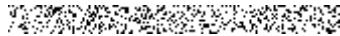

Long-term risk of irritable bowel syndrome associated with adverse childhood and adulthood experiences: a large-scale prospective cohort study

Received: 2 June 2025

Revised: 11 December 2025

Accepted: 20 January 2026



Cite this article as: Zhou, Y., Liu, S., Xie, S. *et al.* Long-term risk of irritable bowel syndrome associated with adverse childhood and adulthood experiences: a large-scale prospective cohort study. *Transl Psychiatry* (2026). <https://doi.org/10.1038/s41398-026-03833-w>

Yesheng Zhou, Si Liu, Sian Xie, Qian Zhang, Shutian Zhang, Shengtao Zhu & Shanshan Wu

We are providing an unedited version of this manuscript to give early access to its findings. Before final publication, the manuscript will undergo further editing. Please note there may be errors present which affect the content, and all legal disclaimers apply.

If this paper is publishing under a Transparent Peer Review model then Peer Review reports will publish with the final article.

Long-term risk of irritable bowel syndrome associated with adverse childhood and adulthood experiences: a large-scale prospective cohort study

Author affiliations

Yesheng Zhou¹, Si Liu¹, Sian Xie¹, Qian Zhang¹, Shutian Zhang¹, Shengtao Zhu^{1*} and Shanshan Wu^{1*}

¹Department of Gastroenterology, Beijing Friendship Hospital, Capital Medical University; State Key Laboratory of Digestive Health; National Clinical Research Center for Digestive Disease; Beijing Key Laboratory of Early Gastrointestinal Cancer Medicine and Medical Devices, Beijing 100050, China

***Corresponding Author**

Shengtao Zhu and Shanshan Wu contributed equally to the study.

Professor Shanshan Wu, Department of Gastroenterology, Beijing Friendship Hospital, Capital Medical University; State Key Laboratory for Digestive Health; National Clinical Research Center for Digestive Diseases, Beijing 100050, China.

Email: shanshanwu@ccmu.edu.cn.

Professor Shengtao Zhu, Department of Gastroenterology, Beijing Friendship Hospital, Capital Medical University; State Key Laboratory for Digestive Health; National Clinical Research Center for Digestive Diseases, Beijing 100050, China. Email: zhushengtao@ccmu.edu.cn.

Word count: 250 words for the abstract; 3597 words for the main text.

Short title: ACEs, AAEs and IBS risk**Abstract**

The impact of adverse childhood experiences (ACEs), adverse adulthood experiences (AAEs), and their combined effects on the risk of incident irritable bowel syndrome (IBS) remains unclear. We aimed to investigate the risk of IBS associated with ACEs and AAEs. Participants free of IBS with available ACEs and AAEs data were included (N=126,735). ACEs and AAEs were assessed separately using the Childhood Trauma Screener-5 item and custom-built questions, with different patterns identified through latent profile analysis. The primary endpoint was incident IBS. Cox proportional hazards models were used to estimate the relationship. During a median follow-up of 14.5 years, 2,492 (2.0%) incident IBS cases were identified. Overall, 95,040 (75.0%), 3,011 (2.4%), 17,409 (13.7%), and 11,275 (8.9%) participants were classified as low ACEs, high physical neglect, high emotional neglect, and high abuse patterns, respectively. Compared with low ACEs, those with high emotional neglect ($HR=1.38$, 95%CI: 1.24-1.54) and abuse ($HR=1.64$, 95%CI: 1.46-1.84) patterns during childhood showed an increased IBS risk. Similarly, 111,776 (88.2%), 7,039 (5.6%), and 7,920 (6.2%) participants were classified as low AAEs, high physical neglect, and high abuse. Compared to low AAEs, high physical neglect and abuse in adulthood had a 1.34-fold (95%CI: 1.15-1.56) and 1.54-fold (95%CI: 1.36-1.77) increased IBS risk. Joint analysis indicated that individuals with high abuse or emotional neglect in ACEs, combined with any pattern in AAEs, had a 39%-161% higher IBS risk compared to those with low ACEs and AAEs. Both ACEs and AAEs are associated with higher IBS risk, with their joint effects aggravating the risk.

Keywords: Adverse childhood experiences; Adverse adulthood experiences; Irritable bowel

syndrome; Cohort studies

ARTICLE IN PRESS

Introduction

Irritable bowel syndrome (IBS) is a common gut-brain interaction disorder, characterized by recurrent abdominal pain or discomfort and altered bowel habits [1]. It affects approximately 10% of the world's population, severely compromises health-related quality of life, and imposes substantial economic burdens on individuals and society [2]. Given incomplete understanding of pathophysiology and absence of effective treatments, identifying modifiable risk factors is crucial to inform better prevention and management strategies.

Adverse childhood experiences (ACEs), including various forms of abuse, neglect, and other potentially traumatic events during childhood, are increasingly recognized for their profound and lasting effects on both psychological and physiological health [3]. ACEs are consistently linked to psychological vulnerabilities, such as difficulties in emotion regulation, anxiety, and depression, which frequently co-occur with IBS [4-8]. These psychological factors, particularly alexithymia-related difficulties in emotion regulation, may contribute to dysfunctional eating behaviors, heightened perception of IBS symptoms (e.g., abdominal pain), and even some inflammatory processes in IBS [5, 6, 8, 9]. Furthermore, accumulating experimental evidence also supports the potential association between ACEs and IBS, implicating mechanisms involving dysregulation of the stress-response system, impaired neurodevelopment, gut dysbiosis, and increased systemic inflammation [10-16]. However, epidemiological evidence regarding the ACEs-IBS association has been inconsistent, owing to limitations of cross-sectional or case-control designs, small sample sizes, and uncontrolled confounders [17-19]. Meanwhile, previous research has only focused on each item or cumulative number of ACEs associated with IBS risk, rather than comprehensive

assessment of ACEs patterns identified via Latent Profile Analysis (LPA)—a clustering method that enables the identification of complex patterns and distinct subgroups [20].

Additionally, adverse adulthood experiences (AAEs), involving traumatic and stressful events occurring after the age of 18, may also trigger IBS symptoms and intensify the effects of ACEs on IBS risk [21]. Nevertheless, to the best of our knowledge, there is currently a lack of evidence regarding the effects of AAEs, as well as joint effects of AAEs and ACEs, on IBS risk.

To address these knowledge gaps, we aimed to examine the risk of incident IBS associated with different patterns, numbers, types of ACEs and AAEs, as well as joint patterns of ACEs and AAEs, in a large long-term prospective cohort.

Methods

Study population

Details of UK Biobank (UKB) study design and population were described previously. Briefly, it is a large population-based prospective cohort study enrolled over 500,000 participants aged 37 to 73 years across England, Scotland, and Wales from 2006 to 2010. At recruitment, all participants provided written informed consent, completed baseline questionnaires, and underwent various physical and biochemical tests. In 2016, an online mental health questionnaire, including adverse experiences during childhood and adulthood, was administered [22].

Participants free of IBS at baseline and responding to all questions about ACEs and AAEs were included. Those who withdrew ($N=12$) or had a diagnosis of cancer ($N=12,477$), inflammatory bowel disease ($N=1,446$), coeliac disease ($N=843$) at enrollment were excluded. All disease diagnoses were determined via International Classification of Disease-10 (ICD-10) codes (**Table S1**). Finally, 126,735 participants were included (**Fig. S1**).

Assessment of ACEs and AAEs

ACEs were evaluated using Childhood Trauma Screener-5 item, a validated and cost-efficient screening tool with five questions representing physical neglect, emotional neglect, sexual abuse, physical abuse, and emotional abuse (**Table S2**) [23]. AAEs were assessed using bespoke (custom-built) questions adapted from UK National Crime Survey concerning experiences of being a crime victim and adult domestic violence, with similar five questions (**Table S3**) [22]. Since the average age of participants at enrollment was 56 years old and AAEs were assessed across the entire adulthood period, thus we assumed AAE exposure was occurred before enrollment for most

participants. Responses to each question were recorded on a 5-point Likert scale (“Never true”, “Rarely true”, “Sometimes true”, “Often true”, and “Very often true”). Each item was dichotomized into 0 (absence) or 1 (presence) based on established cutoff points, and subsequently summed to yield cumulative number of ACEs or AAEs (ranging from 0 to 5, with higher scores reflecting greater exposure) [24].

For separate analysis of ACEs or AAEs, we considered presence of each type (i.e., physical neglect, emotional neglect, sexual abuse, physical abuse, and emotional abuse) as exposure while their absence as reference. Meanwhile, we also categorized ACEs or AAEs according to cumulative numbers: per 1 increase, binary (<2 , ≥ 2), and categorical (0, 1, 2-3, 4-5).

For joint analysis of each type of ACEs and AAEs, individuals were categorized into four groups: no in childhood or adulthood (reference group), only in childhood, only in adulthood, and both in childhood and adulthood. Similarly, joint analysis of cumulative numbers of ACEs and AAEs was performed as follows: per 1 increase of ACEs and AAEs, binary (<2 ACEs and <2 AAEs, <2 ACEs and ≥ 2 AAEs, ≥ 2 ACEs and <2 AAEs, ≥ 2 ACEs and ≥ 2 AAEs), and categorical (0 ACE and 0 AAE, 0 ACE and 1 AAE, 0 ACE and ≥ 2 AAEs, 1 ACE and 0 AAE, 1 ACE and 1 AAE, 1 ACE and ≥ 2 AAEs, ≥ 2 ACEs and 0 AAE, ≥ 2 ACEs and 1 AAE, ≥ 2 ACEs and ≥ 2 AAEs).

Furthermore, comprehensive assessments of ACEs or AAEs patterns were conducted using LPA, identifying four patterns for ACEs (low ACEs, high physical neglect, high emotional neglect, and high abuse; **Fig. 1a-b, Table S4**) and three patterns for AAEs (low AAEs, high physical neglect, and high abuse; **Fig. 1c-d, Table S5**). Individuals with low ACEs or AAEs patterns were considered reference group, while those with other patterns were considered exposure group.

Additionally, joint analyses of ACEs and AAEs patterns were conducted based on overall 12 joint patterns, including both low ACEs and low AAEs (reference group), low ACEs and high physical neglect in AAEs, low ACEs and high abuse in AAEs, high physical neglect in ACEs and low AAEs, both high physical neglect in ACEs and AAEs, high physical neglect in ACEs and high abuse in AAEs, high emotional neglect in ACEs and low AAEs, high emotional neglect in ACEs and high physical neglect in AAEs, high emotional neglect in ACEs and high abuse in AAEs, high abuse in ACEs and low AAEs, high abuse in ACEs and high physical neglect in AAEs, and both high abuse in ACEs and AAEs.

Ascertainment of IBS

The primary outcome was incident IBS (ICD-10 code K58), with a censoring date of September 30th, 2023. Incident IBS was identified using self-reports that met the Rome III criteria via the Digestive Health Questionnaire, or through linkage to primary care and/or hospital admission records across the UK. Since the UKB relies on routine health record linkage rather than scheduled visits, follow-up points and timing varied and were not summarized.

Covariates

Based on prior epidemiological evidence and data availability [1, 25, 26], we selected potential confounders at baseline as covariates: age (continuous), sex (male, female), Townsend Deprivation Index (TDI; quartiles), education level (non-university, university), ethnicity (White, non-White), smoking status (never, previous, current), alcohol drinking (never, previous, current), physical activity (low, moderate, high), healthy diet (yes, no), body mass index (BMI; <18.5, 18.5-24.9, 25.0-29.9, $\geq 30 \text{ kg/m}^2$), and type 2 diabetes (yes, no). A healthy diet was defined as adherence to at

least four of the seven commonly consumed food groups (i.e., fruits, vegetables, fish, processed meats, unprocessed red meats, whole grains, and refined grains) [27]. Physical activity levels were categorized according to International Physical Activity Questionnaire.

Statistical analysis

Patterns of ACEs and AAEs were identified through LPA, a method using Gaussian mixture models for person-centered clustering, with standardized scores of each type [20]. Optimal number of profiles for ACEs and AAEs was assessed using model-fit statistics, including Bayesian Information Criterion (BIC), sample-size-adjusted BIC (SABIC), Akaike's Information Criterion (AIC), entropy, and Bootstrap Likelihood Ratio Test (BLRT) P-value. Means of five dimensions for ACEs and AAEs were freely estimated across profiles, with equal variance and covariance.

Cumulative incidence of incident IBS among different ACEs/AAEs exposure groups was depicted by Kaplan-Meier curves. Cox proportional hazards model was used to investigate relationship between patterns, numbers, and types of ACEs or AAEs, as well as joint patterns, numbers, and types of ACEs and AAEs, with risk of incident IBS. The proportional hazards assumption was tested using Schoenfeld residuals, and no violations were found (all $P>0.05$). Follow-up period started from enrollment date until date of first IBS diagnosis, death, lost to follow-up, or end of study (September 30th, 2023), whichever occurred first. Participants were right-censored at death or lost to follow-up, assumed to be non-informative. In addition to univariable analysis, three adjustment models were implemented: Model 1 adjusted for age and sex; Model 2 additionally adjusted for TDI, education level, ethnicity, smoking status, alcohol drinking, physical activity, healthy diet, and BMI; Model 3 additionally adjusted for type 2 diabetes.

Given a very small percentage of missing values for most variables, missing indicators were used.

To further explore the joint associations of ACEs and AAEs with IBS risk, we assessed their additive interactions, including the relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI), as well as their multiplicative interaction, using the R package “interactionR” (version 0.1.7).

Subgroup analyses stratified by age (<60, \geq 60 years), sex (male, female), smoking status (never, previous/current), drinking status (never/previous, current), and BMI (<25 , ≥ 25 kg/m²) were conducted. Potential effect modifications were examined by including a cross-product interaction item as an independent variable in model separately.

Several sensitivity analyses were performed to validate our findings. Firstly, participants who had an IBS diagnosis within 1 or 2 years after recruitment were excluded to avoid reverse causation. Secondly, baseline depression (ICD-10 code: F32) and anxiety (ICD-10 code: F40, F41) were further adjusted. Thirdly, Fine-Gray competing risk model was performed by considering death and loss to follow-up as competing events. Lastly, age-scaled Cox regression stratified by 5-year birth cohort was conducted to illustrate the impact of different time scales.

All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC) and R version 4.3.0, with a two-tailed P value <0.05 being considered as statistically significant.

Results

Baseline characteristics

Among 126,735 participants, 95,040 (75.0%), 3,011 (2.4%), 17,409 (13.7%) and 11,275 (8.9%) participants were classified into low ACEs, high physical neglect, high emotional neglect and high abuse patterns through LPA, respectively (**Table 1**). Compared with low ACEs pattern, participants with high physical neglect pattern were more likely to be non-White, had a lower level of education and socioeconomic status, a higher BMI and proportion of type 2 diabetes, depression and anxiety. Participants with high emotional neglect pattern had a lower level of education and socioeconomic status, and a higher proportion of depression and anxiety, whereas those with high abuse tended to be younger, female, lower socioeconomic status, higher BMI and proportion of smoking, depression and anxiety. Additionally, similar characteristics were shown in participants with higher numbers of ACEs (**Table S6**).

Regarding AAEs, 111,776 (88.2%), 7,039 (5.6%) and 7,920 (6.2%) were classified as low AAEs, high physical neglect and high abuse patterns through LPA (**Table 1**). Compared to low AAEs, similar characteristics were observed in participants with high physical neglect pattern, high abuse pattern and higher numbers of AAEs (**Table S6**).

Patterns of ACEs and AAEs with risk of incident IBS

During a median follow-up period of 14.5 years, 2,492 (2.0%) participants developed IBS. The 14-year cumulative incidence of IBS for ACEs patterns was lowest in the low ACEs group (1.7%, 95% CI: 1.7-1.8%), followed by high physical neglect (2.0%, 95% CI: 1.5-2.5%), high emotional neglect (2.4%, 95% CI: 2.2-2.6%), and high abuse (3.1%, 95% CI: 2.8-3.5%) (**Fig. S2-S3**). For

AAEs patterns, the 14-year cumulative incidence was 1.8% (95% CI: 1.7-1.9%) for low AAEs, 2.6% (95% CI: 2.2-2.9%) for high physical neglect, and 3.4% (95% CI: 3.0-3.8%) for high abuse. Additional cumulative incidence estimates are provided in **Fig. S4-S10**. Participants with high emotional neglect ($HR=1.38$, 95% CI: 1.24-1.54) and high abuse ($HR=1.64$, 95% CI: 1.46-1.84) during childhood showed increased risk of IBS versus low ACEs pattern, respectively (**Table 2**). Similarly, compared to low AAEs pattern, those with high physical neglect and high abuse in adulthood had a 34% ($HR=1.34$, 95% CI: 1.15-1.56) and 55% ($HR=1.55$, 95% CI: 1.36-1.77) greater IBS risk, respectively.

Joint analysis indicated individuals with both high abuse in ACEs and AAEs ($HR=2.61$, 95% CI: 2.12-3.21), high abuse in ACEs and high physical neglect in AAEs ($HR=2.21$, 95% CI: 1.61-3.05), high emotional neglect in ACEs with high physical neglect ($HR=1.62$, 95% CI: 1.13-2.33) or high abuse in AAEs ($HR=1.39$, 95% CI: 1.02-1.91) had a 39%-161% excess IBS risk versus those with both low ACEs and AAEs (**Table 2**). A positive significant additive interaction was observed between ACEs and AAEs patterns in their synergistic associations with IBS risk ($RERI=0.78$, 95% CI: 0.16-1.40; $AP=0.29$, 95% CI: 0.10-0.48; $SI=1.86$, 95% CI: 1.15-3.01; **Table S7**). However, no significant multiplicative interaction was detected ($HR=1.27$, 95% CI: 0.94-1.72).

In subgroup analysis, increased IBS risk associated with high emotional neglect and high abuse patterns of ACEs, high physical neglect and high abuse patterns of AAEs, as well as the above joint patterns of ACEs and AAEs, was generally observed across age, sex, smoking, alcohol drinking and BMI subgroups (**Table S8-S22**).

Numbers of ACEs and AAEs with risk of incident IBS

Regarding numbers of ACEs, a 17% higher IBS risk was observed with per 1 ACE increment (HR=1.17, 95% CI: 1.13-1.20; **Fig. 2a, Table S23**). Individuals with ≥ 2 ACEs exhibited a HR of 1.44 (95% CI: 1.32-1.58) versus those with <2 ACEs (**Fig. 2b, Table S23**). Meanwhile, individuals with 4-5 ACEs had a 2.01-fold (95% CI: 1.71-2.37) IBS risk versus those without ACEs, with significant dose-response relationship ($P_{trend} < 0.001$, **Fig. 2c, Table S23**).

Similarly, each additional AAE increment was associated with a 16% increase of IBS risk (HR=1.16, 95% CI: 1.12-1.20; **Fig. 2a, Table S24**). Individuals with ≥ 2 AAEs had a 1.38-fold (95% CI: 1.26-1.51) IBS risk versus those with <2 AAEs (**Fig. 2b, Table S24**). Moreover, individuals with 4-5 AAEs had a 1.77-fold (95% CI: 1.47-2.13) IBS risk versus those without AAEs, with significant dose-response relationship ($P_{trend} < 0.001$, **Fig. 2c, Table S24**).

As for joint analyses, individuals with ≥ 2 ACEs and ≥ 2 AAEs had a 1.80-fold (95%CI: 1.60-2.03) higher risk of IBS versus those with <2 ACEs and <2 AAEs, and a 1.97-fold (95%CI: 1.72-2.25) higher IBS risk versus those without none of ACEs or AAEs. Generally, a higher risk of developing IBS was observed with accumulation of more ACEs and AAEs (**Fig. 3a-b, Table S25**).

While a positive significant additive interaction was identified between ACEs and AAEs numbers in their association with IBS risk (RERI=0.28, 95% CI: 0.01-0.54; AP=0.15, 95% CI: 0.01-0.29; SI=1.52, 95% CI: 1.00-2.36; **Table S7**), no significant multiplicative interaction was observed (HR=1.13, 95% CI: 0.94-1.36).

Regarding subgroup analysis, increased IBS risk associated with per 1 ACEs/AAEs increment, ≥ 2 ACEs/AAEs, 4-5 ACEs/AAEs, as well as the above joint numbers of ACEs and AAEs, was

generally observed across age, sex, smoking, alcohol drinking and BMI subgroups (**Table S8-S22**).

Types of ACEs and AAEs with risk of incident IBS

All ACEs types were associated with a 25%-44% higher IBS risk, with emotional neglect (HR=1.44, 95% CI: 1.32-1.57) and emotional abuse (HR=1.42, 95% CI: 1.29-1.57) posing the highest IBS risks (**Fig. 2d, Table S23**). Similarly, all AAEs types were associated with a 16%-43% higher IBS risk, with physical abuse (HR=1.43, 95% CI: 1.29-1.59) and emotional abuse (HR=1.41, 95% CI: 1.30-1.54) presenting the greatest IBS risks (**Fig. 2d, Table S24**). Moreover, individuals who encountered specific types of adverse experiences in both childhood and adulthood had an even higher risk of developing IBS, particularly for sexual abuse, physical abuse and emotional abuse, with an 80%, 69% and 86% greater risk versus none in childhood and adulthood (**Fig. 3c, Table S25**).

In subgroup analysis, a greater IBS risk associated with each type of ACEs/AAEs and the above joint type of ACEs and AAEs, was generally observed across age, sex, smoking, alcohol drinking and BMI subgroups (**Table S8-S22**).

Sensitivity analysis

The results of the sensitivity analyses, whether examining patterns, numbers, or types of adverse experiences, remained consistent with the primary findings (**Table S26-S40**).

Discussion

In this prospective cohort study involving over 120,000 participants, we found that individuals experiencing high emotional neglect and abuse pattern during childhood had a 38% and 64% higher IBS risk versus those with low ACEs pattern. Similarly, individuals experiencing high physical neglect and abuse pattern during adulthood showed a 34% and 55% greater IBS risk versus low AAEs pattern. Joint analysis indicated that individuals with high abuse or emotional neglect in ACEs, combined with any pattern in AAEs, had a 39%-161% higher IBS risk. A significant positive additive interaction between ACEs and AAEs on IBS risk was also detected. Similar findings were demonstrated for different numbers or types of ACEs and AAEs.

Several cross-sectional, case-control, and retrospective cohort studies have supported positive association between ACEs exposure and IBS, aligning with our findings [17-19]. However, significant inconsistencies persist regarding the association between different types of ACEs and IBS [17-19]. A cross-sectional study in Mexico, involving 290 participants, identified emotional and physical abuse/neglect elevated IBS risk [17]. Another cross-sectional study with 798 participants, found emotional and sexual abuse increased IBS risk by 83% and 81%, respectively [18]. Additionally, a case-control study with 302 individuals revealed only emotional abuse significantly increased IBS occurrence [19]. These inconsistent results might be attributed to different measurement instruments, limited sample size and different study designs, or cultural differences in reporting and perceiving adverse experiences. To date, all prior studies have only investigated IBS risk associated with specific types of ACEs, rather than examining patterns or cumulative numbers.

Regarding AAEs, a cross-sectional study within 186 participants indicated severity of IBS symptoms was significantly linked to experiences of adult sexual abuse, whereas this association was not observed with physical abuse [28]. Similar findings were reported in a cross-sectional study from China with 388 participants, which found a higher prevalence of sexual abuse among IBS patients rather than physical abuse [29]. These discrepancies may be attributed to different survey questionnaires, and the un-temporal cross-sectional design. Currently, no research has yet examined the link between patterns or cumulative numbers of AAEs and IBS, as well as joint effects of ACEs and AAEs on IBS risk.

The exact mechanisms linking adverse experiences to IBS are not fully understood and likely involve psychological, biological, and behavioral pathways. Firstly, adverse experiences are closely related to psychological vulnerabilities, such as difficulties in emotion regulation (especially alexithymia), anxiety, and depression, which commonly co-occur with IBS [4-8]. These psychological dysfunctions may mediate or moderate the impact of adversities on IBS development by triggering stress-related biological changes and amplifying effects, including impaired stress regulation, sustained low-grade inflammation, and heightened visceral hypersensitivity [30, 31]. Secondly, dysregulation of the stress-response system (e.g., the hypothalamic-pituitary-adrenal axis and autonomic nervous system) due to adverse experiences may cause excessive cortisol secretion or prolonged stress responses, subsequently affecting visceral sensitivity and gut motility [10, 11]. Thirdly, trauma-induced neurodevelopmental impairments (e.g., changes in brain structure and function), intestinal dysbiosis, and increased systemic inflammation (e.g., C-reactive protein and interleukin-1 β) may disrupt the gut-brain axis

and intestinal motility, increase gut permeability and pain perception [12-16]. Lastly, adverse experiences and associated psychological issues may lead to unhealthy behaviors, such as disordered eating and sleep disturbances, further increasing IBS risk [32, 33].

To the best of our knowledge, this is the first large-scale prospective cohort study to comprehensively investigate risk of incident IBS associated with ACEs and AAEs exposures, including not only cumulative numbers and specific types but also distinct patterns. Moreover, we also highlighted joint effects of ACEs and AAEs on IBS risk for the first time, and further established a dose-response relationship. Additionally, we conducted a series of subgroup and sensitivity analyses to validate the reliability of our results.

However, several limitations should be considered. Firstly, recall bias in reporting ACEs and AAEs during adulthood could not be avoided, potentially leading to misclassification in exposure assessments. Secondly, absence of detailed information on duration and frequency of adverse experiences, as well as additional traumas such as family dysfunction or community violence, may limit a comprehensive understanding of these exposures. Thirdly, since AAEs were assessed in 2016, there may be a small portion of AAE exposures that occurred between enrollment and 2016, which could impact causal inference. Fourthly, incident IBS may be underdiagnosed since some IBS cases do not seek medical consultation, although we ascertained IBS cases using ICD-10 codes from both primary care and hospital admission sources. Fifthly, predominantly White ethnicity of our population may limit the generalizability of our findings to other populations.

Our study suggested early life adversities could persist into adulthood and, along with AAEs, further elevated IBS risk. Thus, it's important to adopt comprehensive strategies to address both

ACEs and AAEs issues. Individuals experiencing early-life and/or adulthood adversities, particularly both adversities, should be prioritized for psychological and IBS screenings to identify potential disorders and ensure appropriate interventions. Given the association of ACEs and AAEs with various other diseases, screening IBS patients for these experiences might also help reduce incidence of other related conditions. Future prospective cohorts should collect detailed information to examine the relationship of adverse experiences with specific IBS subtype and IBS severity.

Conclusions

In conclusion, this large-scale prospective cohort study identified an increased risk of IBS associated with exposures to ACEs and AAEs, particularly high emotional neglect and abuse pattern during childhood and high physical neglect and abuse pattern during adulthood. Meanwhile, joint effects of ACEs and AAEs aggravated IBS risk, highlighting the importance of comprehensive life-course health strategies targeting adverse experiences for the prevention and management of IBS. Future epidemiologic studies across diverse ethnic populations and experimental studies are necessary to confirm our findings and clarify underlying mechanisms.

References

- 1 Ford AC, Sperber AD, Corsetti M, Camilleri M. Irritable bowel syndrome. Lancet. 2020;396:1675-88.
- 2 Black CJ, Ford AC. Global burden of irritable bowel syndrome: trends, predictions and risk factors. Nat Rev Gastroenterol Hepatol. 2020;17:473-86.
- 3 Madigan S, Thiemann R, Deneault AA, Fearon RMP, Racine N, Park J, *et al.* Prevalence of

Adverse Childhood Experiences in Child Population Samples: A Systematic Review and Meta-Analysis. *JAMA Pediatr.* 2024.

- 4 Cole E, Diaz A. Specific emotion regulation deficits differentiate and mediate the relationship between adverse childhood experiences and internalizing psychopathology. *Journal of Affective Disorders Reports.* 2024;16:100722.
- 5 Phillips K, Wright BJ, Kent S. Psychosocial predictors of irritable bowel syndrome diagnosis and symptom severity. *J Psychosom Res.* 2013;75:467-74.
- 6 Sibelli A, Chalder T, Everitt H, Chilcot J, Moss-Morris R. Positive and negative affect mediate the bidirectional relationship between emotional processing and symptom severity and impact in irritable bowel syndrome. *J Psychosom Res.* 2018;105:1-13.
- 7 Carrozzino D, Porcelli P. Alexithymia in Gastroenterology and Hepatology: A Systematic Review. *Front Psychol.* 2018;9:470.
- 8 Rzeszutek M, Kowalkowska J, Drabarek K, Van Hoy A, Schier K, Lis-Turlejska M, *et al.* Adverse childhood experiences and alexithymia intensity as predictors of temporal dynamics of functioning in individuals with irritable bowel syndrome: A three-wave latent transition analysis. *J Psychosom Res.* 2024;187:111904.
- 9 Conti C, Caraffa A, Kritas SK, Ronconi G, Fulcheri M. Alexithymia and its relationships with inflammatory response mediated by IL-1 family members. *J Biol Regul Homeost Agents.* 2017;31:21-8.
- 10 Kano M, Muratsubaki T, Van Oudenhove L, Morishita J, Yoshizawa M, Kohno K, *et al.* Altered brain and gut responses to corticotropin-releasing hormone (CRH) in patients with

- irritable bowel syndrome. *Sci Rep.* 2017;7:12425.
- 11 Hong S, Zheng G, Wiley JW. Epigenetic regulation of genes that modulate chronic stress-induced visceral pain in the peripheral nervous system. *Gastroenterology.* 2015;148:148-57 e7.
- 12 Jeong HJ, Durham EL, Moore TM, Dupont RM, McDowell M, Cardenas-Iniguez C, *et al.* The association between latent trauma and brain structure in children. *Transl Psychiatry.* 2021;11:240.
- 13 Siehl S, Sicorello M, Herzog J, Nees F, Kleindienst N, Bohus M, *et al.* Neurostructural associations with traumatic experiences during child- and adulthood. *Transl Psychiatry.* 2022;12:515.
- 14 Margolis KG, Cryan JF, Mayer EA. The Microbiota-Gut-Brain Axis: From Motility to Mood. *Gastroenterology.* 2021;160:1486-501.
- 15 Chang H, Perkins MH, Novaes LS, Qian F, Zhang T, Neckel PH, *et al.* Stress-sensitive neural circuits change the gut microbiome via duodenal glands. *Cell.* 2024;187:5393-412 e30.
- 16 Tursich M, Neufeld RW, Frewen PA, Harricharan S, Kibler JL, Rhind SG, *et al.* Association of trauma exposure with proinflammatory activity: a transdiagnostic meta-analysis. *Transl Psychiatry.* 2014;4:e413.
- 17 Priego-Parra BA, Triana-Romero A, Lajud-Barquin FA, de Fatima Higuera-DelaTijera M, Martinez-Vazquez SE, Salgado-Alvarez GA, *et al.* Association of adverse childhood experiences with irritable bowel syndrome in Mexican adults: A cross-sectional study. *Neurogastroenterol Motil.* 2024;36:e14743.

- 18 Lee AH, Mahurkar-Joshi S, Naliboff B, Gupta A, Labus J, Tillisch K, *et al.* Role of Sex, Anxiety, and Resilience in the Association between Adverse Childhood Experiences and Irritable Bowel Syndrome. *Clin Gastroenterol Hepatol*. 2024.
- 19 Park SH, Videlock EJ, Shih W, Presson AP, Mayer EA, Chang L. Adverse childhood experiences are associated with irritable bowel syndrome and gastrointestinal symptom severity. *Neurogastroenterol Motil*. 2016;28:1252-60.
- 20 Beattie MM, Kontinen HM, Volanen SM, Hankonen NE. Latent profile analysis as a method for process evaluations: Discovering response subgroups in a mindfulness intervention. *Soc Sci Med*. 2022;296:114748.
- 21 Zia JK, Lenhart A, Yang PL, Heitkemper MM, Baker J, Keefer L, *et al.* Risk Factors for Abdominal Pain-Related Disorders of Gut-Brain Interaction in Adults and Children: A Systematic Review. *Gastroenterology*. 2022;163:995-1023 e3.
- 22 UK Biobank. Mental well-being web questionnaire. 2023. https://biobank.ctsu.ox.ac.uk/crystal/ukb/docs/mwb_overview.pdf. Accessed 6 Dec 2024.
- 23 Grabe HJ, Schulz A, Schmidt CO, Appel K, Driessen M, Wingenfeld K, *et al.* A brief instrument for the assessment of childhood abuse and neglect: the childhood trauma screener (CTS). *Psychiatr Prax*. 2012;39:109-15.
- 24 Glaesmer H, Schulz A, Hauser W, Freyberger HJ, Brahler E, Grabe HJ. The childhood trauma screener (CTS) - development and validation of cut-off-scores for classificatory diagnostics. *Psychiatr Prax*. 2013;40:220-6.
- 25 Fu T, Sun Y, Lu S, Zhao J, Dan L, Shi W, *et al.* Risk Assessment for Gastrointestinal Diseases

- via Clinical Dimension and Genome-Wide Polygenic Risk Scores of Type 2 Diabetes: A Population-Based Cohort Study. *Diabetes Care.* 2024;47:418-26.
- 26 Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, *et al.* UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med.* 2015;12:e1001779.
- 27 Mozaffarian D. Dietary and Policy Priorities for Cardiovascular Disease, Diabetes, and Obesity: A Comprehensive Review. *Circulation.* 2016;133:187-225.
- 28 Melchior C, Wilpart K, Midenfjord I, Trindade IA, Tornblom H, Tack JF, *et al.* Relationship Between Abuse History and Gastrointestinal and Extraintestinal Symptom Severity in Irritable Bowel Syndrome. *Psychosom Med.* 2022;84:1021-33.
- 29 Lee HF, Liu PY, Wang YP, Tsai CF, Chang FY, Lu CL. Sexual Abuse Is Associated With an Abnormal Psychological Profile and Sleep Difficulty in Patients With Irritable Bowel Syndrome in Taiwan. *J Neurogastroenterol Motil.* 2018;24:79-86.
- 30 Schneider KM, Blank N, Alvarez Y, Thum K, Lundgren P, Litichevskiy L, *et al.* The enteric nervous system relays psychological stress to intestinal inflammation. *Cell.* 2023;186:2823-38 e20.
- 31 Luo QQ, Wang B, Chen X, Qiu HY, Li WT, Yan XJ, *et al.* Acute stress induces visceral hypersensitivity via glucocorticoid receptor-mediated membrane insertion of TRPM8: Involvement of a non-receptor tyrosine kinase Pyk2. *Neurogastroenterol Motil.* 2020;32:1514-28.
- 32 Testa A, Zhang L, Jackson DB, Ganson KT, Raney JH, Nagata JM. Adverse childhood

experiences and unhealthy dietary behaviours in adulthood. *Public Health Nutr.* 2024;27:e40.

- 33 Yu HJ, Liu X, Yang HG, Chen R, He QQ. The association of adverse childhood experiences and its subtypes with adulthood sleep problems: A systematic review and meta-analysis of cohort studies. *Sleep Med.* 2022;98:26-33.

Declarations**Authors' contributions**

SSW and STZhu designed the study. YSZ and SSW drafted the manuscript. YSZ analyzed the data.

SSW and QZ verified the analysis. SL, STZhu, STZhang and SAX interpreted the results, incorporated comments for the co-authors and finalized the manuscript. All authors approved the final version of the paper.

Financial support

This work was supported by National Natural Science Foundation of China (No. 82570631), Beijing Nova Program (No. 20230484349), and The Beijing High-Level Innovation and Entrepreneurship Talent Support Program Young Backbone Talent Projects (No. G202533237).

Potential competing interests

All authors have declared no potential conflicts of interest relevant to this article.

Ethics approval

The UK Biobank study was approved by the North West Multicenter Research Ethical Committee (21/NW/0157), and all participants or their proxy respondents provided written informed consent. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Patient and public involvement

Patients and the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Acknowledgements

This research has been conducted using the UK Biobank Resource under application number 74444.

Data Availability Statement

All data relevant to the study were using the UK Biobank Resource under application number 74444. No additional data available.

Figure Legends

Fig. 1. Patterns of ACEs and AAEs identified through latent profile analysis. (a) Standardized mean scores of ACEs across four profiles identified by LPA; (b) Standardized mean scores of five ACEs indicators across four profiles identified by LPA; (c) Standardized mean scores of AAEs across three profiles identified by LPA; (d) Standardized mean scores of five AAEs indicators across three profiles identified by LPA.

Note: ACEs and AAEs indicators refer to physical neglect, emotional neglect, sexual abuse, physical abuse, and emotional abuse.

Abbreviations: ACEs, adverse childhood experiences; AAEs, adverse adulthood experiences; LPA, latent profile analysis.

Fig. 2. Risk of incident IBS associated with different numbers and types of ACEs and AAEs.

(a) Per 1 number of ACEs/AAEs increase; (b) ≥ 2 ACEs/AAEs versus < 2 ACEs/AAEs; (c) 1, 2-3, and 4-5 ACEs/AAEs versus 0 ACEs/AAEs; (d) Types of ACEs/AAEs (with no each indicator as reference).

Note: Model 1: age and sex were adjusted; Model 2: Townsend Deprivation Index, education level, ethnicity, smoking status, alcohol drinking, physical activity, healthy diet, and body mass index were additionally adjusted; Model 3: type 2 diabetes was additionally adjusted. P for trend was calculated by using median values within each category.

Abbreviations: IBS, irritable bowel syndrome; ACEs, adverse childhood experiences; AAEs, adverse adulthood experiences; HR, hazard ratio; CI, confidence interval.

Fig. 3. Joint analysis of different numbers and types of ACEs and AAEs on risk of incident IBS.

(a) Per 1 number of ACEs and AAEs increase, and binary ACEs and AAEs (with < 2 ACEs and < 2 AAEs as reference); (b) Categorical ACEs and AAEs (with 0 ACEs and 0 AAEs as reference); (c) Types of ACEs and AAEs (with the absence of specific types of adverse events in both childhood and adulthood as reference).

Note: Model 1: age and sex were adjusted; Model 2: Townsend Deprivation Index, education level, ethnicity, smoking status, alcohol drinking, physical activity, healthy diet, and body mass index were additionally adjusted; Model 3: type 2 diabetes was additionally adjusted.

Abbreviations: ACEs, adverse childhood experiences; AAEs, adverse adulthood experiences; IBS, irritable bowel syndrome; HR, hazard ratio; CI, confidence interval.

Table 1. Baseline characteristics according to different patterns of ACEs and AAEs.

Characteri stics	ACEs patterns				AAEs patterns					
	Total (N=1267 35)	Low ACEs (N=950 40)	High physic al neglec t (N=30 11)	High emotio nal neglect (N=174 09)	Hig h a bus e (N= 112 75)	P	Low AAEs (N=1117 76)	High physic al neglec t (N=70 39)	High abuse (N=79 20)	
Age (years) ^a	55.61 (7.73)	55.8 (7.71)	57.38 (7.70)	55.55 (7.67)	5 (7.7 0)	53.6 <0.0	55.71 (7.72)	56.04 (7.94)	53.86 (7.52)	<0.0 01
Sex						<0.0 01				<0.0 01
Male	58240 (46.0)	44243 (46.6)	1502 (49.9)	8684 (49.9)	1 (33. 8)	381 746	53248 (47.6)	3384 (48.1)	1608 (20.3)	
Female	68495 (54.0)	50797 (53.4)	1509 (50.1)	8725 (50.1)	4 (66. 2)	58528 (52.4)	3655 (51.9)	6312 (79.7)		
Ethnicity						<0.0 01				<0.0 01
Non- White	3786 (3.0)	2286 (2.4)	315 (10.5)	554 (3.2)	631 (5.6)	2912 (2.6)	550 (7.8)	324 (4.1)		
White	122602 (96.7)	92536 (97.4)	2689 (89.3)	16783 (96.4)	94 (94. 0)	108574 (97.1)	6465 (91.8)	7563 (95.5)		
Unknown	347 (0.3)	218 (0.2)	7 (0.2)	72 (0.4)	50 (0.4)	290 (0.3)	24 (0.3)	33 (0.4)		
Education level						<0.0 01				<0.0 01
Non- university	66961 (52.8)	49386 (52.0)	2060 (68.4)	9420 (54.1)	609 5	57486 (51.4)	4660 (66.2)	4815 (60.8)		

					(54. 1) 507				
Universit y	58617 (46.3)	44825 (47.2)	897 (29.8)	7817 (44.9)	8 (45. 0)	53322 (47.7)	2270 (32.2)	3025 (38.2)	
Unknown n	1157 (0.9)	829 (0.9)	54 (1.8)	172 (1.0)	102 (0.9)	968 (0.9)	109 (1.5)	80 (1.0)	
TDI					<0.0 01				<0.0 01
Mean (SD)	-1.7 (2.84)	-1.83 (2.76)	-1.27 (3.13)	-1.51 (2.90)	0.98 (3.1 5)	<0.0 01	-1.8 (2.77)	-1.07 (3.20)	-0.83 (3.20)
Q1 (\leq - 3.63)	31666 (25.0)	24748 (26.0)	678 (22.5)	4069 (23.4)	1 (19. 3)	28756 (25.7)	1458 (20.7)	1452 (18.3)	
Q2 (- 3.63 to - 2.11)	31623 (25.0)	24386 (25.7)	694 (23.0)	4160 (23.9)	3 (21. 1)	28413 (25.4)	1584 (22.5)	1626 (20.5)	
Q3 (- 2.11 to 0.58)	31640 (25.0)	23756 (25.0)	701 (23.3)	4341 (24.9)	2 (25. 2)	28026 (25.1)	1688 (24.0)	1926 (24.3)	
Q4 (> 0.58)	31640 (25.0)	22029 (23.2)	934 (31.0)	4814 (27.7)	3 (34. 3)	26441 (23.7)	2300 (32.7)	2899 (36.6)	
Unknown n	166 (0.1)	121 (0.1)	4 (0.1)	25 (0.1)	16 (0.1)	140 (0.1)	9 (0.1)	17 (0.2)	
Smoking status					<0.0 01				<0.0 01
Never	73026 (57.6)	56635 (59.6)	1668 (55.4)	9415 (54.1)	8 (47. 1)	65692 (58.8)	3678 (52.3)	3656 (46.2)	
Previous	44172 (34.9)	31984 (33.7)	1069 (35.5)	6521 (37.5)	459 8	38376 (34.3)	2572 (36.5)	3224 (40.7)	

					(40. 8) 132			
	9250 (7.3)	6224 (6.5)	260 (8.6)	1437 (8.3)	9 (11. 8)	7470 (6.7)	757 (10.8)	1023 (12.9)
Current								
Unknown n	287 (0.2)	197 (0.2)	14 (0.5)	36 (0.2)	40 (0.4)	238 (0.2)	32 (0.5)	17 (0.2)
Alcohol drinking					<0.0 01			<0.0 01
Never	3423 (2.7)	2457 (2.6)	160 (5.3)	441 (2.5)	365 (3.2)	2908 (2.6)	293 (4.2)	222 (2.8)
Previous	3262 (2.6)	2063 (2.2)	114 (3.8)	537 (3.1)	548 (4.9)	2630 (2.4)	283 (4.0)	349 (4.4)
Current	119949 (94.6)	90455 (95.2)	2733 (90.8)	16416 (94.3)	45 (91. 8)	106155 (95.0)	6454 (91.7)	7340 (92.7)
Unknown n	101 (0.1)	65 (0.1)	4 (0.1)	15 (0.1)	17 (0.2)	83 (0.1)	9 (0.1)	9 (0.1)
IPAQ					<0.0 01			<0.0 01
Low	19108 (15.1)	14198 (14.9)	374 (12.4)	2880 (16.5)	165 6 (14. 7)	16955 (15.2)	958 (13.6)	1195 (15.1)
Moderat e	45783 (36.1)	34753 (36.6)	979 (32.5)	6240 (35.8)	381 1 (33. 8)	40836 (36.5)	2261 (32.1)	2686 (33.9)
High	41584 (32.8)	31074 (32.7)	1056 (35.1)	5498 (31.6)	395 6 (35. 1)	36465 (32.6)	2442 (34.7)	2677 (33.8)
Unknown n	20260 (16.0)	15015 (15.8)	602 (20.0)	2791 (16.0)	185 2 (16. 4)	17520 (15.7)	1378 (19.6)	1362 (17.2)

	878									
Healthy diet (n, %) ^b	98092 (77.4)	73817 (77.7)	2261 (75.1)	13225 (76.0)	9 (78.0)	<0.0 01	86615 (77.5)	5242 (74.5)	6235 (78.7)	<0.0 01
Healthy diet score ^{a,b}	4.64 (1.56)	4.65 (1.55)	4.59 (1.62)	4.60 (1.59)	4.69 (1.58)	<0.0 01	4.64 (1.55)	4.56 (1.63)	4.74 (1.57)	<0.0 01
BMI (kg/m ²)	<0.0 01									
Mean (SD)	26.79 (4.53)	26.70 (4.45)	27.39 (4.61)	26.91 (4.61)	0 (5.0)	<0.0 01	26.72 (4.47)	27.48 (4.89)	27.22 (5.06)	<0.0 01
< 18.5	644 (0.5)	478 (0.5)	13 (0.4)	92 (0.5)	61 (0.5)	560 (0.5)	31 (0.4)	53 (0.7)		
18.5-24.9	47958 (37.8)	36614 (38.5)	941 (31.3)	6413 (36.8)	0 (35.4)	42832 (38.3)	2287 (32.5)	2839 (35.8)		
25.0-29.9	52824 (41.7)	39704 (41.8)	1333 (44.3)	7305 (42.0)	2 (39.8)	46719 (41.8)	2961 (42.1)	3144 (39.7)		
≥ 30.0	25009 (19.7)	18028 (19.0)	713 (23.7)	3552 (20.4)	6 (24.1)	21415 (19.2)	1733 (24.6)	1861 (23.5)		
Unknown	300 (0.2)	216 (0.2)	11 (0.4)	47 (0.3)	26 (0.2)	250 (0.2)	27 (0.4)	23 (0.3)		
Diabetes (n, %)	1929 (1.5)	1376 (1.4)	71 (2.4)	285 (1.6)	197 (1.7)	<0.0 01	1648 (1.5)	165 (2.3)	116 (1.5)	<0.0 01
Depression (n, %)	9131 (7.2)	5417 (5.7)	220 (7.3)	1807 (10.4)	168 (15.0)		7316 (6.5)	681 (9.7)	1134 (14.3)	<0.0 01
Anxiety (n, %)	4042 (3.2)	2596 (2.7)	104 (3.5)	713 (4.1)	629 (5.6)	<0.0 01	3288 (2.9)	271 (3.8)	483 (6.1)	<0.0 01

Note: Categorical variables are presented as frequencies and percentages.

^a Data are presented as the mean ± standard deviation.

^b A healthy diet was based on adherence to at least four of seven commonly eaten food groups following recommendations on dietary priorities for cardiometabolic health.

Abbreviations: ACEs, adverse childhood experiences; AAEs, adverse adulthood experiences; TDI, Townsend Deprivation Index; SD, standard deviation; IPAQ, International Physical Activity Questionnaire; BMI, body mass index.

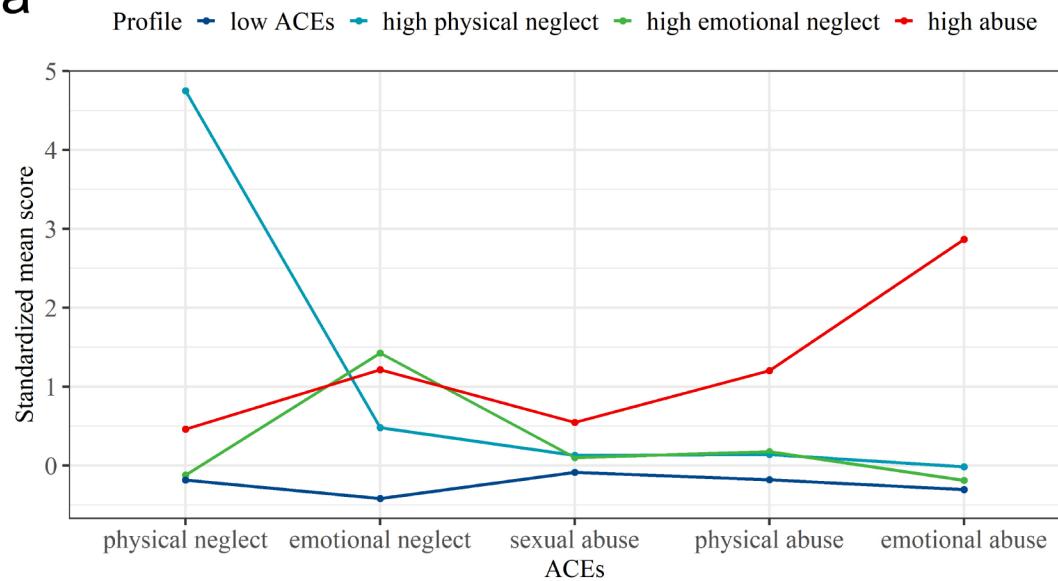
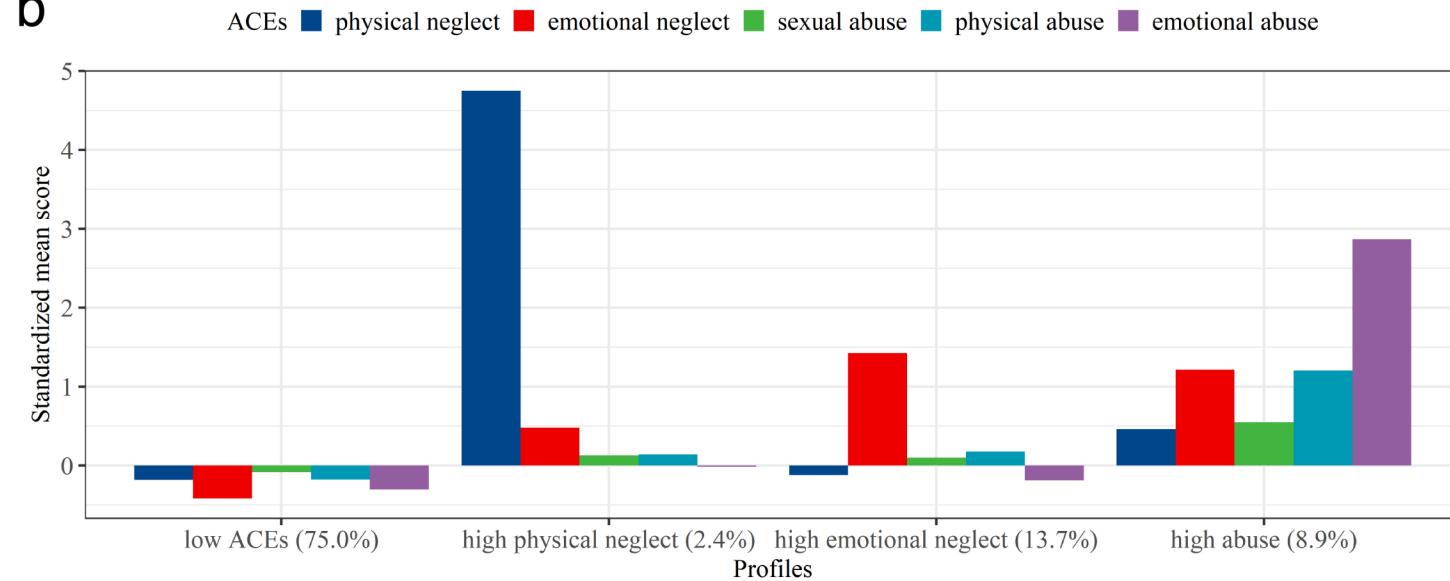
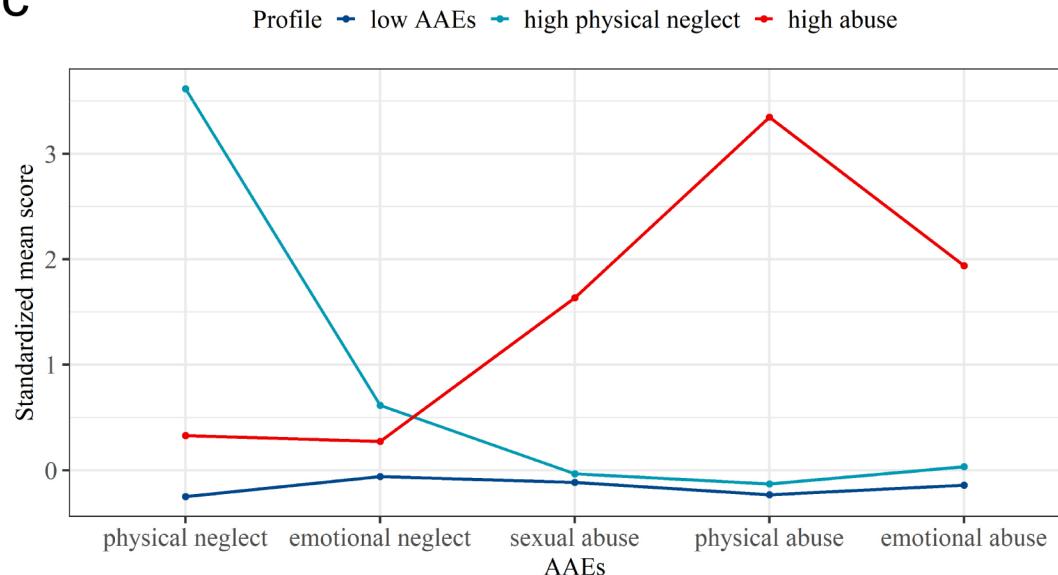
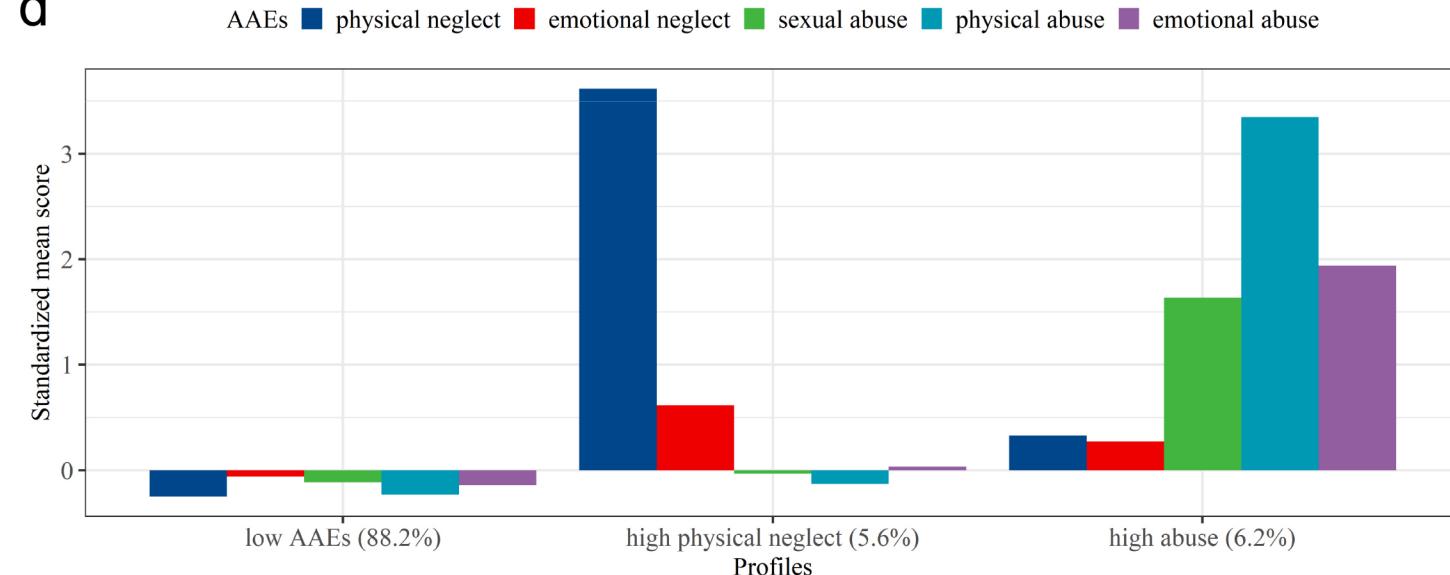
Table 2. Risk of incident IBS associated with different patterns of ACEs and AAEs.

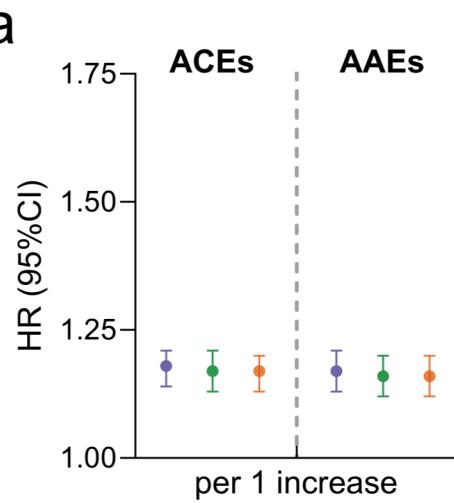
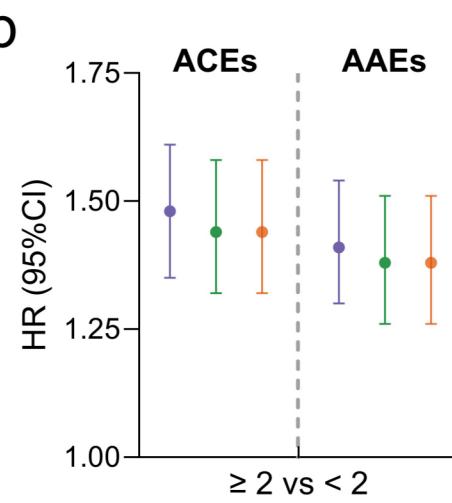
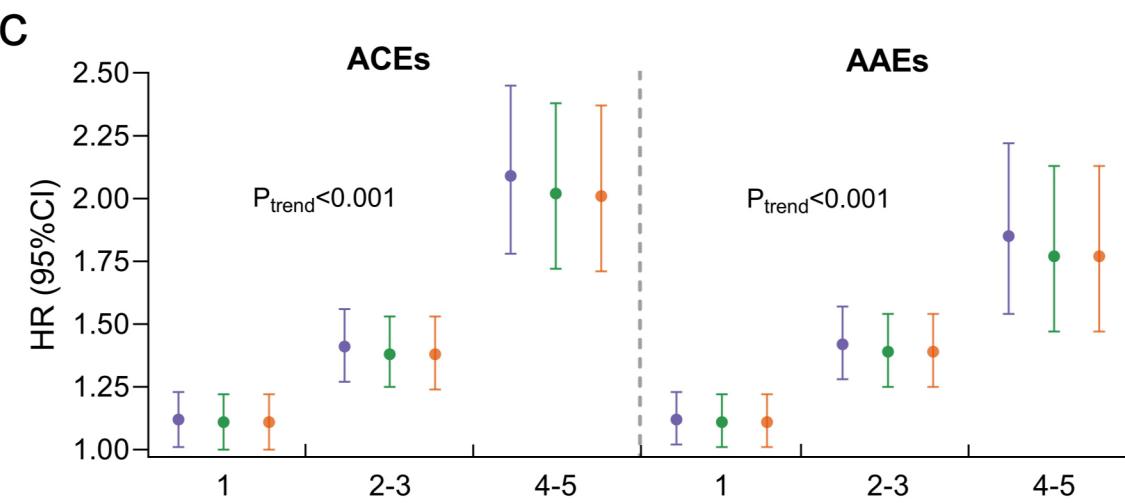
Patterns	Events/ participants	Unadjusted HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Patterns of ACEs					
Low ACEs	1665/95040	Reference	Reference	Reference	Reference
High physical neglect	59/3011	1.12 (0.87- 1.46)	1.14 (0.88- 1.48)	1.10 (0.85- 1.43)	1.10 (0.85- 1.43)
High emotional neglect	417/17409	1.37 (1.23- 1.53)***	1.40 (1.26- 1.56)***	1.38 (1.24- 1.54)***	1.38 (1.24- 1.54)***
High abuse	351/11275	1.79 (1.60- 2.01)***	1.68 (1.49- 1.88)***	1.64 (1.46- 1.84)***	1.64 (1.46- 1.84)***
Patterns of AAEs					
Low AAEs	2048/111776	Reference	Reference	Reference	Reference
High physical neglect	178/7039	1.39 (1.19- 1.62)***	1.39 (1.19- 1.62)***	1.34 (1.15- 1.56)***	1.34 (1.15- 1.56)***
High abuse	266/7920	1.85 (1.63- 2.10)***	1.61 (1.41- 1.83)***	1.55 (1.36- 1.77)***	1.55 (1.36- 1.77)***
Joint patterns of ACEs and AAEs					
Both low ACEs and AAEs	1453/86711	Reference	Reference	Reference	Reference
Low ACEs and high physical neglect in AAEs	92/4031	1.37 (1.11- 1.69)**	1.37 (1.11- 1.69)**	1.32 (1.07- 1.64)**	1.32 (1.07- 1.63)*
Low ACEs and high abuse in AAEs	120/4298	1.68 (1.39- 2.02)***	1.46 (1.21- 1.77)***	1.43 (1.18- 1.72)***	1.43 (1.18- 1.72)***
High physical neglect in ACEs and low AAEs	36/1852	1.16 (0.84- 1.62)	1.18 (0.85- 1.64)	1.14 (0.82- 1.59)	1.14 (0.82- 1.58)
Both high physical neglect in ACEs and AAEs	17/946	1.08 (0.67- 1.74)	1.13 (0.70- 1.82)	1.10 (0.68- 1.77)	1.10 (0.68- 1.77)
High physical neglect in ACEs and high abuse in AAEs	6/213	1.69 (0.76- 3.78)	1.47 (0.66- 3.27)	1.40 (0.63- 3.13)	1.39 (0.62- 3.10)
High emotional neglect in ACEs and low AAEs	347/14845	1.40 (1.25- 1.57)***	1.44 (1.28- 1.62)***	1.42 (1.26- 1.60)***	1.42 (1.26- 1.60)***
High emotional neglect in ACEs and high physical neglect in AAEs	30/1088	1.67 (1.16- 2.39)**	1.69 (1.17- 2.42)**	1.63 (1.13- 2.34)**	1.62 (1.13- 2.33)**
High emotional neglect in ACEs and high abuse in AAEs	40/1476	1.63 (1.19- 2.23)**	1.44 (1.05- 1.97)*	1.40 (1.02- 1.91)*	1.39 (1.02- 1.91)*

High abuse in ACEs and low AAEs	212/8368	1.52 (1.32-1.76)***	1.44 (1.25-1.67)***	1.43 (1.23-1.65)***	1.42 (1.23-1.65)***
High abuse in ACEs and high physical neglect in AAEs	39/974	2.43 (1.76-3.33)***	2.33 (1.70-3.20)***	2.21 (1.61-3.05)***	2.21 (1.61-3.05)***
Both high abuse in ACEs and AAEs	100/1933	3.15 (2.57-3.86)***	2.69 (2.20-3.30)***	2.62 (2.13-3.22)***	2.61 (2.12-3.21)***

Note: *P < 0.05, **P < 0.01, ***P < 0.001. Adjusted model 1: age and sex were adjusted; Adjusted model 2: Townsend Deprivation Index, education level, ethnicity, smoking status, alcohol drinking, physical activity, healthy diet, and body mass index were additionally adjusted; Adjusted model 3: type 2 diabetes was additionally adjusted.

Abbreviations: IBS, irritable bowel syndrome; ACEs, adverse childhood experiences; AAEs, adverse adulthood experiences; HR, hazard ratio; CI, confidence interval.

a**b****c****d**

a**b****c****d**