

Published in final edited form as:

Am J Gastroenterol. 2008 March ; 103(3): . doi:10.1111/j.1572-0241.2007.01722.x.

Early life risk factors that contribute to irritable bowel syndrome in adults: a systematic review

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Abstract

Background—IBS is a common disorder that occurs in adults. The natural history of symptoms and risk factors that contribute to IBS may begin in the childhood period. The aim of this systematic review of the published medical literature was to determine what early life factors have been demonstrated to contribute to the development of IBS in adolescents and adults.

Methods—A computer-assisted search of the PubMed database from 1966 to 2007 was performed. The selection criteria were: (1) studies conducted in adolescents or adults with IBS that (2) investigate pre-morbid factors occurring specifically during the childhood period and are (3) associated with the outcomes of symptoms, quality of life, health care utilization, and interferences with work or disability.

Results—Twenty-five articles met inclusion criteria. The studies were categorized into articles examining the persistence of childhood gastrointestinal symptoms into adulthood, affluent childhood socioeconomic status and adult IBS, infantile and childhood trauma associated with the development of adult IBS, and social learning of illness behavior as predictors of adult IBS.

Conclusion—Pediatricians should be aware that potentially modifiable childhood factors such as early symptom management of recurrent functional abdominal pain with cognitive therapies and parent education about social learning may alter illness behavior and the manifestation of IBS. Research in examining the effect of affluent childhood socioeconomic status and early childhood trauma in the evolution of functional gastrointestinal disorders may help identify causative factors of IBS.

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Conflict of interest statements

- A. Dr. Chitkara is the guarantor of the paper.
- B. Each authors contribution to the paper.
 1. Denesh K. Chitkara, M.D. Primary development of the concept, research of the background, primary author of the initial and final draft.
 2. Miranda van Tilburg, Ph.D. Development of the concept, editorial revisions of each draft.
 3. Nannette Bloise-Martin, R.N. Development of the concept and research of the background.
 4. William E. Whitehead. Development of the concept, editorial revision of each draft.
- C. There is no further financial report was received other than what has been acknowledged.
- D. There are no potential competing interests.

Keywords

abdominal pain; pediatrics; functional gastrointestinal disorders; irritable bowel syndrome

Introduction

Irritable Bowel Syndrome (IBS) is a gastrointestinal disorder characterized by chronic abdominal pain or discomfort and disturbed bowel function without a readily identified etiology. IBS is a common disorder experienced by 10-15% of the general adult population¹. This disorder accounts for a high societal burden of disease and accounts for an estimated \$1.7 billion in annual direct medical costs in the U.S., and an estimated \$20 billion in indirect costs due to worker absenteeism².

Functional abdominal pain and constipation are also frequently observed in children. Population based studies have demonstrated that approximately 8% of children experience functional recurrent abdominal pain, and 18-61% of these children will continue to report symptoms of abdominal pain or IBS 5-30 years later³. Pathophysiologic mechanisms that are associated with symptoms such as altered intestinal motility and heightened visceral sensitivity are common features observed in both children and adults with functional gastrointestinal disorders⁴⁻⁷. In addition, co-morbid extra-intestinal symptom complaints such as back pain, headache, limb pain, anxiety and depression are also common to both children and adults with functional gastrointestinal disorders^{3, 8}. These observations suggest that in a proportion of adults, the natural history of their symptoms of IBS began during the childhood period.

The aim of this systematic review of the published medical literature was to determine what early life factors have been demonstrated to contribute to the development of IBS in adolescents and adults. We hypothesize that identifying modifiable early childhood factors that contribute to IBS may help improve health outcomes such as decreased health care utilization and disability associated with symptoms when children become adults.

Methods

Literature search

A computer-assisted search of the PubMed database from 1966 to 2007 was performed using medical subject heading (MeSH) and title words for the terms “irritable bowel syndrome”, OR “functional diseases colonic”, OR “functional gastrointestinal disorders”, AND “risk” OR “risk factors”, AND “early”, OR “childhood” OR “infant”. Reference lists of relevant articles were reviewed for additional citations.

Study selection criteria

The titles and abstracts of all citations identified by the literature search were reviewed. Potentially relevant studies were retrieved, reviewed in full, and the selection criteria were applied. The selection criteria were: (1) studies conducted in adolescents or adults with IBS that (2) investigate pre-morbid factors occurring specifically during the childhood period and are (3) associated with the outcomes of symptoms, quality of life, health care utilization, and interferences with work or disability. All studies conducted in both clinical settings and population-based samples were considered.

Selected studies

The initial search of the PubMed database yielded 107 articles. Twenty-five articles met inclusion criteria. The studies were categorized into articles examining the persistence of childhood gastrointestinal symptoms into adolescence and adulthood, affluent childhood socioeconomic status and adult IBS, traumatic events during infancy and childhood, and social learning of illness behavior and adult IBS. Table 1. summarizes the study results.

Persistence of childhood gastrointestinal symptoms into adolescence and adulthood

There is evidence from prospective studies that adults with IBS began experiencing recurrent functional abdominal pain and constipation as a child. Utilizing a prospective longitudinal birth cohort, Howell et al demonstrated that IBS at age 26 yr was significantly more common among individuals with a history of chronic abdominal pain between ages 7 and 9, as assessed by history (OR = 1.85; $p=0.02$), parental report (OR = 1.82; $p=0.03$), and medical service encounters (OR = 3.75; $p=0.03$)⁹.

These findings have been corroborated by other studies in which children with functional recurrent abdominal pain (RAP) and constipation have been re-surveyed as adolescents and adults. Apley et al. interviewed patients who 8-20 years previously experience symptoms of recurrent abdominal pain. In this study, 38% of subjects continued to experience abdominal pain. However, there was no comparison group to assess the prevalence of gastrointestinal symptoms in the general population, and the sample studied was small ($n=30$)¹⁰. Christensen et al. reported a higher prevalence of gastrointestinal symptoms among 34 individuals admitted for recurrent abdominal pain as a child compared to individuals without a childhood history of abdominal pain, and 53% continued to have gastrointestinal symptoms 30 years later¹¹. In a case/control study, Walker et al. reassessed children who were initially seen in a clinic for recurrent abdominal pain and healthy controls after 5 years^{12, 13}. Female subjects with RAP as a child were more likely to meet the Manning criteria for IBS as an adolescent compared to control subjects ($p=0.03$), but this trend was not seen in boys¹³. In a similarly designed study, Kahn et al. surveyed adults for symptoms of IBS (median age 22) who had been previously evaluated for functional childhood constipation compared to children who had a tonsillectomy between 1-8 years of age¹⁴. Although the frequency of functional constipation in adults was not different between cases and controls, the frequency of IBS was higher in adults with a history of childhood constipation as a child compared to the children who underwent a tonsillectomy as a child (control) (55% vs. 24%; $p<0.05$)¹⁴.

Claar et al. examined factors that moderate the relationship between disability and symptoms in adolescents and adults with IBS who had previously experienced symptoms of functional abdominal pain as a child 5 years prior¹⁵. In patients who met the criteria for IBS and had abdominal pain as children, the relation between symptoms and disability was stronger at lower levels of perceived academic competence¹⁵. Among females with IBS, increased symptoms and disability were associated with lower levels of perceived social competence whereas among males with IBS, increased symptoms and disability were associated with lower levels of perceived athletic competence¹⁵.

Retrospective data from adults with IBS also suggest that adult IBS may represent the persistence of gastrointestinal symptoms from childhood in at least a subset of patients. In semi structured interviews, Lowman et al asked adult patients and non-patients (individuals who met symptom criteria for IBS but had not consulted a doctor) and individuals without IBS (healthy controls) to recall what gastrointestinal symptoms they experienced as a

child¹⁶. Patients with IBS differed from non-patients with IBS by reporting more severe current gastrointestinal symptoms and more frequent doctor visits during childhood¹⁶. Compared to healthy controls, patients and non-patients with IBS reported poorer current general health and more childhood headaches, stomachaches, and bowel complaints¹⁶.

Other studies have failed to find a significant association between childhood abdominal pain and adult IBS but have reported that childhood abdominal pain is a risk factor for having an adult psychiatric diagnosis. In a population-based birth cohort survey, Hotopf et al reported that children with abdominal pain during the previous year on three occasions (at ages 7, 11, 15) were more likely to have a psychiatric disorder in adulthood, but they were not more likely to have a gastrointestinal disorder after adjustment for psychiatric conditions¹⁷. However, in this study, the type of psychiatric disorder was not specified and individuals with a functional gastrointestinal disorder may not have been accurately identified¹⁷. Similarly, Campo et al. interviewed a group of 28 subjects with recurrent functional abdominal pain and 28 matched subjects with tonsillectomy and adenoidectomy an average of 11 years after their index visit¹⁸. Patients with childhood RAP were more likely to meet the criteria for having a lifetime history (46.4% vs. 17.9%) and current symptoms (21.4% vs. 0%) of anxiety compared to controls¹⁸. However, group differences in current abdominal pain among patients with RAP as a child were not statistically significant from controls (70.4% vs. 44.4%)¹⁸. However, due to the small sample size (n=28 RAP cases and 28 controls), this study may have been underpowered to detect statistical differences¹⁸.

Overall, these studies suggest that in a proportion of individuals with IBS, the onset of abdominal or bowel complaints begin in the childhood period. Although all children with episodic functional abdominal pain are not likely at risk, children with recurrent abdominal complaints and other identified risk factors such as co-morbid psychosocial stressors may be at the highest risk for continuing to manifest symptoms of IBS as an adult. Mulvaney et al. examined factors associated with symptom persistence in children with functional abdominal pain¹⁹. Over a 5 year period, children with persistent abdominal pain tended to have more anxiety, depression, lower self worth, and more negative life events¹⁹. Patients with IBS and symptoms of abdominal pain persisting from childhood to adulthood may experience less ability to manage their long-standing and unexplained symptoms. This inability to address unexplained symptoms may lead to illness related behaviors such as experiencing a disproportionate degree of disability from symptoms, or frequently seeking health care for ill defined symptoms. This problem is compounded by the limited ability of pediatricians to treat chronic functional abdominal pain as there is little evidence of effective pharmacologic treatments for this condition²⁰, and current pharmacological treatments used in adults and children with functional gastrointestinal disorders are associated with unacceptable risks²¹⁻²⁴.

One possible management strategy to address continued and prolonged symptoms of functional abdominal pain and IBS would be to utilize cognitive therapies. Cognitive therapies such as education, cognitive behavioral therapy, and hypnosis have the advantage of teaching children self-management strategies that can be utilized throughout their lives. These treatment have been utilized in children with success^{21, 25, 26}. Although access to specialized therapy is limited, home based treatments are currently being developed and the initial results appear promising²⁷. Cognitive therapies may positively influence immediate symptoms in children with functional abdominal pain and potentially provide long term management strategies to decrease illness behavior as children become adults with IBS.

Affluent childhood socioeconomic status and adult IBS

Two studies demonstrated a relationship between childhood economic affluence and symptoms of IBS in adults^{28, 29}. Mendall et al. surveyed subjects in a general practice clinic for symptoms of IBS as defined by the Manning criteria²⁹. For their survey, an association was found between subjects with IBS and the recollection of a childhood living density of <1 person per room (O.R. 3.47; 95% C.I. 1.57-7.64.)²⁹. Howell et al. examined the association between childhood economic status and IBS in a prospective longitudinal birth cohort in New Zealand²⁸. Childhood social class was assigned according to the highest socioeconomic (SES) level of either parent from interviews across the first 15 yr of life²⁸. For this study, an affluent childhood social class was associated with IBS in gender adjusted models²⁸. Furthermore, this trend was characterized as a linear decrease in the odds of IBS across decreasing levels of social class²⁸.

The results of these studies are somewhat contradictory to studies which have demonstrated childhood socioeconomic disadvantage to be associated with multiple poor adult health outcomes^{30, 31}. One hypothesis to explain this observation is that factors associated with socioeconomic disadvantage such as crowded living conditions at an early age may actually protect against the development of post-infectious IBS through increased exposure to intestinal organisms and development of immune tolerance³². Gwee³² has proposed this “hygiene hypothesis” to explain the dissimilar prevalence’s of IBS reported in western countries compared to Asian countries³². Individuals in Asian countries with presumably more exposures to enteric pathogens at an earlier age tend to report lower prevalence rates of adult IBS compared to individuals in Western countries³². Although preliminary, two studies suggest that an affluent childhood is an independent risk factor for IBS, and support a hygiene hypothesis for the development of IBS in adulthood.

Traumatic events during infancy and IBS

Two studies have identified risk factors during infancy related to trauma may influence symptoms in adults with IBS^{33, 34}. Bengston et al. theorized that, because it is known to contribute to the development of other chronic conditions such as cardiovascular disease, early neonatal growth delays may influence the development of IBS³³. This study consisted of a cross section survey of 12,700 Norwegian twins born between 1967 and 1979³³. Twins with a birth weight below 1500 grams (g) were significantly more likely to develop IBS (adjusted odds ratio 2.4 (95% C.I. 1.1-5.3). In addition, individuals with a birth weight <1500 g had a significantly younger age of onset of IBS that individuals with a higher birth weight³³. This study suggests that pre-natal traumatic events that effect neonatal growth may contribute to the development of IBS.

Anand et al. examined the role of early infant trauma on the development of IBS. In this study, a multivariate logistic regression analysis showed that gastric suction at birth was associated with being discharged from the hospital with a diagnostic code for a functional intestinal disorder later in life (odds ratio, 2.99; 95% confidence interval, 1.32-6.79; P=.009), whereas maternal, perinatal, or other confounding variables were not significant³⁴.

Traumatic events during childhood and IBS

A number of studies have examined the association of traumatic events such as abuse and loss of a parent during childhood to the development of IBS. Drossman et al. surveyed individuals who presented for IBS in a university based gastroenterology clinic³⁵. They demonstrated that patients with functional gastrointestinal disorders were more likely to report a history of physical or sexual abuse during childhood or later in life compared to individuals with organic disorders³⁵. Although some studies have combined childhood and

adult abuse to demonstrate an association with IBS^{36,37}, other studies have specifically investigated whether abuse during the childhood period was associated with IBS³⁸. In a case control study of outpatients with IBS and organic gastrointestinal disorders, Salmon et al. reported that adult patients with IBS recalled more sexual and physical abuse as a child³⁹. These individuals also tended to have more symptoms of anxiety, depression, somatization, and dissociation as an adult³⁹.

In a large age and sex stratified random population based sample, Talley et al. reported a significant association between adult IBS and sexual abuse, emotional or verbal abuse, and physical abuse specifically in childhood⁴⁰. The odds of visiting a physician for symptoms of IBS as an adult were highest in those reporting abuse in childhood⁴⁰. Talley et al. performed an additional study to try to explain the relationship between childhood abuse, psychological symptoms, and IBS⁴¹. In this study, a population based sample was surveyed for symptoms of childhood abuse, psychological factors, and IBS. Although a univariate association between childhood abuse and IBS was demonstrated (O.R. 2.02; 95% C.I. 1.29-3.15), when adjusting for age, gender, and psychological factors such as neuroticism, childhood abuse was not independently associated with IBS (O.R. 1.34; 95% C.I. 0.83-2.17)⁴¹.

Hislop suggested that parental deprivation during childhood may also be associated with IBS⁴². In a study in which consecutive patients with IBS were interviewed, 61% reported unsatisfactory relationship between their parents, and 31% reported losing a parent through either death, divorce, or separation⁴². However, there was no comparison group to determine if the experience of parental deprivation was unique to subjects with IBS.

Taken together, these studies suggest that possibly prenatal, early infancy, and childhood traumatic events may sensitize an individual to the manifestation of functional gastrointestinal symptoms later in life. One explanation is that childhood traumatic events such as physical or sexual abuse may predispose an individual to psychological distress which would lead to exaggerated reactions to stress and manifest as symptoms of IBS or increased disability when confronted with unexplained gastrointestinal symptoms. Evidence that supports this theory is the consistent demonstration of higher levels of anxiety, depression, and somatization in both referral and community based patients with IBS and the increased likelihood of individuals with psychological distress to develop IBS after a gastrointestinal infection^{43, 44}.

Alternatively, injurious childhood events or possibly prenatal insults may act as contributory factors toward the sensitization of intestinal visceral afferents with lifelong consequences. In support of this, experimental animal models of IBS are based upon inducing visceral sensitivity by manipulating early life events. Coutinho et al. demonstrated that the early life event of maternal separation predisposed Long-Evans rats to develop visceral hyperalgesia, reduced somatic analgesia, and increased colonic motility as they matured⁴⁴. Al-Chaer et al. utilized Sprague-Dawley rats to demonstrate that colonic irritation in neonates, but not in adults, resulted in chronic visceral hypersensitivity associated with central neuronal sensitization in the absence of identifiable peripheral pathology⁴⁵. These studies mimic the physiologic findings that have been demonstrated in humans with IBS, and suggest that there may be a critical time period during which traumatic events are more likely to affect the development of visceral hypersensitivity.

Neonatal or early childhood trauma may play a role in chronic visceral hypersensitivity or psychological hypervigilance of altered gastrointestinal symptoms. Both observational clinical and experimental data support early childhood as a critical time period in which trauma can induce visceral sensitivity and the manifestation of a functional gastrointestinal disorder.

Social learning of illness behavior and adult IBS

Whitehead et al. proposed that individuals with IBS may develop illness behavior as a consequence of social learning from parental reactions to symptom complaints. Social learning of illness behavior occurs when parents respond to abdominal complaints of their children with increased attention (reinforcement), or when parents with IBS behave in a manner that demonstrates a preoccupation with illness (modeling)⁴⁶. Whitehead et al. initially reported retrospective data on parental reinforcement of illness in adults with IBS⁴⁷. In a telephone survey of metropolitan Cincinnati, individuals with IBS were found to be more likely than the general population to report somatic complaints, to view cold symptoms as a more serious condition, and were more likely to consult a physician for minor illnesses⁴⁷. In this study, individuals with IBS and illness behavior were also more likely to recall childhood reinforcement of illness behavior by recalling being given gifts or special foods when they had an illness as a child⁴⁷.

Levy et al. examined the role of modeling of illness behavior and heredity in IBS⁴⁸. In a survey of more than 60,000 twin pairs, the concordance for IBS was significantly greater ($P = 0.030$) in monozygotic (MZ) (17.2%) than in dizygotic (DZ) (8.4%) twins, supporting a genetic contribution to IBS⁴⁸. However, the proportion of DZ twins with IBS who have mothers with IBS (15.2%) was greater than the proportion of DZ twins with IBS who have co-twins with IBS (6.7%, $P < 0.001$), and logistic regression analysis demonstrated that having a parent with IBS was an independent predictor for the individual having IBS ($P < 0.001$)⁴⁸. Although other twin studies have supported either a genetic^{33, 49} or environmental⁵⁰ cause for IBS, no other studies have examined factors that occur specifically during the childhood period.

Hill et al. reported that adults with non-organic abdominal pain and IBS reported having more siblings (i.e., larger families) than individuals with organic cause for abdominal pain such as peptic ulcer disease⁵¹. Individuals with non-organic abdominal pain reported an average of 5.4 siblings versus an average of 4 siblings in the organic abdominal pain group⁵¹. The authors theorized that individuals tend to report symptoms to gain attention in a larger family, and reflects a type of social learning⁵¹.

Since adults with IBS and illness behaviors tend to recall experiencing positive attention or reinforcement of illness behavior as children, parental behavioral intervention may have both short and long term consequences as children become adults⁵². Levy et al. reported that children, whose mothers made more statements that reinforced illness behavior, independently reported more severe stomachaches⁴⁶. Addressing the parents reactions to a child's abdominal complaints may be one mechanism to affect to the degree of disability an individual experiences due to their symptoms. Walker et al. demonstrated that parents utilizing distraction techniques as opposed to sympathy were able to decrease the level of discomfort that their children with functional abdominal pain experienced when undergoing an experiment designed to trigger abdominal pain by drinking water until completely full (a water load test)⁵³. This intervention may have potential long term beneficial consequences as distraction decreases the reinforcement received from symptom complaints. It is important that pediatric practitioners recognize the potential benefits of responding to symptoms of chronic abdominal pain with distraction and to discuss this with parents of children with chronic functional abdominal pain.

Study Limitations

A number of limitations need to be considered in the studies examining childhood risk factors for adult IBS. Many studies relied on the retrospective recollection of childhood experiences including the onset of symptoms, parenting patterns, and history of physical and

sexual abuse. These studies cannot completely exclude cognitive bias: That is, currently experiencing pain symptoms may positively influence selective recollections of past memories of pain experiences during childhood. Another limitation of many reviewed studies is that they examined childhood factors in a selective population who sought medical care. The findings in these subjects may not be generalizable to the public as only a proportion of individuals who experience gastrointestinal symptoms consistent with IBS seek out medical care.

Prospective population based cohorts have been used to examine the role of childhood factors in the development of functional gastrointestinal disorders in adults, and these studies provide the ideal methodology to assess the association between childhood factors and adult outcomes. However, these studies provide information only after decades of observation. The limitations of studies that derive information from recollection of childhood events, selected clinic populations, and in some case uncontrolled observations (Table 1) should be understood in the interpretation of studies examining childhood factors that contribute to functional gastrointestinal disorders in adults. However, together these studies provide preliminary information that can be used as a guide for modifying early childhood factors that appear to contribute to symptoms and illness behavior in adults with functional gastrointestinal disorders.

Summary

This review summarizes factors that are specific to the early childhood time period in the development and manifestation of illness behavior and symptoms in adults with IBS. Factors such as the early manifestation of GI symptoms, affluent childhood socioeconomic status, prenatal, infant, and childhood trauma, as well as reinforcement and modeling of illness behavior are all potential early life mediators of symptoms and illness behavior in adults with IBS. Clinicians should be aware of techniques for potentially modifying early life factors including early symptom management with cognitive therapies and parental education about social learning of illness behavior in children. The effect of affluent childhood socioeconomic status and early childhood trauma in the evolution of functional gastrointestinal disorders are areas for which further research may help identify causative factors for IBS.

Acknowledgments

Supported by grants R24 DK67674 and RO1 DK31369. Dr. Chitkara has received research grant support through the AGA Foundation Outcomes Research Award.

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Table 1

Summary of Studies Examining Early Life Risk Factors that Contribute to IBS in Adulthood.

Study	Method to determine IBS/abdominal pain diagnosis/ additional factors surveyed	Pertinent risk factor surveyed	Method to determine risk factor	Location of survey	Population	Sample Size	Comparison or control group
<i>Persistence of childhood gastrointestinal symptom into adulthood</i>							
Howell et al. ⁹	Questionnaire/IBS Manning and Rome criteria	Childhood chronic abdominal pain	Prospective data collection	New Zealand	Longitudinal Birth Cohort	N=912	Yes
Apley et al. ¹⁰	Interview/continued abdominal pain	Childhood recurrent abdominal pain	Prospective data collection	United Kingdom	Follow-up study/clinic sample	N=30	No
Christensen et al. ¹¹	Questionnaire/abdominal pain and GI symptoms	Childhood recurrent abdominal pain	Prospective data collection	Denmark	Follow-up clinic sample	N=30 cases childhood RAP; n=45 non RAP controls	Yes
Stieckler et al. ⁵⁴	Questionnaire and interview/abdominal pain and GI symptoms	Childhood recurrent abdominal pain	Prospective data collection	United States	Follow-up clinic sample	N=161 cases with childhood abdominal pain	No
Magni et al. ⁵⁵	Semi-structured interview/GI and somatic symptoms	Childhood recurrent abdominal pain	Prospective data collection	Italy	Follow-up clinic sample	N=22	No
Walker et al. ¹³	Interview/IBS Manning criteria, clinic visits, psychosocial symptoms	Childhood recurrent abdominal pain	Prospective data collection	United States	Follow-up Sample	N=76 cases childhood RAP/N=49 nonRAP control	Yes
Kahn et al. ¹⁴	Questionnaire/IBS and Functional GI disorders	Functional childhood constipation	Prospective data collection	United States	Follow-up clinic patients	N=20 cases childhood constipation; n=17 childhood tonsillectomy	Yes
Clarr et al. ¹⁵	Questionnaire/IBS social and athletic competence, functional disability	Childhood recurrent abdominal pain	Prospective data collection	United States	Follow-up Sample	N=76 cases childhood RAP; N=49 control	Yes
Lowman et al. ¹⁶	Questionnaire/IBS	Childhood abdominal and bowel complaints, headaches physician visits	Recollection	United States	GI clinic patients/non-patients	N=88 IBS patients; N=67 IBS non-patients; N=79 healthy control	Yes
Hocopf et al. ¹⁷	Questionnaire/Physical and psychiatric symptoms	Abdominal pain at 7, 11, and 15 years	Prospective data collection	United Kingdom	Longitudinal birth cohort	N=3637	Yes
Campo et al. ¹⁸	Questionnaire and interview/IBS and psychiatric symptoms	Childhood recurrent abdominal pain	Prospective data collection	United States	Follow up clinic patients	N=28 with childhood RAP; N=28 childhood tonsillectomy and adenotomectomy patients	Yes
<i>Adjuvant childhood socioeconomic status and adult IBS</i>							
Mendall et al. ²⁹	Questionnaire and interview/IBS Manning criteria	Childhood living density, antibiotic use, parental occupation	Recollection	United Kingdom	General practice	N=421	Yes
Howell et al. ²⁸	Questionnaire/IBS Manning and Rome criteria	Childhood socio-demographic class	Prospective data collection	New Zealand	Longitudinal Birth Cohort	N=980	Yes
<i>Low birth weight and infantile trauma</i>							
Bengston et al. ³³	Questionnaire/ IBS self report	Birth weight	Prospective data collection	Norway	Population based sample of twins	N=12700	Yes
Anand et al. ³⁴	Diagnostic codes for being hospitalized for "functional intestinal complaints"	Peri-natal record of gastric suction	Retrospective data collection	Sweden	Consecutive medical records of births between 1935-1945	N=1110	Yes
<i>Traumatic childhood events</i>							
Drossman et al. ³⁵	Questionnaire/IBS	Sexual or physical abuse in childhood or later in life	Recollection	United States	Consecutive university Gastroenterology clinic attendees	N=206	Yes/organic GI disorders
Koloski et al. ³⁶	Questionnaire/Rome criteria	Sexual, physical, emotional abuse as a child and adult	Recollection	United States	Population based survey	N=307	Yes
Walker et al. ³⁷	Physician diagnosed IBS/structured interview	Sexual trauma or victimization	Recollection	United States	Primary and tertiary care clinic patients	N=28 IBS and N=19 IBD	Yes
Salmon et al. ³⁹	Physician diagnosed IBS/ Questionnaire, Manning criteria	Sexual, physical, or psychological abuse as a child and adult	Recollection	United Kingdom	Sequential Gastroenterology Clinic Patients	N=61 IBS and N=64 IBD	Yes

Study	Method to determine IBS/abdominal pain diagnosis/ additional factors surveyed	Pertinent risk factor surveyed	Method to determine risk factor	Location of survey	Population	Sample Size	Comparison or control group
Talley et al ⁴⁰ .	Questionnaire/Manning criteria	Sexual, verbal, emotional abuse as a child and adult	Recollection	United States	Community based sample	N=919	Yes
Talley et al ⁴¹ .	Questionnaire/Rome criteria	Childhood and adult abuse, psychologic comorbidity	Recollection	Australia	Community based sample	N=730	Yes
Hislop et al ⁴² .	Physician diagnosis of IBS/interview	Parental relationships during childhood	Recollection	Australia	Clinic sample	N=333	No
Social learning of illness behavior and adult IBS							
Whitehead et al ⁴⁷ .	Telephone interview/IBS and somatic complaints, physician consultations	Illness behaviors as a child	Recollection	United States	General population	N=832	Yes
Levy et al ⁴⁸ .	Questionnaire/self report of IBS	IBS in family members	Recollection	United States	Population based sample of twins	N=10699	Yes
Hill et al ⁵¹ .	Physician diagnosis of non-organic abdominal pain/interview	Number of siblings in family	Recollection	United Kingdom	Gastroenterology clinic	N=31 non-organic abdominal pain; N=31 PUD and organic abdominal pain	Yes