Original research

Association of healthy lifestyle behaviours with incident irritable bowel syndrome: a large population-based prospective cohort study

Fai Fai Ho ,[1] Hui Sun,[2] Hong Zheng,[3] David C N Wong,[3] Yin-Yan Gao,[2] Chen Mao ,[4] Yin Ting Cheung,[5] Chun Sing Lam,[5] Maggie H Wang,[3] Irene Xin-Yin Wu,[2] Justin C Y Wu,[6] Vincent C H Chung[3]

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[1]School of Chinese Medicine, The Chinese University of Hong Kong, Hong Kong, Hong Kong
[2]Xiangya School of Public Health, Central South University, Changsha, Hunan, China
[3]The Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong, Hong Kong
[4]Department of Epidemiology, Southern Medical University School of Public Health, Guangzhou, Guangdong, China
[5]School of Pharmacy, The Chinese University of Hong Kong, Hong Kong, Hong Kong
[6]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong

Correspondence to
Professor Irene Xin-Yin Wu, Xiangya School of Public Health, Central South University, Changsha, Hunan, China; irenexywu@csu.edu.cn

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ABSTRACT

Objectives To evaluate the association between healthy lifestyle behaviours and the incidence of irritable bowel syndrome (IBS).

Design Population-based prospective cohort study.

Setting The UK Biobank.

Participants 64 268 adults aged 37 to 73 years who had no IBS diagnosis at baseline were enrolled between 2006 and 2010 and followed up to 2022.

Main exposure The five healthy lifestyle behaviours studied were never smoking, optimal sleep, high level of vigorous physical activity, high dietary quality and moderate alcohol intake.

Main outcome measure The incidence of IBS.

Results During a mean follow-up of 12.6 years, 961 (1.5%) incident IBS cases were recorded. Among the 64 268 participants (mean age 55.9 years, 35 342 (55.0%) female, 7604 (11.8%) reported none of the five healthy lifestyle behaviours, 20 662 (32.1%) reported 1 behaviour, 21 901 (34.1%) reported 2 behaviours and 14 101 (21.9%) reported 3 to 5 behaviours at baseline. The multivariable adjusted hazard ratios associated with having 1, 2 and 3 to 5 behaviours for IBS incidence were 0.79 (95% confidence intervals 0.65 to 0.96), 0.64 (0.53 to 0.78) and 0.58 (0.46 to 0.72), respectively (P for trend <0.001). Never smoking (0.86, 0.76 to 0.98, P=0.02), high level of vigorous physical activity (0.83, 0.73 to 0.95, P=0.006) and optimal sleep (0.73, 0.60 to 0.88, P=0.001) demonstrated significant independent inverse associations with IBS incidence. No significant interactions were observed between these associations and age, sex, employment status, geographic location, gastrointestinal infection, endometriosis, family history of IBS or lifestyle behaviours.

Conclusions Adhering to a higher number of healthy lifestyle behaviours is significantly associated with a lower incidence of IBS in the general population. Our findings suggest the potential of lifestyle modifications as a primary prevention strategy for IBS.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Currently, there is no established primary prevention strategy for irritable bowel syndrome (IBS).

⇒ Previous studies showed that five modifiable lifestyle factors, including smoking, sleeping, physical activity, diet and alcohol consumption are associated with IBS. However, their combined association with the incidence of IBS is currently unknown.

⇒ Current guidelines do not recommend any lifestyle modification interventions as primary prevention measures for IBS.

WHAT THIS STUDY ADDS

⇒ Adhering to a higher number of the five healthy lifestyle behaviours is significantly associated with a lower IBS incidence in a middle-aged population.

⇒ Our findings suggest the potential of lifestyle modifications as a primary prevention strategy for IBS.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The individual or combined effect of the five healthy lifestyle behaviours on IBS incidence will guide further basic research on discovering potential underlying mechanisms.

⇒ Coordinated efforts and support at individual and community levels are required to promote the adoption of the five beneficial lifestyle behaviours among the general population for IBS prevention and for other health benefits.

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterised by recurrent abdominal pain and disordered bowel habits with abnormal stool form or frequency.[1] IBS affects 5% to 10% of the population worldwide[2] and causes substantial annual direct and indirect expenditure related to disease management in various countries.[3–5]

Although the pathophysiology of IBS is not fully understood, the dysfunction of the gut–brain axis, which causes intestinal motility disturbances, visceral hypersensitivity and altered processing in the central nervous system, is well recognised.[6] Current treatments for IBS only aim to improve troublesome symptoms of abdominal pain and bowel habits, but they are either of uncertain efficacy or have adverse events.[6] Patients with IBS often report experiencing comorbid psychiatric disorders,[7] heightened thoughts of suicide because of their symptoms[8] and lower quality of life.[9] Finding a primary prevention strategy for IBS is essential for reducing its disease burden.

In previous studies, some modifiable lifestyle factors, including smoking,[10] sleeping,[11] physical activity,[11] diet[12] and alcohol consumption,[13 14] were found to be independently associated with IBS. It can be hypothesised that the combination of these healthy lifestyle behaviours might also protect against the occurrence of IBS. We assessed the combined association of the above-mentioned five healthy lifestyle behaviours—never smoking, optimal sleep, high level of vigorous physical activity, high dietary quality and moderate alcohol intake—with the incidence of IBS in a large prospective cohort from the UK Biobank.

METHODS

Study setting and participants

The UK Biobank study is a large-scale prospective cohort study that recruited 502 492 participants aged 37 to 73 years by sending invitation letters to their homes between 2006 and 2010. The participants completed a touchscreen questionnaire and a verbal interview on demographics, health and lifestyles as baseline assessments at one of 22 assessment centres throughout the UK. They also provided biological samples and received physical examinations. The participants were followed up to update their health status. The details of the UK Biobank study have been described elsewhere.[15 16]

For the assessment of dietary habits, de Boer *et al* recommended administering 24-hour dietary recall questionnaires on at least two non-consecutive days,[17] and this approach has shown acceptable reproducibility.[18] Following this suggestion, we included only participants who completed at least two 24-hour dietary recall questionnaires (n=126 841, including alcohol intake assessment) from the whole cohort. Participants reporting unrealistic energy intake (outside the range of 800–5000 kcal/day for men and 500–4000 kcal/day for women, n=200),[19] participants who were missing data on any of the five lifestyle behaviours (physical activity, n=17 900; smoking, n=170; sleeping, n=266) or key covariates (employment status, n=131; family history of IBS, n=41 020) and participants with prevalent IBS at baseline (n=2886) were excluded to reduce the probability of inferential bias. Ultimately, 64 286 participants were included in the analysis (figure 1).

Ascertainment of exposure

The five healthy lifestyle behaviours were never smoking, optimal sleep, high level of vigorous physical activity, high dietary quality and moderate alcohol intake. The participants were grouped based on how many of the five healthy lifestyle behaviours they had (0, 1, 2 or 3 to 5). The relatively small number of individuals who had 3 (n=11 079), 4 (n=2767) and 5 (n=255) healthy lifestyle behaviours were pooled together as a single group to increase the sample size for analysis. All the lifestyle behaviours were assessed using structured questionnaires on a self-report basis. Details can be found in online supplemental text S1.

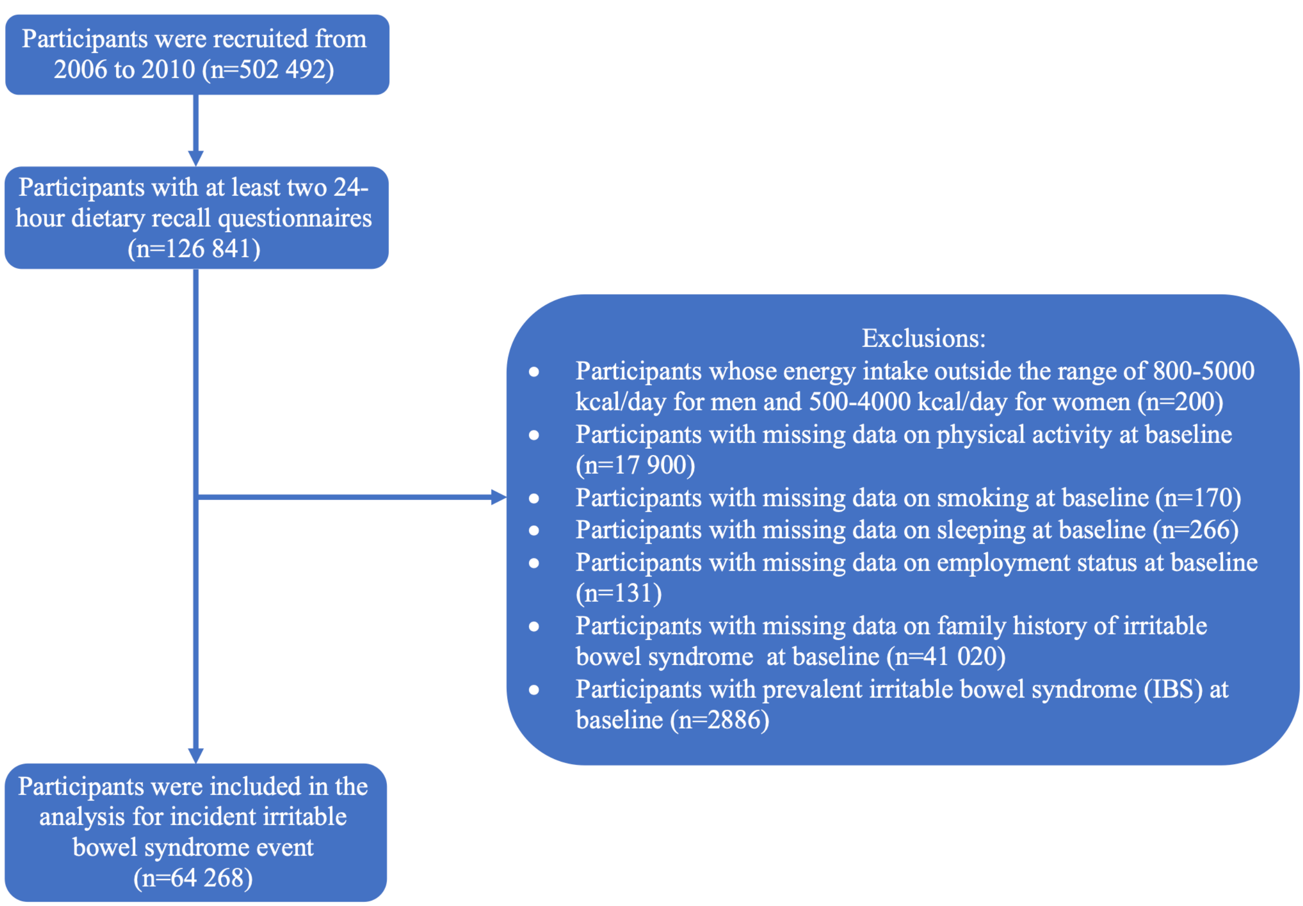

Figure 1 Flow chart of UK Biobank participants

Ascertainment of outcome

The outcome of interest of the study was the incidence of IBS, which was defined as code K58 under the International Classification of Diseases, 10th revision (ICD-10) after baseline assessment. The UK Biobank has summarised the dates of the first occurrences of a range of health-related outcomes mapped to ICD-10 codes from various sources, including primary care data, hospital inpatient data, death register records and self-reported medical conditions (online supplemental text S1), which are updated regularly. Therefore, the date when the diagnosis of IBS was first made could be identified.

Ascertainment of covariates

A number of covariates associated with healthy lifestyle behaviours and/or IBS were determined by reviews of relevant observational studies, systematic reviews and consensus reports (online supplemental table S1). These covariates included sociodemographic factors (age, sex, body mass index (BMI), geographic location, marital status and employment status) and medical factors (depression, anxiety, back pain or joint pain, headaches, osteoporosis, asthma, gastrointestinal infection, endometriosis, ectopic pregnancy and family history of IBS). The sociodemographic covariates were assessed using a touchscreen questionnaire at baseline in assessment centres and family history of IBS was collected using a web-based digestive health questionnaire during the follow-up period. The baseline status of existing diseases was confirmed through primary care data, hospital inpatient data, death register records and self-reported medical conditions, with dates of their first occurrence recorded. Details of these assessments and data linkages are available on the UK Biobank website (www.ukbiobank.ac.uk).

Patient and public involvement

The analysis was based on data from the UK Biobank, which included extensive public consultation in its design. Patients were not involved in setting the research question or the outcome measures, nor were they involved in developing plans for the design or implementation of the study. No patients were asked to advise on the interpretation or writing up of the results.

Statistical analyses

Baseline characteristics were described across the number of healthy lifestyle behaviours. Continuous variables were presented as the mean (SD) and compared among groups using analysis of variance test or Welch test, as appropriate. Categorical variables were presented as the number (percentage) and compared among groups using X^2 test or Fisher's exact test, as appropriate. At the time of analysis, the UK Biobank data were available up to 1 February 2022, so this date was considered the end of the study. Person years of follow-up were computed from the first interview at baseline until the occurrence of IBS, death, loss of follow-up or the end of the study, whichever occurred first.

Cox proportional hazard models were used to estimate the hazard ratios and 95% confidence intervals for the associations between healthy lifestyle behaviours and the incidence of IBS. To improve confounding control in the analysis process, observational studies often employ data-driven approaches to adjust seemingly related covariates, but inappropriate confounder selection and adjustment (eg, failing to adjust for a confounder or inappropriately adjusting a collider or mediator) might unwittingly introduce more bias and impair the validity of results.[20] To improve the confounder selection process, a graphical tool called directed acyclic graphs (DAGs) has been introduced.[21] DAGs have several advantages over traditional statistical approaches for appropriate confounder selection. First, DAGs provide a visual representation of causal relations between the exposure variable, the outcome variables and other variables that play a role in the causal question of concern.[22] In this way, DAGs enable researchers to identify different types of biases (eg, confounding, selection, overadjustment and detection bias) more efficiently and to consider them early in the study design and subsequent data analysis process.[22] Second, when confounding control is not adequate, DAGs can help researchers identify the bias and assess its direction in specific situations.[23 24] Third, DAGs provide a more comprehensive and transparent process to select confounders. Traditional statistical approaches may not fully capture the intricate interrelationships between variables, which could result in the omission of important confounders and the subsequent introduction of potential bias into the estimate of causal effects.[25] However, DAGs summarise prior knowledge on the complex inter-relationships between variables; they identify and adjust for confounders based on causal relationships rather than relying solely on statistical associations.[26] Each pair of causal relationships is systematically assessed and explicitly documented; supporting evidence is provided when needed, allowing for high transparency and reproducibility.[27]

We decided to use the DAG method, given the benefits stated above. We constructed a DAG to summarise prior knowledge of the causal relationships between healthy behaviours, IBS and their covariates to guide potential confounder selection.[28] The construction of the DAG followed the evidence synthesis for constructing directed acyclic graphs protocol, which integrates evidence synthesis strategies and causal inference principles.[27] Briefly, a pool of covariates related to healthy lifestyle behaviours and/or IBS was determined by a series of systematic literature reviews on: (i) observational studies on the healthy lifestyle behaviours–IBS relationship; (ii) systematic reviews on IBS and (iii) consensus reports on IBS from several databases. Furthermore, the relationship between every pair of variables in the DAG was assessed by sequential causal criteria, including temporality, validity and theoretical support. More information about the building of DAGs can be found in online supplemental text S2and Online supplemental figure S1.'

The proposed DAG in online supplemental figure S2 was found to be consistent with the UK Biobank data and it indicated that adjustments should be made for the following covariates when estimating the association between healthy behaviours and the incidence of IBS: age (<40, 40–49, 50–59 or ≥60 years), sex (female or male), employment status (in paid employment or self-employed or not employed), geographic location (England area or non-England area, including Wales and Scotland), gastrointestinal infection (yes or no), endometriosis (yes or no) and family history of IBS (yes or no). The proportional hazards assumption of the models was tested using Schoenfeld residuals, and no significant deviation from the assumption was found.

Subgroup analyses by age, sex, employment status, geographic location, gastrointestinal infection and endometriosis were conducted to examine potential modifying effects. Interaction was assessed by including a product term of one of the stratifying variables with healthy lifestyle behaviours in the model.

We also performed several sensitivity analyses. First, we excluded participants whose IBS diagnosis was made solely based on self-report. Second, we applied a different definition for healthy alcohol drinking behaviours: instead of moderate alcohol drinking, only those who abstained from alcohol were considered to be healthy. Third, we used a looser definition for a healthy level of physical activity following the UK Chief Medical

Table 1 Baseline characteristics of the study participants by the number of healthy lifestyle behaviours*

Characteristics	Overall (n=64 268)	Number of healthy lifestyle behaviours 0 (n=7604)	1 (n=20 662)	2 (n=21 901)	3–5 (n=14 101)	P value
Mean (SD) age (years)	55.9 (7.7)	57.0 (7.4)	56.1 (7.6)	55.6 (7.7)	55.3 (7.8)	<0.001
Female	35 342 (55.0)	3643 (47.9)	11 027 (53.4)	12 244 (55.9)	8428 (59.8)	<0.001
Mean (SD) BMI (kg/m^2)	26.5 (4.4)	27.8 (4.9)	26.9 (4.6)	26.2 (4.3)	25.4 (3.9)	<0.001
England area	58 633 (91.2)	6920 (91.0)	18 894 (91.4)	19 977 (91.2)	12 842 (91.1)	0.551
Married	51 565 (80.4)	5967 (78.6)	16 411 (79.6)	17 723 (81.0)	11 464 (81.4)	<0.001
Paid employment or self-employment	40 829 (63.5)	4599 (60.5)	13 182 (63.8)	14 015 (64.0)	9033 (64.1)	<0.001
Family history of IBS	9707 (15.1)	1168 (15.4)	3203 (15.5)	3340 (15.3)	1996 (14.2)	0.004
Depression	8496 (13.2)	1309 (17.2)	2944 (14.2)	2743 (12.5)	1500 (10.6)	<0.001
Anxiety	1778 (2.8)	243 (3.2)	619 (3.0)	606 (2.8)	310 (2.2)	<0.001
Back pain or joint pain	19 869 (39.3)	3007 (49.4)	6812 (42.2)	6533 (38.1)	3517 (31.5)	<0.001
Headaches	5411 (12.8)	697 (15.3)	1878 (14.2)	1826 (12.6)	1010 (10.3)	<0.001
Osteoporosis	1070 (1.7)	143 (1.9)	336 (1.6)	356 (1.6)	235 (1.7)	0.465
Asthma	7510 (11.7)	968 (12.7)	2466 (11.9)	2569 (11.7)	1507 (10.7)	<0.001
Gastrointestinal infection	1109 (1.7)	155 (2.0)	335 (1.6)	391 (1.8)	228 (1.6)	0.067
Endometriosis	953 (1.5)	113 (1.5)	314 (1.5)	306 (1.4)	220 (1.6)	0.6
Ectopic pregnancy	137 (0.2)	16 (0.2)	44 (0.2)	46 (0.2)	31 (0.2)	0.998
Lifestyle behaviours:						
Never smoking	37 653 (58.6)	0 (0.0)	9380 (45.4)	15 746 (71.9)	12 527 (88.8)	<0.001
Optimal sleep	11 505 (17.9)	0 (0.0)	1418 (6.9)	4089 (18.7)	5998 (42.5)	<0.001
Mean (SD) physical activity (MET-h/week)	39.8 (38.2)	22.8 (24.1)	33.2 (35.3)	43.7 (39.5)	52.5 (41.2)	<0.001
High level of vigorous physical activity (>median, MET-h/week)	31 136 (48.4)	0 (0.0)	6249 (30.2)	13 116 (59.9)	11 771 (83.5)	<0.001
Mean (SD) alcohol intake (g/day)	17.7 (19.9)	26.2 (24.9)	20.0 (21.7)	16.3 (18.4)	12.2 (13.0)	<0.001
Moderate alcohol intake (5–15 g/day)	13 986 (21.8)	0 (0.0)	1704 (8.2)	5062 (23.1)	7220 (51.2)	<0.001
Mean (SD) DASH diet score (range, 8–38)	23.0 (4.8)	20.6 (3.7)	21.7 (4.2)	23.3 (4.7)	25.9 (4.8)	<0.001
High dietary quality (highest quartile of DASH diet score)	15 764 (24.5)	0 (0.00)	1911 (9.2)	5789 (26.4)	8064 (57.2)	<0.001

*Values are numbers (percentages) unless stated otherwise.
BMI, body mass index; DASH, Dietary Approaches to Stop Hypertension; IBS, irritable bowel syndrome; MET, metabolic equivalent task.

Officers' Physical Activity Guidelines,[29] according to which performing moderate physical activity for 150 min or more per week or vigorous physical activity for 75 min or more per week is recommended. Participants who met either of these recommendations were considered to have a healthy level of physical activity. Fourth, as a sensitivity analysis, we repeated our analysis by including participants who completed at least one dietary questionnaire. Finally, to explore the individual impact of each of the five lifestyle behaviours, we conducted separate analyses for each while adjusting the models for the other behaviours.

All the analyses were performed using IBM SPSS Statistics software version 26.0 (IBM Corporation, Armonk, New York, USA). All the tests were two-sided, with P<0.05 considered statistically significant.

RESULTS

Baseline characteristics

Table 1 presents the baseline characteristics of the study participants across the number of healthy lifestyle behaviours they had. Among the 64 268 participants (mean age 55.9 years, 55.0% female), 7604 (11.8%) had none of the 5 studied healthy lifestyle behaviours, 20 662 (32.1%) had 1 behaviour, 21 901 (34.1%) had 2 behaviours and 14 101 (21.9%) had 3 to 5 behaviours. In comparison with participants who did not perform any of the five healthy lifestyle behaviours, those who adhered to 3 to 5 behaviours were more likely to be younger, female, have a lower BMI, married and in paid employment or self-employed and less likely to have a family history of IBS. In addition, they had a lower prevalence of depression, anxiety, back pain or joint pain, headaches, asthma and gastrointestinal infection. The two comparison groups had similar baseline prevalence of osteoporosis, endometriosis and ectopic pregnancy. Participants excluded from the analysis because of missing information had similar adherences to the five healthy lifestyle behaviours to those of the participants included, with similar age, BMI, percentage of female participants, geographic location (living in England), marital status (being married), IBS family history (yes) and prevalent diseases, although they were less likely to be in paid employment or self-employed (online supplemental table S2).

Healthy lifestyle behaviours and IBS

During a mean follow-up of 12.6 years, 961 (1.5%) incident IBS cases were recorded. In table 2, after adjusting for age (<40, 40–49, 50–59 or ≥60 years), sex (female or male), employment status (in paid employment or self-employed or not), geographic location (England or non-England area, including Wales and Scotland), gastrointestinal infection (yes or no), endometriosis (yes or no) and family history of IBS (yes or no), we found that adherence to a higher number of healthy lifestyle behaviours was significantly associated with a lower risk of incident IBS (all P<0.05). Compared with not performing any of the five healthy lifestyle behaviours, the adjusted hazard ratios associated with adhering to 1, 2 and 3 to 5 behaviours were 0.79 (0.65 to 0.96), 0.64 (0.53 to 0.78) and 0.58 (0.46 to 0.72), respectively (P for trend <0.001).

Table 2 Associations between healthy lifestyle behaviours and the risk of incident irritable bowel syndrome (IBS)*

	Number of healthy lifestyle behaviours†				
	0	1	2	3–5	P value for trend
No. of participants	7604 (11.8)	20 662 (32.1)	21 901 (34.1)	14 101 (21.9)	
Person years	95 763	260 868	277 306	178 802	
No. of IBS events	153 (2.0)	339 (1.6)	297 (1.4)	172 (1.2)	
Adjusted hazard ratio‡ (95% CI)	1 (reference)	0.79 (0.65 to 0.96)	0.64 (0.53 to 0.78)	0.58 (0.46 to 0.72)	<0.001

*Values are numbers (percentages) unless stated otherwise
†Healthy lifestyle behaviours included never smoking, a high level of vigorous physical activity (in the highest 50% of the cohort), high dietary quality (in the highest quartile of the Dietary Approaches to Stop Hypertension diet score), moderate alcohol intake (5–15 g/day) and optimal sleep (having a sleep duration of between 7 and 9 h/day, finding it fairly easy or very easy to get up in the morning and never or rarely having insomnia and narcolepsy).
‡Hazard ratios were adjusted for age (<40, 40–49, 50–59 or ≥60 years), sex (female or male), employment status (in paid employment or self-employment or not), geographic location (England area or non-England area, including Wales and Scotland), gastrointestinal infection (yes or no), endometriosis (yes or no) and family history of IBS (yes or no).

Subgroup, sensitivity and separate analyses

We conducted subgroup analyses by age, sex, employment status, geographic location, gastrointestinal infection, endometriosis and family history of IBS to identify potential effect modifiers, but no significant interactions were found (all P for interaction ≥0.05; table 3). In the sensitivity analysis excluding participants whose IBS diagnosis was made solely based on self-report (n=85), the estimates of the association were similar to those of the main analysis shown in Table 2 (online supplemental table S3). However, in both the sensitivity analysis considering zero alcohol consumption as a healthy drinking behaviour (online supplemental table S4) and the sensitivity analysis of relaxing the definition of a healthy level of physical activity for those who met the recommendation of moderate or vigorous physical activity (online supplemental table S5), the estimates of the association were weakened slightly compared with the main analysis. After relaxing the eligibility criteria from completing at least two dietary questionnaires to one, the number of participants included in the analysis increased from 64 268 to 85 937 (online supplemental figure S3). Similar to the main analysis, such sensitivity analysis showed that adherence to a higher number of healthy lifestyle behaviours was significantly associated with a

Table 3 Associations between healthy lifestyle behaviours and the risk of incident irritable bowel syndrome (IBS) stratified by subgroups

	Adjusted hazard ratio* (95% CI)					
	Number of healthy lifestyle behaviours†					
Subgroups	0	1	2	3 to 5	P value for trend	P value for interaction
Age:						0.52
40–49 (n=15 394)	1 (reference)	0.66 (0.45 to 0.97)	0.51 (0.34 to 0.75)	0.45 (0.29 to 0.70)	<0.001	
50–59 (n=24 113)	1 (reference)	0.73 (0.54 to 0.99)	0.58 (0.42 to 0.79)	0.57 (0.40 to 0.80)	<0.001	
≥60 (n=24 761)	1 (reference)	0.96 (0.70 to 1.33)	0.85 (0.61 to 1.18)	0.69 (0.48 to 1.01)	0.03	
Sex:						0.21
Female (n=35 342)	1 (reference)	0.75 (0.60 to 0.94)	0.61 (0.48 to 0.77)	0.50 (0.39 to 0.65)	<0.001	
Male (n=28 926)	1 (reference)	0.88 (0.61 to 1.25)	0.72 (0.50 to 1.04)	0.81 (0.54 to 1.21)	0.16	
Employment status:						0.46
Not in paid employment or self-employment (n=23 439)	1 (reference)	0.88 (0.65 to 1.19)	0.63 (0.46 to 0.86)	0.54 (0.38 to 0.77)	<0.001	
Paid employment or self-employment (n=40 829)	1 (reference)	0.74 (0.58 to 0.95)	0.66 (0.51 to 0.85)	0.60 (0.46 to 0.80)	<0.001	
Geographic location:						0.22
Non-England area (n=5635)	1 (reference)	0.90 (0.47 to 1.72)	0.42 (0.20 to 0.87)	0.67 (0.32 to 1.38)	0.06	
England area (n=58 633)	1 (reference)	0.78 (0.64 to 0.95)	0.67 (0.54 to 0.81)	0.57 (0.45 to 0.71)	<0.001	
Gastrointestinal infection:						0.98
No (n=63 159)	1 (reference)	0.79 (0.65 to 0.96)	0.65 (0.53 to 0.79)	0.58 (0.46 to 0.72)	<0.001	
Yes (n=1109)	1 (reference)	0.77 (0.26 to 2.30)	0.53 (0.17 to 1.64)	0.54 (0.15 to 1.90)	0.24	
Endometriosis:						0.05
No (n=63 315)	1 (reference)	0.77 (0.63 to 0.93)	0.62 (0.51 to 0.75)	0.58 (0.46 to 0.72)	<0.001	
Yes (n=953)	1 (reference)	2.20 (0.49 to 9.85)	2.90 (0.67 to 12.64)	0.54 (0.08 to 3.85)	0.60	
Family history of IBS:						0.27
No (n=54 561)	1 (reference)	0.75 (0.59 to 0.96)	0.68 (0.53 to 0.86)	0.54 (0.41 to 0.71)	<0.001	
Yes (n=9707)	1 (reference)	0.86 (0.63 to 1.18)	0.58 (0.42 to 0.81)	0.64 (0.45 to 0.92)	0.001	

*Hazard ratios were adjusted for age (<40, 40–49, 50–59 or≥60 years), sex (female or male), employment status (in paid employment or self-employment or not), geographic location (England area or non-England area, including Wales and Scotland), gastrointestinal infection (yes or no), endometriosis (yes or no), and family history of IBS (yes or no).
†Healthy lifestyle behaviours included never smoking, a high level of vigorous physical activity (in the highest 50% of the cohort), high dietary quality (in the highest quartile of the Dietary Approaches to Stop Hypertension diet score), moderate alcohol intake (5–15 g/day), and optimal sleep (having a sleep duration between 7 and 9 h/day, finding it fairly easy or very easy to get up in the morning, and never or rarely having insomnia and narcolepsy).

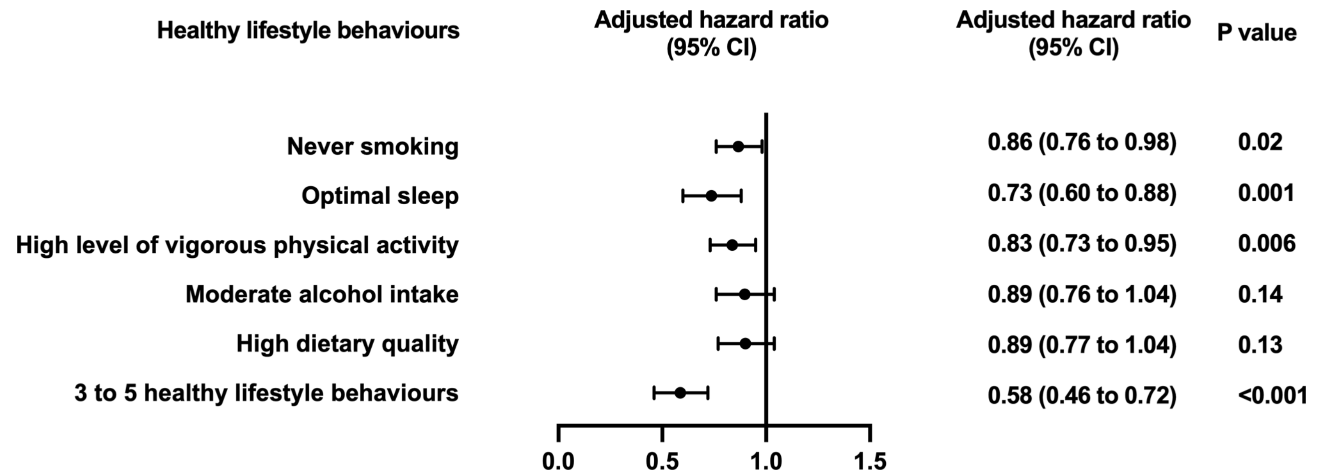

Figure 2 Associations of each healthy lifestyle behaviour with the risk of irritable bowel syndrome (IBS). Healthy lifestyle behaviours included never smoking, a high level of vigorous physical activity (in the highest 50% of the cohort), high dietary quality (in the highest quartile of the dietary approaches to stop hypertension diet score), moderate alcohol intake (5–15 g/day) and optimal sleep (having a sleep duration between 7 and 9 h/day, finding it fairly easy or very easy to get up in the morning, and never or rarely having insomnia and narcolepsy). Hazard ratios were adjusted for age (<40, 40–49, 50–59 or ≥60 years), sex (female or male), employment status (in paid employment or self-employed or not), geographic location (England area or non-England area, including Wales and Scotland), gastrointestinal infection (yes or no), endometriosis (yes or no) and family history of IBS (yes or no). The healthy lifestyle behaviours were also adjusted for each other: never smoking (yes or no), optimal sleep (yes or no), a high level of vigorous physical activity (yes or no), moderate alcohol (yes or no) and high dietary quality (yes or no); 'no' was the reference group for each behaviour. For estimates of the association between adhering to 3 to 5 healthy lifestyle behaviours, the reference group comprised those who did not perform any of the behaviours.

lower risk of incident IBS (all $P<0.05$; online supplemental table S6), although the estimate of association was slightly weakened. Nevertheless, the 95% CIs of all three adjusted hazard ratios (1, 2 and 3 to 5 healthy lifestyle behaviours) in the two samples were overlapping. Finally, in separate analyses of each of the five lifestyle behaviours, never smoking (0.86, 0.76 to 0.98, P=0.02), high level of vigorous physical activity (0.83, 0.73 to 0.95, P=0.006) and optimal sleep (0.73, 0.60 to 0.88, P=0.001) demonstrated significant independent inverse associations with the incidence of IBS, although of a smaller magnitude than adhering to 3 to 5 behaviours (figure 2). No significant independent associations were observed for healthy diet and moderate alcohol consumption, but their effect sizes were very close to being statistically significant (figure 2).

DISCUSSION

Our analysis showed that adopting a combination of healthy lifestyle behaviours—never smoking, optimal sleep, high level of vigorous physical activity, high dietary quality and moderate alcohol intake—was significantly associated with a lower risk of subsequent incident IBS even when we adjusted for potential confounders. This primary finding was further supported in subgroup analyses, which indicated that age, sex, employment status, geographic location, gastrointestinal infection and endometriosis did not substantially modify the estimated hazard ratios. To the best of our knowledge, this is one of the first prospective cohort studies to confirm the causal relationship between combinations of healthy lifestyle behaviours and subsequent lower incidence of IBS. These results are consistent with those of a recent cross-sectional study among 3363 Iranian adults, which found that an overall healthy lifestyle was associated with a lower prevalence of IBS.[30]

Consensus reports have provided recommendations on the diagnosis and treatment of IBS, but none of them have recommended any preventive measures.[31–33] Although lifestyle modification is recommended as a means of managing IBS symptoms,[6 31–33] its potential role in preventing the onset of the condition has not been given due attention. IBS has a complex aetiology, involving biological, genetic, psychosocial and environmental factors.[6 34] Our findings underscore the value of lifestyle modification in the primary prevention of IBS and suggest that healthy lifestyle choices could significantly attenuate the effects of aetiological factors on the incidence of IBS.

To prevent IBS, it is important for primary healthcare providers to take an active role in delivering appropriate interventions to change health behaviours during routine consultations, as they are often the first point of contact for patients accessing the health system.[35 36] Moreover, support from national and local authorities is required to establish a supportive macroenvironment for changing unhealthy lifestyle behaviours or maintaining healthy behaviours.[37] Coordinated efforts are required at many levels to promote the adoption of the five recommended lifestyle behaviours among the general population for prevention of IBS.

Previous studies have assessed the individual impact of each of the five healthy lifestyle behaviours on the incidence of IBS. The role of smoking in causing IBS is a subject of debate.[38] Our study found that never smoking was independently associated with a lower incidence of IBS. Although existing studies suggest this might be due to smoking's effect on delaying the gastric emptying of food and mouth–caecum transit time,[39 40] this hypothesis needs to be tested in more up-to-date mechanistic studies. Meanwhile, it is widely acknowledged that the pathogenesis of IBS involves dysregulated communication between the gut and the brain via the gut–brain axis.[6] Several prospective cohort studies found that the gut–brain pathway is bidirectional, showing that anxiety and depression could predict the development of IBS and vice versa.[41 42] Furthermore, previous studies have indicated that individuals with mental illness have significantly higher smoking rates than those without.[43 44] Nearly half of the 148 studies, which included a systematic review, indicated an association between baseline anxiety or depression and subsequent smoking behaviours.[45] According to these findings, smoking may be a surrogate for mental health conditions and mediate the association between mental health conditions and the risk of IBS. While no research to date has provided direct evidence to deal with this question, further research is needed to explore the potential mediating role of smoking in the relationship between mental health and IBS incidence.

Our research revealed that optimal sleep is significantly associated with a reduction in IBS incidence, which is consistent with the findings of an earlier meta-analysis of 36 observational studies.[46] This meta-analysis revealed a high pooled prevalence of sleep disorders (37.6%) among patients with IBS and a strong and significant association between sleep disorders and IBS, with a pooled OR of 2.618.[46] Sleep disturbance could cause an upregulation of inflammatory cytokines such as interleukin-1 and interleuking-6,[47] which can negatively affect the neural control of gastrointestinal motor, sensory and secretory functions.[6] Changes in the levels of these cytokines have been observed in some gastrointestinal diseases, including IBS.[47] This might explain why quality sleep plays a crucial role in preventing the development of IBS.

Although our study found that both moderate and vigorous physical activity were inversely associated with incident IBS, the sensitivity analysis revealed that vigorous intensity outperformed moderate intensity exercise. The benefits of exercise, such as reducing intestinal inflammation and regulating the gut microbiota, might explain the underlying mechanisms of its effect on lowering the risk of IBS.[48] These mechanisms might be more effectively activated by vigorous physical activity; however, these observations require further investigations in future studies.

In contrast to the findings of a cross-sectional study in Iran,[12] our study did not find an independent association between dietary quality and the incidence of IBS, but the result is very close to statistical significance. The DASH diet emphasises a high intake of fruits, vegetables and legumes, which are rich in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs).[49] The fermentative and osmotic effects of FODMAPs may contribute to IBS symptoms such as diarrhoea and bloating.[49] A low-FODMAP diet has been shown to effectively improve IBS symptoms[50] and has been recommended as an IBS self-management strategy.[32] However, our study participants were IBS-free at baseline, and hence, it is reasonable to assume that they had a relatively healthy gut environment and normal gastrointestinal function relative to patients with IBS. This might partly explain why adherence to the DASH diet did not have a significant protective or harmful effect on the development of IBS in our study.

Research has suggested that alcohol consumption can affect gastrointestinal motility, absorption and intestinal permeability in both animals and humans.[51] However, our results showed that moderate alcohol consumption, similar to the DASH diet, was not associated with IBS incidence. This finding is in agreement with a previous case–control study.[52] Among the five healthy behaviours investigated, DASH diet adherence and moderate alcohol intake had the weakest links to IBS prevention, but their combined effect with the remaining three behaviours was significant. Given the other benefits of these behaviours beyond IBS prevention, adherence to all five positive lifestyle factors is still prudent.

Strengths and limitations

Our study has several strengths. First, the use of a population-based cohort data from the UK Biobank allowed us to demonstrate the positive real-world impact of a healthy lifestyle in reducing IBS incidence. Second, the large sample size and sufficiently long follow-up duration provided adequate statistical power for examining the causal relationship between healthy lifestyle behaviours and incident IBS over a decade. Finally, the use of a DAG provided a transparent and evidence-based approach to guide the appropriate selection of potential confounders based on prior knowledge of the possible causal relationships between healthy lifestyle behaviours, IBS and their covariates.

This study also has some limitations. First, as mentioned previously, only participants who completed at least two dietary questionnaires were included in this study. We compared the baseline characteristics between participants with and without at least two dietary questionnaires. While the two groups were similar in almost all aspects, there were statistically significant differences in most characteristics between these two groups (online supplemental table S7). This difference was clearly due to the very large sample sizes in both groups, of which high statistical power would cause the P values to rapidly approach zero, but indeed, there was no meaningful practical significance between these two groups. In this scenario, we followed existing recommendations to focus on the practical significance rather than the statistical significance of P values when considering their differences.[53 54] Based on the figures presented in online supplemental table S7), we observed no substantial practical difference between the two groups, and hence our current sample was not at risk of selection bias within the UK Biobank cohort.

Second, a large portion of participants was excluded owing to missing data on the family history of IBS (n=41 020). This is because the data were collected using a web-based digestive health questionnaire during the follow-up period, which was sent out to participants who provided a valid email address (n=331 832, 66% of the entire UK Biobank cohort) in 2017, and only about half (n=172 949, 52.1%) fully completed the questionnaire as of July 2018.[55] Moreover, this exclusion is supported by a previous study using data from the UK Biobank cohort, which found that people with a family history of IBS had a 3.7-fold increased risk of having IBS compared with those without.[56]

Third, the use of self-reported data on lifestyle behaviours might raise concerns about data accuracy. However, the high comprehension and acceptability indicated by participants in pilot studies might dispel that concern.[57] Moreover, it is worth noting that self-reported data have been used to measure lifestyle factors in many similar large-scale population-based studies.[58 59]

Fourth, as one of the lifestyle behaviours of interest, sleep quality was self-reported at baseline in our study. However, discrepancies have been found between subjective self-reported sleep experience and objective sleep measurements among patients with sleep problems in previous studies.[60–62] Individuals with only self-reported sleep disturbances are more likely to overestimate sleep onset latency (ie, the time taken to fall asleep) and underestimate total sleep time.[60 63] Therefore, in our analysis, the quality of sleep might be underestimated among participants. Future research should use both self-reported data and objective measurements (eg, polysomnography) to assess sleep quality.

Fifth, when comparing the baseline characteristics of study participants whose IBS diagnosis was made based on different data sources, we found that participants whose IBS diagnosis was made solely based on self-report data were more likely employed and were less likely to have back pain or joint pain and headaches than participants whose IBS diagnosis was retrieved from a trustworthy data source (ie, primary care data, hospital inpatient or death register records), with no significant differences found in other characteristics (online supplemental table S8). However, the sensitivity analysis in which participants whose IBS diagnosis was made solely based on self-report (n=85) were excluded found similar estimates of the association between healthy lifestyle behaviours and the risk of developing IBS (online supplemental table S3), compared with the main analysis in table 2, which included cases of incident IBS from both self-reported data and the trustworthy data source. The similarity suggested that differences in some of the baseline characteristics between these two groups did not have a substantial impact on the effect estimate of interest.

Sixth, we only used ICD-10 code K58 to identify the outcome of incident IBS, and the symptom-based diagnostic criteria of Rome III were not applied. However, the process of outcome ascertainment can still be considered trustworthy because the majority of incident IBS cases were confirmed based on reliable clinical diagnostic data from primary care, hospital inpatient or death register records. In addition, when compared with the updated Rome IV IBS diagnostic criteria, the benefits of using the Rome III criteria are limited owing to their excessive sensitivity, which would inflate the prevalence of IBS.[64]

Seventh, gastrointestinal infection is one of the important risk factors for developing IBS, and our DAG also indicated that it was one of the confounders that should be adjusted when evaluating the association between healthy lifestyle behaviours and incident IBS. In our study, the confounding effect of baseline gastrointestinal infection was eliminated when estimating the effects of healthy lifestyle behaviours on the risk of developing IBS, but subsequent infections were not adjusted, and this might remain a confounder in our analysis.

The eighth limitation is the lack of consideration for changes in healthy lifestyle behaviours during the follow-up period. Future longitudinal studies with repeated measurements are needed to examine the cumulative exposure over time and verify the combined benefit of healthy lifestyle factors in preventing IBS.

Finally, a meta-analysis on IBS found that individuals aged 50 years and older had a lower prevalence of IBS (OR= 0.75; 95% CI 0.62 to 0.92) than those under 50.[65] However, this prospective cohort study was based on the UK Biobank cohort, which only consists of middle-aged and older people with an average age of 55.9 years. Therefore, caution should be exercised when extrapolating the findings to younger populations.

POTENTIAL FUTURE RESEARCH

In addition to the focal association between healthy lifestyle behaviours and IBS, we observed some interesting potential associations that require further investigations. First, we found that the percentage of women increased across the number of healthy lifestyle behaviours (table 1). Most women in our study were postmenopausal, and there are several possible health-related reasons motivating them to choose a more healthy lifestyle: (i) improve menopausal symptoms[66] and (ii) reduce the risk of developing breast cancer.[67] It is unlikely that this gender difference is linked to the presence of osteoarthritis, as its prevalence across men and women is similar.[68] Future studies may explore other possible gender-differentiated factors associated with choosing healthy lifestyles in middle-aged populations.

Another interesting finding is that the percentage of baseline depression decreases across the number of healthy behaviours (table 1). The relationship between depression and healthy lifestyle behaviours has been a subject of interest in various studies. Research has demonstrated an inverse relationship between depression and healthy lifestyle behaviours.[69] This observation aligns with a previous prospective cohort study of 667 participants with coronary heart disease, which found that there was a bidirectional relationship between depressive symptoms and lifestyle behaviours.[70] Other studies suggest that individuals with depression might have specific health-related beliefs and behaviours that influence their adherence to a healthy lifestyle.[71] Additionally, studies have found that depression is negatively correlated with health-promoting behaviours, indicating that individuals with depression might engage in fewer health-promoting activities.[72] Further studies should be conducted to confirm or refute the bidirectional relationship between healthy behaviours and depression among the general population.

Moreover, the percentage of participants who had a high level of vigorous physical activity increased while the mean age of participants slightly decreased across the number of healthy behaviours (table 1). If the association truly exists, osteoarthritis (OA), an age-related disease,[73] is probably one of the reasons explaining this observation. An existing study investigating the experience of living with knee OA showed that it can lead to negative attitudes and perceptions about physical activity due to activity limitations and the impact on functional performance.[74] This is further supported by the finding that a large proportion of individuals with OA involving the hips or knees are sedentary,[75] explaining our observation that OA might be a reason for the lower physical activity level among older participants. The potential association between age, vigorous physical activity, and their covariates, including OA, is an area requiring further investigation.

In this study, age, sex, employment status, geographical location, gastrointestinal infection, endometriosis and family history of IBS were treated as confounders and adjusted when evaluating the association between healthy lifestyle behaviours and the risk of developing IBS (ie, the association of interest). Moreover, we assessed if they were effect modifiers on the association of interest, but no significant results were found. However, as they were not our exposure of interest in this study, we did not estimate their effects on the risk of incident IBS. Previous studies with different populations reported these effect estimates.[76–80] Future studies can repeat these analyses using the UK Biobank cohort data to allow comparison.

CONCLUSIONS

This study provides evidence that adherence to a higher number of healthy lifestyle behaviours—never smoking, optimal sleep, high level of physical activity, high dietary quality and moderate alcohol intake—is significantly associated with a lower risk of subsequent IBS incidence. These findings suggest that lifestyle modifications should be considered as key primary prevention strategies for IBS. Future research with repeated measurements of lifestyle factors is required to further verify our observations.

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ORCID iDs
Fai Fai Ho http://orcid.org/0000-0003-0525-2621
Chen Mao http://orcid.org/0000-0002-6537-6215

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