associated risk factors. Cancer Commun (Lond). 2021;41(11):1137–51. https://doi.org/10.1002/cac2.12220
4. Zhang F, Aschenbrenner D, Yoo JY, Zuo T. The gut mycobiome in health, disease, and clinical applications in association with the gut bacterial microbiome assembly. Lancet Microbe. 2022;3(12):e969–83. https://doi.org/10.1016/S2666-5247(22)00203-8

5. Zhang Y, Wang H, Sang Y, Liu M, Wang Q, Yang H, Li X. Gut microbiota in health and disease: advances and future prospects. MedComm (2020). 2024;5(12):e70012. https://doi.org/10.1002/mco2.70012
6. Liu Y, Baba Y, Ishimoto T, Gu X, Zhang J, Nomoto D, Okadome K, Baba H, Qiu P. Gut microbiome in gastrointestinal cancer: a friend or foe? Int J Biol Sci. 2022;18(10):4101–17. https://doi.org/10.7150/ijbs.69331
7. Meng C, Bai C, Brown TD, Hood LE, Tian Q. Human gut microbiota and gastrointestinal cancer. Genomics Proteom Bioinf. 2018;16(1):33–49. https://doi.org/10.1016/j.gpb.2017.06.002
8. Wong CC, Yu J. Gut microbiota in colorectal cancer development and therapy. Nat Rev Clin Oncol. 2023;20(7):429–52. https://doi.org/10.1038/s41571-023-00766-x
9. Li Y, Jia X, Li C, Sun H, Nie S, Giovannucci EL, Liu L. The global incident gastrointestinal cancers attributable to suboptimal diets from 1990 to 2018. Gastroenterology. 2024;167(6):1141–51. https://doi.org/10.1053/j.gastro.2024.07.009
10. García-Montero C, Fraile-Martínez O, Gómez-Lahoz AM, Pekarek L, Castellanos AJ, Noguerales-Fraguas F, et al. Nutritional components in western diet versus mediterranean diet at the gut microbiota-Immune system interplay. Implications for health and disease. Nutrients. 2021;13(2). https://doi.org/10.3390/nu13020699
11. Soldán M, Argalášová Ľ, Hadvinová L, Galileo B, Babjaková J. The effect of dietary types on gut microbiota composition and development of non-communicable diseases: a narrative review. Nutrients. 2024;16(18). https://doi.org/10.3390/nu16183134
12. Tong Y, Gao H, Qi Q, Liu X, Li J, Gao J, Li P, Wang Y, Du L, Wang C. High fat diet, gut microbiome and gastrointestinal cancer. Theranostics. 2021;11(12):5889–910. https://doi.org/10.7150/thno.56157
13. Kase BE, Liese AD, Zhang J, Murphy EA, Zhao L, Steck SE. The development and evaluation of a literature-based dietary index for gut microbiota. Nutrients. 2024;16(7). https://doi.org/10.3390/nu16071045
14. Herrera-Luis E, Benke K, Volk H, Ladd-Acosta C, Wojcik GL. Gene-environment interactions in human health. Nat Rev Genet. 2024;25(11):768–84. https://doi.org/10.1038/s41576-024-00731-z
15. Jin G, Lv J, Yang M, Wang M, Zhu M, Wang T, et al. Genetic risk, incident gastric cancer, and healthy lifestyle: a meta-analysis of genome-wide association studies and prospective cohort study. Lancet Oncol. 2020;21(10):1378–86. https://doi.org/10.1016/S1470-2045(20)30460-5
16. Laskar RS, Qu C, Huyghe JR, Harrison T, Hayes RB, Cao Y, et al. Genome-wide association studies and Mendelian randomization analyses provide insights into the causes of early-onset colorectal cancer. Ann Oncol. 2024;35(6):523–36. https://doi.org/10.1016/j.annonc.2024.02.008
17. Schröder J, Chegwidden L, Maj C, Gehlen J, Speller J, Böhmer AC, et al. GWAS meta-analysis of 16 790 patients with Barrett's oesophagus and oesophageal adenocarcinoma identifies 16 novel genetic risk loci and provides insights into disease aetiology beyond the single marker level. Gut. 2023;72(4):612–23. https://doi.org/10.1136/gutjnl-2021-326698
18. Briggs SEW, Law P, East JE, Wordsworth S, Dunlop M, Houlston R, Hippisley-Cox J, Tomlinson I. Integrating genome-wide polygenic risk scores and non-genetic risk to predict colorectal cancer diagnosis using UK biobank data: population based cohort study. BMJ. 2022;379:e071707. https://doi.org/10.1136/bmj-2022-071707
19. Huntley C, Torr B, Sud A, Rowlands CF, Way R, Snape K, et al. Utility of polygenic risk scores in UK cancer screening: a modelling analysis. Lancet Oncol. 2023;24(6):658–68. https://doi.org/10.1016/S1470-2045(23)00156-0
20. Cai Y, Hong C, Han J, Fan L, Xiao X, Xiao J, et al. Healthy dietary patterns, genetic risk, and gastrointestinal cancer incident risk: a large-scale prospective cohort study. Am J Clin Nutr. 2024;119(2):406–16. https://doi.org/10.1016/j.ajcnut.2023.11.015
21. Liu W, Wang T, Zhu M, Jin G, Healthy Diet. Polygenic risk score, and upper gastrointestinal cancer risk: a prospective study from UK Biobank. Nutrients. 2023;15(6). https://doi.org/10.3390/nu15061344
22. Allen NE, Lacey B, Lawlor DA, Pell JP, Gallacher J, Smeeth L, et al. Prospective study design and data analysis in UK biobank. Sci Transl Med. 2024;16(729):eadf4428. https://doi.org/10.1126/scitranslmed.adf4428
23. Lu X, Wu L, Shao L, Fan Y, Pei Y, Lu X, Borné Y, Ke C. Adherence to the EAT-Lancet diet and incident depression and anxiety. Nat Commun. 2024;15(1):5599. https://doi.org/10.1038/s41467-024-49653-8
24. Perez-Cornago A, Pollard Z, Young H, van Uden M, Andrews C, Piernas C, Key TJ, Mulligan A, Lentjes M. Description of the updated nutrition calculation of the Oxford WebQ questionnaire and comparison with the previous version among 207,144 participants in UK biobank. Eur J Nutr. 2021;60(7):4019–30. https://doi.org/10.1007/s00394-021-02558-4
25. Greenwood DC, Hardie LJ, Frost GS, Alwan NA, Bradbury KE, Carter M, et al. Validation of the Oxford WebQ online 24-hour dietary questionnaire using biomarkers. Am J Epidemiol. 2019;188(10):1858–67. https://doi.org/10.1093/aje/kwz165
26. Liu B, Young H, Crowe FL, Benson VS, Spencer EA, Key TJ, Appleby PN, Beral V. Development and evaluation of the Oxford WebQ, a low-cost, web-based method for assessment of previous 24 h dietary intakes in large-scale prospective studies. Public Health Nutr. 2011;14(11):1998–2005. https://doi.org/10.1017/S1368980011000942
27. Bycroft C, Freeman C, Petkova D, Band G, Elliott LT, Sharp K, et al. The UK biobank resource with deep phenotyping and genomic data. Nature. 2018;562(7726):203–9. https://doi.org/10.1038/s41586-018-0579-z
28. Choi J, Jia G, Wen W, Long J, Zheng W. Evaluating polygenic risk scores in assessing risk of nine solid and hematologic cancers in European descendants. Int J Cancer. 2020;147(12):3416–23. https://doi.org/10.1002/ijc.33176
29. Fernandez-Rozadilla C, Timofeeva M, Chen Z, Law P, Thomas M, Schmit S, et al. Deciphering colorectal cancer genetics through multi-omic analysis of 100,204 cases and 154,587 controls of European and East Asian ancestries. Nat Genet. 2023;55(1):89–99. https://doi.org/10.1038/s41588-022-01222-9
30. Gharahkhani P, Fitzgerald RC, Vaughan TL, Palles C, Gockel I, Tomlinson I, et al. Genome-wide association studies in oesophageal adenocarcinoma and Barrett's oesophagus: a large-scale meta-analysis. Lancet Oncol. 2016;17(10):1363–73. https://doi.org/10.1016/S1470-2045(16)30240-6
31. Zhang X, Yang Q, Huang J, Lin H, Luo N, Tang H. Association of the newly proposed dietary index for gut microbiota and depression: the mediation effect of phenotypic age and body mass index. Eur Arch Psychiatry Clin Neurosci. 2024. https://doi.org/10.1007/s00406-024-01912-x
32. Piernas C, Perez-Cornago A, Gao M, Young H, Pollard Z, Mulligan A, et al. Describing a new food group classification system for UK biobank: analysis of food groups and sources of macro- and micronutrients in 208,200 participants. Eur J Nutr. 2021;60(5):2879–90. https://doi.org/10.1007/s00394-021-02535-x
33. Wang W, Chang Y, Chen G. Association between healthy eating Index-2020, alternative mediterranean diet scores, and Gastrointestinal cancer risk in NHANES 2005–2018. Sci Rep. 2025;15(1):3983. https://doi.org/10.1038/s41598-025-88317-5
34. Adolph TE, Tilg H. Western diets and chronic diseases. Nat Med. 2024;30(8):2133–47. https://doi.org/10.1038/s41591-024-03165-6
35. Castelló A, Rodríguez-Barranco M, Fernández de Larrea N, Jakszyn P, Dorronsoro A, Amiano P, et al. Adherence to the western, prudent and mediterranean dietary patterns and colorectal cancer risk: findings from the Spanish cohort of the European prospective investigation into cancer and nutrition (EPIC-Spain). Nutrients. 2022;14(15). https://doi.org/10.3390/nu14153085
36. Chen C-C, Liou J-M, Lee Y-C, Hong T-C, El-Omar EM, Wu M-S. The interplay between Helicobacter pylori and gastrointestinal microbiota. Gut Microbes. 2021;13(1). https://doi.org/10.1080/19490976.2021.1909459
37. Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. Cancer Epidemiol Biomarkers Prev. 2014;23(5):700–13. https://doi.org/10.1158/1055-9965.EPI-13-1057
38. Aune D, Chan DSM, Lau R, Vieira R, Greenwood DC, Kampman E, Norat T. Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. BMJ. 2011;343:d6617. https://doi.org/10.1136/bmj.d6617
39. Bouvard V, Loomis D, Guyton KZ, Grosse Y, Ghissassi FE, Benbrahim-Tallaa L, Guha N, Mattock H, Straif K. Carcinogenicity of consumption of red and processed meat. Lancet Oncol. 2015;16(16):1599–600. https://doi.org/10.1016/S1470-2045(15)00444-1
40. De Filippis F, Pasolli E, Ercolini D. The food-gut axis: lactic acid bacteria and their link to food, the gut microbiome and human health. FEMS Microbiol Rev. 2020;44(4):454–89. https://doi.org/10.1093/femsre/fuaa015
41. Zhang K, Dai H, Liang W, Zhang L, Deng Z. Fermented dairy foods intake and risk of cancer. Int J Cancer. 2019;144(9):2099–108. https://doi.org/10.1002/ijc.31959
42. Gill SK, Rossi M, Bajka B, Whelan K. Dietary fibre in gastrointestinal health and disease. Nat Rev Gastroenterol Hepatol. 2021;18(2):101–16. https://doi.org/10.1038/s41575-020-00375-4
43. Holscher HD. Dietary fiber and prebiotics and the gastrointestinal microbiota. Gut Microbes. 2017;8(2):172–84. https://doi.org/10.1080/19490976.2017.1290756

44. Ross FC, Patangia D, Grimaud G, Lavelle A, Dempsey EM, Ross RP, Stanton C. The interplay between diet and the gut microbiome: implications for health and disease. Nat Rev Microbiol. 2024;22(11):671–86. https://doi.org/10.1038/s41579-024-01068-4
45. Volokh O, Klimenko N, Berezhnaya Y, Tyakht A, Nesterova P, Popenko A, Alexeev D. Human gut microbiome response induced by fermented dairy product intake in healthy volunteers. Nutrients. 2019;11(3). https://doi.org/10.3390/nu11030547
46. Wang C, Yang Y, Xu W, Yu D, Wu J, Cai Q, Long J, Zheng W, Shu X-O. Legume consumption and gut microbiome in elderly Chinese men and women. J Nutr. 2021;151(8):2399–408. https://doi.org/10.1093/jn/nxab139
47. De Filippo C, Chioccioli S, Meriggi N, Troise AD, Vitali F, Mejia Monroy M, et al. Gut microbiota drives colon cancer risk associated with diet: a comparative analysis of meat-based and pesco-vegetarian diets. Microbiome. 2024;12(1):180. https://doi.org/10.1186/s40168-024-01900-2
48. Whelan K, Bancil AS, Lindsay JO, Chassaing B. Ultra-processed foods and food additives in gut health and disease. Nat Rev Gastroenterol Hepatol. 2024;21(6):406–27. https://doi.org/10.1038/s41575-024-00893-5
49. Huang H, Krishnan HB, Pham Q, Yu LL, Wang TTY. Soy and gut microbiota: interaction and implication for human health. J Agric Food Chem. 2016;64(46):8695–709.
50. Nguyen LH, Ma W, Wang DD, Cao Y, Mallick H, Gerbaba TK, et al. Association between sulfur-metabolizing bacterial communities in stool and risk of distal colorectal cancer in men. Gastroenterology. 2020;158(5):1313–25. https://doi.org/10.1053/j.gastro.2019.12.029
51. He Y, Fu L, Li Y, Wang W, Gong M, Zhang J, et al. Gut microbial metabolites facilitate anticancer therapy efficacy by modulating cytotoxic CD8 + T cell immunity. Cell Metab. 2021;33(5). https://doi.org/10.1016/j.cmet.2021.03.002
52. Crowder SL, Jim HSL, Hogue S, Carson TL, Byrd DA. Gut microbiome and cancer implications: potential opportunities for fermented foods. Biochim Biophys Acta Rev Cancer. 2023;1878(3):188897. https://doi.org/10.1016/j.bbcan.2023.188897
53. Alasalvar C, Chang SK, Kris-Etherton PM, Sullivan VK, Petersen KS, Guasch-Ferré M, Jenkins DJA. Dried fruits: bioactives, effects on gut microbiota, and possible health benefits-an update. Nutrients. 2023;15(7). https://doi.org/10.3390/nu15071611
54. Pérez-Burillo S, Navajas-Porras B, López-Maldonado A, Hinojosa-Nogueira D, Pastoriza S, Rufián-Henares JÁ. Green tea and its relation to human gut microbiome. Molecules. 2021;26(13). https://doi.org/10.3390/molecules26133907
55. Saygili S, Hegde S, Shi X-Z. Effects of coffee on gut microbiota and bowel functions in health and diseases: a literature review. Nutrients. 2024;16(18). https://doi.org/10.3390/nu16183155
56. Byrne S, Boyle T, Ahmed M, Lee SH, Benyamin B, Hyppönen E. Lifestyle, genetic risk and incidence of cancer: a prospective cohort study of 13 cancer types. Int J Epidemiol. 2023;52(3):817–26. https://doi.org/10.1093/ije/dyac238
57. Shen Y, Chen W, Fu C, Liu X, Miao J, Li J, Li N, Hang D. Polygenic risk score, healthy lifestyle score, and colorectal cancer risk: a prospective cohort study. Cancer Epidemiol Biomarkers Prev. 2025;34(2):290–7. https://doi.org/10.1158/1055-9965.EPI-24-1013
58. Liu Y, Yan C, Yin S, Wang T, Zhu M, Liu L, Jin G. Genetic risk, metabolic syndrome, and gastrointestinal cancer risk: a prospective cohort study. Cancer Med. 2023;12(1):597–605. https://doi.org/10.1002/cam4.4923
59. Choi J, Jia G, Wen W, Shu X-O, Zheng W. Healthy lifestyles, genetic modifiers, and colorectal cancer risk: a prospective cohort study in the UK biobank. Am J Clin Nutr. 2021;113(4):810–20. https://doi.org/10.1093/ajcn/nqaa404
60. Hu F-L, Liu J-C, Li D-R, Xu Y-L, Liu B-Q, Chen X, et al. EAT-Lancet diet pattern, genetic risk, and risk of colorectal cancer: a prospective study from the UK biobank. Am J Clin Nutr. 2025. https://doi.org/10.1016/j.ajcnut.2025.02.025
61. D'Aquila P, Carelli LL, De Rango F, Passarino G, Bellizzi D. Gut microbiota as important mediator between diet and DNA methylation and histone modifications in the host. Nutrients. 2020;12(3). https://doi.org/10.3390/nu12030597
62. Krautkramer KA, Kreznar JH, Romano KA, Vivas EI, Barrett-Wilt GA, Rabaglia ME, Keller MP, Attie AD, Rey FE, Denu JM. Diet-microbiota interactions mediate global epigenetic programming in multiple host tissues. Mol Cell. 2016;64(5):982–92. https://doi.org/10.1016/j.molcel.2016.10.025
63. Shock T, Badang L, Ferguson B, Martinez-Guryn K. The interplay between diet, gut microbes, and host epigenetics in health and disease. J Nutr Biochem. 2021;95:108631. https://doi.org/10.1016/j.jnutbio.2021.108631
64. Al-Ishaq RK, Overy AJ, Büsselberg D. Phytochemicals and gastrointestinal cancer: cellular mechanisms and effects to change cancer progression. Biomolecules. 2020;10(1). https://doi.org/10.3390/biom10010105
65. Bhattacharya T, Dutta S, Akter R, Rahman MH, Karthika C, Nagaswarupa HP, Murthy HCA, Fratila O, Brata R, Bungau S. Role of phytonutrients in nutrigenetics and nutrigenomics perspective in curing breast cancer. Biomolecules. 2021;11(8). https://doi.org/10.3390/biom11081176
66. Armet AM, Deehan EC, O'Sullivan AF, Mota JF, Field CJ, Prado CM, Lucey AJ, Walter J. Rethinking healthy eating in light of the gut microbiome. Cell Host Microbe. 2022;30(6):764–85. https://doi.org/10.1016/j.chom.2022.04.016

Publisher's note

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