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Risk Factors for Chronic Diarrhea in the Community in the Absence of Irritable Bowel Syndrome

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Abstract

Objective—In contrast to irritable bowel syndrome (IBS), the prevalence and risk factors for diarrhea in the absence of IBS in the community are unknown. We aimed to evaluate potential risk factors for chronic diarrhea (non-IBS).

Methods—A valid questionnaire that recorded gastrointestinal symptoms required for a diagnosis of chronic diarrhea, self-reported measures of potential risk factors, and a somatic symptom checklist (SSC) was mailed to an age- and gender- stratified random sample of Olmsted County, Minnesota residents (30–64 year). Chronic diarrhea was defined as reporting one or more of the following symptoms more than 25% of the time in the past 3 months: ≥ 3 bowel movements a day, loose or watery stools, or fecal urgency. Subjects with IBS (Rome III) were excluded.

Results—Of 892 eligible subjects, 653 (73%) responded. Among 523 respondents not reporting IBS, chronic diarrhea was reported by 148 (28%); 90 (61%) had chronic painless diarrhea. Chronic diarrhea was significantly associated with self-reported food sensitivity (OR=2.05 [1.31–3.20]) and stress (OR=1.99 [1.03–3.85]). Both remained significant in the adjusted variable models that excluded subjects with any abdominal pain. Female gender (OR=0.67 [0.45–0.98]) and higher education level (OR=0.60 [0.39–0.92]) had smaller odds for chronic diarrhea. No association was detected for age, marital status, body mass index, cigarette or alcohol use, coffee, analgesics, emotional support, pets, or water source.

Conclusion—Chronic diarrhea in the absence of IBS is common; self-reported food sensitivity, male gender and a lower level of education are risk factors.

Keywords

chronic diarrhea; food sensitivity; irritable bowel syndrome; risk factors

INTRODUCTION

Chronic diarrhea is a common problem in the general population, and there are a wide range of disorders to consider in the differential diagnosis.¹ Historically, a myriad of definitions

have been used to define chronic diarrhea including increased frequency of stools (e.g. more than three bowel movements a day), increased liquidity or loose stools, increased stool weight (e.g. more than 200 grams per day), or decreased fecal consistency.¹ Length of symptoms has also varied among clinical studies, but a duration of four weeks has generally been accepted as meeting criteria for “chronic”.¹ However, a universally accepted consensus definition has yet to be formulated. When underlying organic diseases are absent, a functional bowel disorder is thought to be present. The two major functional bowel disorders characterized by diarrhea are the irritable bowel syndrome (IBS) and functional diarrhea (where there is passage of loose or watery stools without abdominal pain or discomfort).²

Given the differences in definition, the exact prevalence and impact of chronic diarrhea is largely unknown. However, available data indicates that chronic diarrhea is a common complaint in the community; with prevalence estimated as high as 27%.³ Available evidence indicates that chronic diarrhea represents a significant health care burden in the United States: in 1998, estimated to account for over 2 million physician office visits, over 400,000 emergency room visits, and over 165,000 inpatient hospital stays; and for the year 2000, estimated to account for \$661 million in both direct and indirect costs.⁴ In addition to the economic burden, quality of life has been shown to be negatively impacted.^{5,6}

Although much has been written about chronic diarrhea as a subtype of IBS, there remains a lack of investigation outside of this symptom complex. In this study, we sought to evaluate for potential risk factors for chronic diarrhea without IBS in the adult community.

MATERIALS AND METHODS

This study reports results from a cross-sectional survey of a population-based cohort of subjects randomly selected from Olmsted County, Minnesota, identified and followed longitudinally since 1988. We have previously used this survey to evaluate risk factors for IBS and chronic constipation.^{7,8} The study was approved by the Mayo Foundation Institutional Review Board.

Subjects

The Olmsted County population is comprised of approximately 120,000 persons, of whom 89% are white. Sociodemographically, this community is similar to the US caucasian population except for a slightly higher education level and higher proportion employed in the health-related services industry.⁹ Eighty percent of the local population resides within 5 miles of Rochester, MN and virtually all residents receive their medical care almost exclusively from two group practices: Mayo Medical Center and Olmsted Medical Center. The Mayo Clinic has maintained a common medical records system with its two affiliated hospitals (St. Marys and Rochester Methodist) for over 100 years. All diagnoses and surgical procedures are recorded and indexed, including all diagnoses made on outpatients seen in the office or clinic consultations, emergency room visits, or nursing home care. Diagnoses are also recorded for hospital inpatients, at autopsy examination, or on death certificates. The Rochester Epidemiology Project (REP) further developed this system by creating similar indices for the records of other providers to local residents, most notably the Olmsted Medical Group and its affiliated Olmsted Community Hospital. This medical records linkage system allows access to details of the medical care provided to Olmsted County residents for research as long as research authorization is provided by subjects. Annually, more than 80% of the entire population is attended by one or both of these two practices, and approximately 96% of the population is seen at least once during a 4-year-period.⁹ Thus, the REP is a medical records linkage system which provides an enumeration of this population from which samples can be drawn.

Using this system, a series of random samples, stratified by age (in 5-year intervals) and gender, of Olmsted County residents were drawn between 1988 and 1993. Results of previous studies from these cohorts have been reported.^{7,8,10–17} Following approval from the Mayo Foundation Institutional Review Board, a random sample of 1290 caucasian Olmsted County residents aged 30–64 years was drawn.

The medical records of the individuals listed in the sample were reviewed. Subjects were excluded if they had significant illnesses that might cause gastrointestinal (GI) symptoms (n=14) or impaired their ability to complete the questionnaire (e.g. metastatic cancer, major stroke; n=20); had a history of major abdominal surgery (n=16); or had a major psychotic episode, mental retardation, or dementia (n=13). Incarcerated individuals in the local Federal Medical Center (n=31) and subjects for whom contact was prohibited for legal reasons (n=1) were excluded. Residency confirmation further excluded 89 subjects that no longer resided within the county. Subsequently during the course of the study, 13 subjects died and two developed severe medical illnesses; nine subjects were found to have a prior history of psychotic illness, mental retardation, or did not understand written English; seven were not actual county residents and 132 moved outside of the county; 34 moved to a new unknown address and 19 were assumed to have moved because they had no medical contacts in 5 years and could not be contacted by mail or telephone. Nine additional subjects were subsequently excluded after they were identified from the questionnaire as having intercurrent illnesses. A total of 892 county residents without significant disease were eligible to receive the survey (discussed below).

Questionnaire

This survey used a derivative of the original Talley Bowel Disease Questionnaire (BDQ).¹⁸ The BDQ is a reliable and valid self-report questionnaire that recorded GI symptoms experienced over the past year; past medical history; healthcare use; sociodemographic variables; and a somatic symptom checklist (SSC), a measure of somatization.^{18,19} Previous testing has demonstrated the BDQ to have adequate validity and reliability with a median κ statistic for the symptom items of 0.78, and a median κ statistic for potential risk factors of 0.81.²⁰ The BDQ has also been shown to have adequate content, predictive, construct, and discriminatory validity in the outpatient setting.²⁰

For the derivative of the BDQ that was used, modifications to the original version included: reformatting to improve the visual appeal; inclusion of only 21 of the original 46 symptom items; omission of questions regarding past illnesses; and specific questions were added to assess potential risk factors: height, weight, marital status, educational level, satisfaction with emotional support, stress, food allergies or sensitivities, pets, source of water supply, and use of cigarettes, alcohol, coffee, aspirin, acetaminophen, and non-steroidal anti-inflammatory drugs (NSAIDs) in the past year. The reliability of the questions added to this derivative of the BDQ has been assessed in a previous study, and the median κ statistic for the added questions was 0.81.⁷ Stress was assessed by asking, 'Have you been under or felt you were under any strain, stress, or pressure during the past month?' which was recorded on a 6-point scale (from 'none at all' to 'almost more than I can stand'). The food allergy or sensitivity question first asked the subjects if they were allergic or sensitive to any foods. If yes, they were asked to: 1) indicate the types of foods to which they thought they were allergic or sensitive (e.g. beans/legumes, dairy products, fruits, leafy vegetables, onions, chocolate, eggs, greasy foods, nuts, spicy foods, or other); and 2) whether they had a rash or swelling of the lips or throat. Subjects taking aspirin, acetaminophen, or NSAIDs were asked to provide the frequency of weekly administration by indicating 1–2, 3–6, 7–10, or more than 10 tablets or capsule a week. These subjects were also asked to indicate the symptoms for which they took these analgesics (e.g. backache, headache, or stomach or bowel problems). A question asking subjects to describe in an open-ended fashion any

changes in health they might have experienced over the past 4 years was also added. All positive responses to this question were reviewed by one of the investigators.

Survey

An explanatory letter and the study questionnaire were mailed to this age- and gender-stratified sample of 892 eligible Olmsted County residents. Reminder letters were mailed as needed after 2, 4, and 7 weeks to non-responders. The remaining non-responders were then contacted by telephone at 10 weeks. At any point, subjects who indicated that they did not wish to participate were not further contacted. Seventy-three percent of eligible subjects (653 subjects) ultimately responded.

Chronic diarrhea definition and exclusion of IBS

Subjects with chronic diarrhea were defined as having one or more of the following symptoms at least 25% of the time in the past 3 months: (i) three or more bowel movements a day; (ii) loose or watery stools; or (iii) fecal urgency.

Subjects with symptoms of IBS were specifically excluded based upon their responses to the questionnaire. Based on the Rome III criteria for irritable bowel syndrome, subjects were excluded if they reported symptoms of frequent abdominal pain that was associated with two or more of the following: pain relieved by a bowel movement, increase or decrease in frequency of bowel movements with pain onset, or looser or harder consistency of stool with pain onset.²

Statistical analysis

A logistic regression model was used to identify statistically significant and independent risk factors for chronic diarrhea. Potential risk factors for the analyses included: age, gender, SSC, marital status, educational level, obesity, use of cigarettes, alcohol, coffee, acetaminophen, aspirin, NSAIDs, satisfaction with emotional support, stress, food allergy or sensitivity, pets, and water supply. Regression coefficients were estimated both unadjusted and adjusted for age, gender, and SSC to assess which potential risk factors predicted chronic diarrhea in the past year. Results have been reported as univariate odds ratios (OR) and OR adjusted for age, gender, and SSC score. Body mass index (BMI) was used as a marker for obesity and calculated by the following formula: weight (kg)/height (m²).

Analysis of subjects with functional painless diarrhea was also performed with subset analysis that excluded subjects reporting any abdominal pain. Univariate and multiple variable analyses as described above were performed and reported for this group.

RESULTS

A total of 653 eligible subjects returned the survey, reflecting a 73% response rate. For this analysis, 42 were excluded because: (i) they were from a facility without IRB approval (n = 25); or (ii) they refused research authorization (n = 17). An additional 87 were excluded because they had symptoms of IBS and one other did not provide enough information to exclude IBS. Of these 88 subjects with symptoms of IBS or where IBS could not be defined, 59% were female. Of the remaining 523 qualifying subjects, the median age was 49 years and 51% were female.

Among the 523 subjects not reporting IBS, chronic diarrhea was reported by 148 (28%) of the respondents, and represented 23% of the total eligible subjects. Of the 148 subjects with chronic diarrhea, 58 (39%) reported a history of any abdominal pain, while 90 (61%)

respondents had chronic painless diarrhea without any report of abdominal pain. Table 1 illustrates the sociodemographic characteristics of the subjects included here.

Risk factors for chronic diarrhea

Table 2 reports by risk factor the proportion of subjects with chronic diarrhea [Table 2a] and chronic painless diarrhea [Table 2b]. Chronic diarrhea was significantly associated with self-reported food sensitivity and SSC. Female gender and higher education level were factors with significantly smaller odds for chronic diarrhea. Although univariate associations were detected for reporting moderate satisfaction with emotional support and ‘quite a bit’ of stress during the past month, the significance of both findings were attenuated in the multiple variable model. For chronic diarrhea, no statistically significant association was detected for age, marital status, BMI, smoking history, acetaminophen, aspirin, NSAIDs, coffee use, alcohol use, pets, or water supply.

Chronic painless diarrhea was significantly associated with self-reported food sensitivity, SSC, and stress during the past month. For chronic painless diarrhea, no statistically significant association was detected for age, gender, marital status, education level, BMI, smoking history, acetaminophen, aspirin, NSAIDs, coffee use, alcohol use, pets, or water supply.

Food sensitivity

After adjusting for age, gender and SSC score, subjects reporting any food sensitivity and food sensitivity without rash or swelling had significantly greater odds of reporting symptoms of chronic diarrhea [OR for any food sensitivity 2.05; 95% CI 1.31–3.20; OR for food sensitivity without rash or swelling 2.76; 95% CI 1.68–4.56]. This latter association with food sensitivity without rash or swelling remained significant in the group with chronic painless diarrhea [OR 2.36; 95% CI 1.20–4.64].

Gender and education level

Female gender and higher education level (‘college graduate and beyond’) were both factors with significantly smaller odds for chronic diarrhea [OR for female gender 0.67; 95% CI 0.45–0.98; OR for ‘college graduate and beyond’ 0.64; 95% CI 0.42–0.96]. After adjusting for age, gender, and SSC score, the above association seen with higher education level remained significant [OR for ‘college graduate and beyond’ 0.60; 95% CI 0.39–0.92]. Both of these associations were not seen in subjects with chronic painless diarrhea.

DISCUSSION

In this study, we evaluated potential risk factors for chronic diarrhea in the absence of IBS and found an association with self-reported food sensitivity (without rash or swelling) and stress. Chronic diarrhea (both painful and painless) in the community has not been carefully investigated outside of it as part of the symptom complex of diarrhea-predominant IBS. This study excluded subjects with symptoms of IBS based on the current Rome criteria, and in subset analyses, further excluded subjects with any abdominal pain. Female gender and higher education level were significantly associated with smaller odds of reporting chronic diarrhea. Chronic diarrhea was not associated with age, marital status, BMI, smoking history, acetaminophen, aspirin, NSAIDs, coffee use, alcohol use, pets, or water supply. This study also evaluated potential risk factors for chronic painless diarrhea and found associations with self-reported food sensitivity and level of stress during the past month.

Despite the relative limited published information on the epidemiology of chronic diarrhea, the prevalence of 23% found in this study is consistent with a national, cross-sectional,

telephone survey of US households.³ In that study, 2510 subjects completed interviews (71% response rate); within the month before the interview, 27% reported diarrhea or loose stools and this was more prevalent in men than women, although IBS was not a specific exclusion. Similarly, we found that 28% of the Olmsted County population reported chronic diarrhea (after exclusion of IBS). Historically, although data is limited, differences between the sexes has not been observed for diarrhea.^{3,21} However, this study found that female gender was significantly associated with smaller odds of reporting symptoms of chronic diarrhea. Caution should be applied in interpreting this finding as it would seem to contradict the traditional female predilection for reporting other functional gastrointestinal disorders or symptoms such as IBS, abdominal pain, or bloating.^{3,22} Nonetheless, this finding supports the view that chronic diarrhea has notable features that make it unique outside of IBS. Similarly, there is a paucity of investigation into the role of socioeconomic factors, such as education level, in chronic diarrhea. This study found that subjects with a higher education level were at decreased odds of reporting symptoms of chronic diarrhea. This may reflect more exposure to environmental pathogens in subjects from lower socioeconomic strata. Those with higher socioeconomic status may also have greater ease adjusting to food sensitivities with dietary modification versus those with more financial constraints.

There has been growing interest in the role of food allergies and antigens and their possible role in irritable bowel syndrome. Based on findings that there appears to be GI mucosal immune system activation in some patients with IBS, it has been hypothesized that possible immune activation by food antigens may contribute to the development of food allergy and IBS.²³ This hypothesis is supported by findings of positive responses to elimination diets and disodium cromoglycate (a mast cell stabilizer) for certain patients with IBS.^{24–30} In this study, subjects with symptoms of IBS based on Rome criteria were excluded. Despite this exclusion, chronic diarrhea was found to be associated with self-reported food sensitivity. This finding was significant for both subjects with chronic diarrhea and those with chronic painless diarrhea, and did not appear to be due to classical food allergy with symptoms of rash or swelling of the lips or throat. It should be noted that these were self-reported sensitivities and not based on objective allergen testing. Nonetheless, the association found between chronic diarrhea and ‘non-classical’ food allergy may be specific to this entity. A prior study observed an association between food allergy or sensitivity and IBS; subjects with classical symptoms of rash or swelling were more likely to endorse symptoms of IBS.⁷ Another study did not detect an association between chronic constipation and food allergy or sensitivity.⁸

Disorders such as lactose intolerance or celiac disease may cause chronic diarrhea. Although an extensive dietary history was not obtained by the survey, analysis of the responses to the available food groups suggests that lactose intolerance was not a likely explanation; thus, sensitivity to ‘dairy products’ was not a significant finding in any group. Undiagnosed celiac disease is another consideration; unrecognized celiac disease may account for at least 5% of IBS in some outpatient clinics.^{22,31} However, Locke et al.³² found that among 150 eligible subjects (drawn from a separate random sample of 904 residents of Olmsted County) only 4% of all subjects had positive tissue transglutaminase titers (TTg); positive TTg serologies were identified in 2.6% of controls, 4.0% of subjects with IBS, and 5.9% of subjects with dyspepsia. Given the low prevalence of positive TTg serology in this population, the findings suggest unrecognized celiac disease would explain few of the cases in the present study.

This study also found that chronic painless diarrhea was significantly associated with self-reported stress during the past month. Although no formal psychometric testing was performed to assess and define ‘stress’, the significant findings with self-reported stress

seem plausible. Stress may lead to disruption of intestinal permeability, and this mechanism might explain any link.³³ Several other risk factors were studied and no other significant associations with chronic diarrhea were found.

This study did not find an association between chronic diarrhea and BMI. Although an association between increasing BMI and diarrhea has been reported, it should be noted that this association was found in a birth cohort in New Zealand that was sampled at the age of 26 years.³⁴ The lack of association in this study may reflect the focus on middle-aged adults and that younger adults were not sampled.

A wide range of criteria are available to define chronic diarrhea, but symptoms are relied upon in population-based research. The multitude of definitions also serves to hamper investigations as there still lacks a globally accepted case definition. This difficulty may be reflected in this study by the high prevalence found in this community. Although a broad definition helps in increasing the sensitivity of identifying subjects with diarrhea, inclusion of other disorders may have occurred and may explain the relatively high prevalence found. The increased sensitivity would also have a tendency to hamper detection of relevant risk factors due to dilution of true cases. However, given that this study continued to detect significant risk factors, this would only serve to strengthen the consideration for our findings.

Valid population-based research requires the generation of random samples, use of suitable instruments for measurement of disease, and sufficient response rates. This study used a medical records linkage system which allowed enumeration of a population from which true random samples could be drawn. The BDQ was used, which has been shown to accurately identify the presence of symptoms of functional GI disorders, and this study had a response rate over 70%.¹⁸ Although the interval development of organic etiologies for diarrhea, such as infection or thyroid dysfunction, were not specifically addressed, it is important to note that subjects with any serious diseases were excluded at the time of recruitment. The investigators had access to the complete medical records for each subject and were able to exclude those with significant illness that may cause gastrointestinal symptoms. Furthermore, given that over the 4-year period this cohort was followed, that only nine subjects reported the onset of significant illness that might impact GI symptoms, it is suspected that the number of people with undiagnosed conditions was small. As such, it is assumed that it is unlikely that etiologies such as infection, thyroid dysfunction, or other medical conditions are the underlying causes of diarrhea in these subjects.

The Rochester Epidemiology Project is a medical records linkage system that provides an enumeration of approximately 96% of the population of Olmsted County, Minnesota.⁹ Although the distribution of the caucasian population in this group is higher than that nationally in the United States population, the age, gender, and income distributions are similar. As a community-based study, the selection biases that might apply to a clinic-based sample were likely avoided. Thus, we believe that the results of this study can be generalized to at least other white populations.

In summary, chronic diarrhea is a common disorder and has been poorly investigated outside the context of irritable bowel syndrome. This study examined numerous potential risk factors and identified associations with self-reported food sensitivity and stress, while female gender and higher levels of education were factors associated with smaller odds of reporting chronic diarrhea. These findings warrant further investigation.

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Table 1

Sociodemographic Characteristics of Study Subjects

	All Subjects (N= 523)	Chronic Diarrhea (N= 148)	No Chronic Diarrhea (N=375)	Chronic Diarrhea [§] (N=90)	No Chronic Diarrhea [§]
Median, age (range) yr	49 yr (30 – 64)	50 yr (30 – 64)	47 yr (30 – 64)	48 yr (30 – 64)	50 yr (30 – 64)
Gender, n (%)					
Male	259 (49.5%)	84 (56.8%)	175 (46.7%)	44 (48.9%)	126 (46.7%)
Female	264 (50.5%)	64 (43.2%)	200 (53.3%)	46 (51.1%)	144 (53.3%)
Educational level, n (%)					
Not high school graduate	24 (4.5%)	6 (4.1%)	18 (4.8%)	3 (3.4%)	16 (6.0%)
High school/Some college	298 (57.0%)	95 (65.1%)	203 (54.6%)	57 (64.0%)	148 (55.2%)
College graduate and beyond	196 (37.5%)	45 (30.8%)	151 (40.6%)	29 (32.6%)	104 (38.8%)
Marital status, n (%)					
Single	26 (5.0%)	9 (6.1%)	17 (4.6%)	4 (4.5%)	13 (4.8%)
Married	430 (82.2%)	117 (79.6%)	313 (84.1%)	73 (81.1%)	229 (85.5%)
Divorced/Widowed/Separated	63 (12.0%)	21 (14.3%)	42 (11.3%)	13 (14.4%)	26 (9.7%)
Median SSC score (range)	0.8 (0 – 6.5)	1.1 (0 – 6.5)	0.8 (0 – 6.0)	1.0 (0 – 6.5)	0.7 (0 – 6.0)

[§]Patients with abdominal pain are not included

Table 2

a: Univariate and Adjusted (for age, gender, SSC score) Associations Between Risk Factors and Chronic Diarrhea Among Olmsted County Residents Aged 30–64 Yr			
	% Chronic Diarrhea	Univariate* OR (95% CI)	Adjusted † OR (95% CI)
Age, yr			
≤50 (n = 286)	29.7	1.0	
>50 (n = 237)	26.6	0.86 (0.58, 1.26)	
Gender			
Male (n = 259)	32.4	1.0	
Female (n = 264)	24.2	‡0.67 (0.45, 0.98)	
SSC score (n = 8 missing)			
≤Median (n = 281)	22.8	1.0	
>Median (n = 234)	35.0	‡1.83 (1.24, 2.69)	
BMI (n = 12 missing)			
1 st quartile, 18.0 – 24.2 (n = 129)	26.4	1.0	1.0
2 nd quartile, 24.2 – 26.7 (n = 132)	20.5	0.73 (0.41, 1.29)	0.62 (0.29, 1.35)
3 rd quartile, 26.7 – 30.0 (n = 128)	29.7	1.19 (0.69, 2.06)	0.98 (0.46, 2.05)
4 th quartile, >30.0 (n = 121)	37.2	1.67 (0.98, 2.86)	1.30 (0.63, 2.66)
Cigarette use (n = 5 missing) (n = 11 pipe/cigar)			
Never (n = 260)	26.5	1.0	1.0
Current (n = 81)	33.3	1.38 (0.81, 2.37)	1.08 (0.53, 2.17)
Past (n = 177)	29.4	1.15 (0.75, 1.76)	0.83 (0.47, 1.47)
Ever (n = 258)	30.6	1.22 (0.83, 1.79)	0.91 (0.55, 1.50)
Alcohol, drinks per wk (n = 4 missing)			
None (n = 280)	27.9	1.0	1.0
1–2 (n = 94)	27.7	0.99 (0.59, 1.67)	0.99 (0.51, 1.95)
3–6 (n = 78)	25.6	0.89 (0.50, 1.58)	0.70 (0.32, 1.53)
≥7 (n = 67)	35.8	1.45 (0.82, 2.54)	1.30 (0.63, 2.69)
Yes, any (n = 239)	29.3	1.07 (0.73, 1.57)	0.97 (0.69, 1.60)
Coffee (n = 3 missing)			
No (n = 75)	25.3	1.0	1.0
Yes (n = 445)	29.0	1.20 (0.69, 2.11)	1.15 (0.57, 2.35)
Acetaminophen, tablets per wk (n = 5 missing) (n = 9 missing/wk)			
None (n = 372)	26.3	1.0	1.0
1–2/wk (n = 84)	38.1	‡1.72 (1.05, 2.83)	1.13 (0.57, 2.27)
3–6/wk (n = 33)	30.3	1.22 (0.56, 2.65)	0.88 (0.27, 2.84)
≥7/wk (n = 25)	32.0	1.32 (0.55, 3.15)	1.10 (0.36, 3.36)

a: Univariate and Adjusted (for age, gender, SSC score) Associations Between Risk Factors and Chronic Diarrhea Among Olmsted County Residents Aged 30–64 Yr			
	% Chronic Diarrhea	Univariate* OR (95% CI)	Adjusted † OR (95% CI)
Yes, any (n = 146)	34.3	1.46 (0.96, 2.20)	1.03 (0.58, 1.84)
Aspirin, tablets per wk (n = 6 missing) (n = 10 missing/wk)			
None (n = 326)	28.5	1.0	1.0
1–2/wk (n = 71)	36.6	1.45 (0.84, 2.48)	2.07 (0.99, 4.31)
3–6/wk (n = 58)	25.9	0.87 (0.46, 1.65)	1.08 (0.47, 2.47)
≥7/wk (n = 58)	24.1	0.80 (0.42, 1.52)	0.82 (0.36, 1.89)
Yes, any (n = 191)	28.8	1.01 (0.68, 1.50)	1.23 (0.73, 2.08)
NSAID, tablets per wk (n = 6 missing) (n = 13 missing/wk)			
None (n = 389)	26.7	1.0	1.0
1–2/wk (n = 61)	31.2	1.24 (0.69, 2.23)	1.80 (0.79, 4.07)
3–6/wk (n = 19)	36.8	1.60 (0.61, 4.17)	1.90 (0.57, 6.36)
≥7/wk (n = 41)	34.2	1.42 (0.72, 2.82)	0.92 (0.32, 2.65)
Yes, any (n = 128)	33.6	1.39 (0.90, 2.13)	1.51 (0.84, 2.71)
Marital status (n = 4 missing)			
Married (n = 430)	27.2	1.0	1.0
Single (n = 26)	34.6	1.42 (0.61, 3.27)	0.91 (0.26, 3.14)
Divorced/widowed/separated (n = 63)	33.3	1.34 (0.76, 2.35)	1.33 (0.63, 2.80)
Educational level (n = 5 missing)			
High school/some college (n = 298)	31.9	1.0	1.0
Not high school graduate (n = 24)	25.0	0.71 (0.27, 1.85)	0.54 (0.14, 2.03)
College graduate and beyond (n = 196)	23.0	‡0.64 (0.42, 0.96)	0.74 (0.44, 1.26)
Satisfaction with emotional support (n = 9 missing)			
Completely (n = 257)	23.0	1.0	1.0
Not at all (n = 13)	46.2	2.88 (0.93, 8.89)	0.94 (0.09, 9.72)
Somewhat (n = 62)	25.8	1.17 (0.62, 2.21)	1.59 (0.72, 3.55)
Moderately (n = 182)	33.5	‡1.69 (1.11, 2.58)	1.57 (0.89, 2.77)
Stress during the last month (n = 7 missing)			
None (n = 83)	20.5	1.0	1.0
A little (n = 95)	31.6	1.79 (0.90, 3.56)	‡ 2.82 (1.10, 7.23)
Some/usual (n = 145)	22.1	1.10(0.57, 2.13)	2.21 (0.87, 5.61)
Some/>usual (n = 78)	33.3	1.94 (0.95, 3.95)	‡ 3.52 (1.26, 9.78)
Quite a bit (n = 115)	33.9	‡1.99 (1.03, 3.85)	‡ 4.16 (1.64,10.53)
Food allergy/sensitivity (n = 11 missing) (n = 30 missing rash/swelling)			

a: Univariate and Adjusted (for age, gender, SSC score) Associations Between Risk Factors and Chronic Diarrhea Among Olmsted County Residents Aged 30–64 Yr			
	% Chronic Diarrhea	Univariate* OR (95% CI)	Adjusted † OR (95% CI)
None (n = 392)	24.2	1.0	1.0
Yes, no rash/swelling (n = 88)	47.7	‡2.86 (1.77, 4.60)	‡ 2.36 (1.20, 4.64)
Yes, rash/swelling (n = 13)	23.1	0.94 (0.25, 3.48)	1.32 (0.25, 7.16)
Yes, any (n = 120)	40.8	‡2.16 (1.40, 3.32)	1.64 (0.90, 2.97)
Pets in past year (n = 4 missing)			
None (n = 248)	26.2	1.0	1.0
Dogs (n = 185)	30.8	1.21 (0.81, 1.79)	1.27 (0.76, 2.13)
Cats (n = 134)	29.1	1.05 (0.68, 1.63)	0.92 (0.52, 1.63)
Any pet versus none (n = 271)	30.3	1.22 (0.83, 1.79)	1.26 (0.75, 2.09)
Water source (n = 4 missing)			
Private well and other (n = 163)	31.9	1.0	1.0
City water (n = 356)	26.7	0.78 (0.52, 1.16)	0.80 (0.47, 1.36)

b: Univariate and Adjusted (for age, gender, SSC score) Associations Between Risk Factors and Chronic Painless Diarrhea Among Olmsted County Residents Aged 30–64 Yr			
	% Chronic Painless Diarrhea§	Univariate*§ OR (95% CI)	Adjusted †§ OR (95% CI)
Age, yr			
≤50 (n = 286)	26.9	1.0	
>50 (n = 237)	23.0	0.81 (0.50, 1.31)	
Gender			
Male (n = 259)	25.9	1.0	
Female (n = 264)	24.2	0.92 (0.57, 1.48)	
SSC score (n = 8 missing)			
≤Median (n = 281)	19.0	1.0	
>Median (n = 234)	34.8	‡2.28 (1.40, 3.71)	
BMI (n = 12 missing)			
1 st quartile, 18.0 – 24.2 (n = 129)	26.7	1.0	1.0
2 nd quartile, 24.2 – 26.7 (n = 132)	17.6	0.60 (0.29, 1.22)	0.62 (0.29, 1.35)
3 rd quartile, 26.7 – 30.0 (n = 128)	25.0	0.93 (0.47, 1.84)	0.98 (0.46, 2.05)
4 th quartile, >30.0 (n = 121)	31.8	1.30 (0.68, 2.50)	1.30 (0.63, 2.66)
Cigarette use (n = 5 missing) (n = 11 pipe/cigar)			
Never (n = 260)	25.0	1.0	1.0
Current (n = 81)	30.9	1.34 (0.69, 2.60)	1.08 (0.53, 2.17)
Past (n = 177)	23.2	0.91 (0.52, 1.57)	0.83 (0.47, 1.47)
Ever (n = 258)	25.8	1.04 (0.64, 1.68)	0.91 (0.55, 1.50)
Alcohol, drinks per wk			

b: Univariate and Adjusted (for age, gender, SSC score) Associations Between Risk Factors and Chronic Painless Diarrhea Among Olmsted County Residents Aged 30–64 Yr			
	% Chronic Painless Diarrhea[§]	Univariate^{*§} OR (95% CI)	Adjusted^{†§} OR (95% CI)
(n = 4 missing)			
None (n = 280)	25.0	1.0	1.0
1–2 (n = 94)	26.2	1.07 (0.55, 2.06)	0.99 (0.51, 1.95)
3–6 (n = 78)	20.0	0.75 (0.36, 1.57)	0.70 (0.32, 1.53)
≥7 (n = 67)	31.3	1.36 (0.68, 2.73)	1.30 (0.63, 2.69)
Yes, any (n = 239)	25.6	1.03 (0.64, 1.67)	0.97 (0.69, 1.60)
Coffee (n = 3 missing)			
No (n = 75)	23.2	1.0	1.0
Yes (n = 445)	25.6	1.14 (0.58, 2.23)	1.15 (0.57, 2.35)
Acetaminophen, tablets per wk (n = 5 missing) (n = 9 missing/wk)			
None (n = 372)	24.0	1.0	1.0
1–2/wk (n = 84)	30.8	1.41 (0.73, 2.71)	1.13 (0.57, 2.27)
3–6/wk (n = 33)	23.5	0.98 (0.31, 3.10)	0.88 (0.27, 2.84)
≥7/wk (n = 25)	33.3	1.59 (0.57, 4.40)	1.10 (0.36, 3.36)
Yes, any (n = 146)	29.2	1.31 (0.77, 2.24)	1.03 (0.58, 1.84)
Aspirin, tablets per wk (n = 6 missing) (n = 10 missing/wk)			
None (n = 326)	24.0	1.0	1.0
1–2/wk (n = 71)	40.0	‡2.11 (1.05, 4.25)	2.07 (0.99, 4.31)
3–6/wk (n = 58)	25.0	1.05 (0.47, 2.37)	1.08 (0.47, 2.47)
≥7/wk (n = 58)	20.9	0.84 (0.38, 1.85)	0.82 (0.36, 1.89)
Yes, any (n = 191)	28.1	1.24 (0.75, 2.03)	1.23 (0.73, 2.08)
NSAID, tablets per wk (n = 6 missing) (n = 13 missing/wk)			
None (n = 389)	23.3	1.0	1.0
1–2/wk (n = 61)	36.4	1.88 (0.88, 4.02)	1.80 (0.79, 4.07)
3–6/wk (n = 19)	41.7	2.35 (0.72, 7.65)	1.90 (0.57, 6.36)
≥7/wk (n = 41)	21.7	0.91 (0.33, 2.55)	0.92 (0.32, 2.65)
Yes, any (n = 128)	32.9	1.61 (0.92, 2.82)	1.51 (0.84, 2.71)
Marital status (n = 4 missing)			
Married (n = 430)	24.2	1.0	1.0
Single (n = 26)	23.5	0.97 (0.31, 3.05)	0.91 (0.26, 3.14)
Divorced/widowed/separated (n = 63)	33.3	1.57 (0.77, 3.21)	1.33 (0.63, 2.80)
Educational level (n = 5 missing)			
High school/some college (n = 298)	27.8	1.0	1.0
Not high school graduate (n = 24)	15.8	0.72 (0.43, 1.21)	0.54 (0.14, 2.03)
College graduate and beyond (n = 196)	21.8	0.72 (0.43, 1.21)	0.74 (0.44, 1.26)
Satisfaction with emotional support (n = 9)			

b: Univariate and Adjusted (for age, gender, SSC score) Associations Between Risk Factors and Chronic Painless Diarrhea Among Olmsted County Residents Aged 30–64 Yr			
	% Chronic Painless Diarrhea[§]	Univariate ^{*§} OR (95% CI)	Adjusted ^{†§} OR (95% CI)
missing)			
Completely (n = 257)	19.3	1.0	1.0
Not at all (n = 13)	25.0	1.40 (0.14, 13.81)	0.94 (0.09, 9.72)
Somewhat (n = 62)	32.5	2.02 (0.95, 4.28)	1.59 (0.72, 3.55)
Moderately (n = 182)	29.3	[‡] 1.74 (1.02, 2.97)	1.57 (0.89, 2.77)
Stress during the last month (n = 7 missing)			
None (n = 83)	12.7	1.0	1.0
A little (n = 95)	25.0	2.30 (0.95, 5.53)	[‡] 2.82 (1.10, 7.23)
Some/usual (n = 145)	21.3	1.86 (0.79, 4.38)	2.21 (0.87, 5.61)
Some/>usual (n = 78)	29.6	2.89 (1.11, 7.49)	[‡] 3.52 (1.26, 9.78)
Quite a bit (n = 115)	37.0	[‡] 4.04 (1.74, 9.42)	[‡] 4.16 (1.64, 10.53)
Food allergy/sensitivity (n = 11 missing) (n = 30 missing rash/swelling)			
None (n = 392)	22.8	1.0	1.0
Yes, no rash/swelling (n = 88)	40.9	[‡] 2.34 (1.21, 4.54)	[‡] 2.36 (1.20, 4.64)
Yes, rash/swelling (n = 13)	28.6	1.35 (0.26, 7.14)	1.32 (0.25, 7.16)
Yes, any (n = 120)	33.3	1.69 (0.95, 3.03)	1.64 (0.90, 2.97)
Pets in past year (n = 4 missing)			
None (n = 248)	22.1	1.0	1.0
Dogs (n = 185)	28.9	1.35 (0.82, 2.21)	1.27 (0.76, 2.13)
Cats (n = 134)	25.8	1.05 (0.61, 1.80)	0.92 (0.52, 1.63)
Any pet versus none (n = 271)	28.0	1.37 (0.85, 2.22)	1.26 (0.75, 2.09)
Water source (n = 4 missing)			
Private well and other (n = 163)	28.9	1.0	1.0
City water (n = 356)	23.6	0.76 (0.46, 1.28)	0.80 (0.47, 1.36)

* Unadjusted odds ratios (OR) and 95% confidence intervals (CI).

[†] Adjusted for age, gender, and SSC score.

[‡] $p < 0.05$.

BMI = body mass index; SSC = somatic symptom checklist; NSAID = nonsteroidal anti-inflammatory drug.

[§] Patients with abdominal pain are not included in this analysis