

Post-traumatic Stress Disorder Is Associated With Irritable Bowel Syndrome in African Americans

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Background/Aims

Psychosocial stressors likely play an important role in irritable bowel syndrome (IBS). The association between IBS and post-traumatic stress disorder (PTSD) in non-minorities has been described. Our aim was to investigate the potential association between IBS and PTSD in an urban African American population.

Methods

Our institution maintains a longitudinal population-based survey of African Americans (AA). The survey utilizes a complex, stratified sampling design. The study group consisted of adult AA meeting Rome III criteria for IBS of any subtype. The 4-item Primary Care PTSD screener was administered; score of ≥ 3 (range, 0-4) was considered positive for PTSD. Depression (Public Health Questionnaire-9 depression) and anxiety (generalized anxiety disorder-7) levels were measured using standardized scales. To assess quality of life, norm-based physical and mental component summary scores from the short-form 36 health survey version 2 were obtained. Descriptive and inferential statistics were calculated using Complex Sample Module of SPSS after weighting of the study sample.

Results

Four hundred nineteen subjects included corresponded to a weighted 21,264 (95% CI, 19,777-22,751) individuals. The prevalence of IBS in our sample of urban AA was 8.2%. In multivariate regression analysis, female gender, age > 40 , higher educational attainment and divorce were independently associated with IBS. Those with IBS were considerably more likely to suffer from PTSD (OR, 4.54; 95% CI, 4.07-5.06). PTSD was independently associated with depression, anxiety, harmful drinking and substance abuse.

Conclusions

In AA, PTSD is independently associated with IBS. PTSD has a significantly negative impact on physical and mental self-assessment of quality of life. Evaluation of minorities presenting with functional gastrointestinal disorders should include screening for PTSD.

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Key Words

African Americans; Irritable bowel syndrome; Rome; Stress disorders, post-traumatic

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Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal discomfort and change in bowel habit that accounts for symptoms affecting 30-45 million US adults each year.¹ The prevalence of IBS in North America has been estimated at 3-20% with a majority of studies reporting 10-15%.^{2,3} A similar prevalence of 11.5% is reported in Western Europe.⁴ Two thirds of IBS sufferers are women.^{2,5} The peak age for IBS symptoms is between 35-44 years.² Women develop symptoms at an earlier age than men (25.6 vs. 30.5 years, $P = 0.069$).⁶ Caucasians are reportedly 2.5 times more likely (95% confidence interval (CI), 1.5-4.0) than African Americans (AA) to have IBS.⁷ However, overall prevalence of IBS by ethnic groups in the US has not been reported.⁸

The impact of IBS varies over time with respect to severity and symptom pattern, both of which affect quality of life (QOL).⁹ The most commonly reported symptoms include abdominal pain (88%), bloating (80%), tiredness (60%), diarrhea (59%) and constipation (53%).⁴ IBS sufferers miss approximately twice as many work days per year due to symptoms compared with non-sufferers.^{2,4} People with IBS also more frequently report fatigue (21.1% vs. 9.9%, $P = 0.001$) and lack of energy (79% vs. 59.5%, $P = 0.000$).¹⁰ IBS has been shown to have a negative impact on QOL in several domains including physical functioning, bodily pain, general health, vitality, social functioning and mental health.^{5,11,12}

Psychosocial stressors play an important role in IBS from predisposition to the disorder to precipitation of symptoms.^{3,12,13} IBS is associated with being unemployed, unmarried and having a lower income.⁵ The use of psychotropic medications for the treatment of IBS is common, particularly tricyclic antidepressants, selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors.^{3,14,15} An important condition potentially associated with IBS is post-traumatic stress disorder (PTSD). PTSD is defined as an exposure to a traumatic physical or emotional event that causes re-experience of the occurrence, avoidance of triggers, development of negative thoughts and moods, and chronic hyper-arousal symptoms.¹⁶ Often PTSD is the result of childhood sexual abuse.^{17,18} Patients with functional gastrointestinal disorders are more likely to have experienced severe abuse or life threat than those with structural disease.¹⁴

In our review of the literature we were unable to find data on the association between PTSD and IBS in the AA population.

Our aim was to investigate the risk factors for IBS and PTSD among AAs and the impact on QOL. Our institution maintains a longitudinal population-based survey of urban AA which allows for investigation of this association while controlling for many relevant confounders.

Materials and Methods

Temple Registry for the Investigation of African American Gastrointestinal Disease Epidemiology (TRIAGE) is an ongoing cohort study of AA residing within the ZIP Code Tabulation Area (ZCTA) incorporating Temple University Hospital. Survey design has been described in detail previously.¹⁹ In summary, our population-based survey utilizes a complex, stratified sampling design. In order to obtain a representative sample of the entire AA community we carefully identified 4 targeted survey zones. We hand-delivered invitations to 1,000 individual dwellings. The invitation stated that to participate in the survey the subject had to be self-described as an AA, older than 18 and a resident of the dwelling for at least 3 years. Only one adult per household could participate. All surveys are conducted at our research department. A research coordinator records demographic information and measures the subject's height, weight, hip and waist circumference. Patients are then seated at a computer terminal. Our survey was developed using Microsoft Access 2007 (Microsoft Corporation, Redmond, WA, USA). A coordinator assists participants with visual impairment and those unable to read at the fifth grade level. Subjects progress through the survey by selecting choices using a computer mouse. Subjects cannot progress through the survey without answering all questions. The survey was approved by our Institutional Review Board. The trial is registered on clinicaltrials.gov (NCT01262755). The results reported here are from the entry survey subjects completed.

Survey Components

Dependent variable

The outcome variable of interest was the presence of IBS as defined by Rome III criteria.²⁰ For analysis purposes, individuals meeting IBS criteria were considered in aggregate regardless of subtype. Subjects were not required to have had a colonoscopy or other testing to be included.

Independent variables

The survey queries the subject's marital status, highest edu-

cational attainment, annual income, medical history and a list of up to 10 prescriptions and over-the-counter medications. To assess for addictive behaviors, subjects completed the Alcohol Use Disorders Identification Test (AUDIT), Drug Abuse Screening Test (DAST) and the Fagerstrom Test for Nicotine Dependence (FTND). Depression (Public Health Questionnaire-9 depression) and anxiety levels (generalized anxiety disorder-7) were assessed using validated instruments. The primary care PTSD (PC-PTSD) screener was administered and a score of ≥ 3 (range, 0-4) was considered "highly likely positive" for PTSD.^{21,22} All subjects completed the medical outcomes study 36-item short-form health survey (SF-36) version 2, a patient-reported health survey consisting of questions grouped into 8 domains: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health.²³ Each domain is scored from 0-100 with the higher score (100) corresponding to less impairment.²³

Survey Analysis

Sample weighting

Two levels of weighting were performed. An initial weight is applied to adjust for the unequal probability of selection within the household. For second-level weighting, we utilize data from the 2010 US Census which stratifies AA living in the ZCTA by sex and age. An additional scaling variable was used to estimate population-level prevalence data. The scale variable (v) represented the ratio of the entire AA population of the ZCTA divided by the number of subjects interviewed ($v = N_B/n_B$).

Sample size

We estimated that the prevalence of IBS would be 7-10% in the community.²⁴ We anticipated that our final regression model would have 3-4 independent predictors. To develop a well-calibrated regression model with ≥ 8 outcome events per predictor variable, our protocol called for the recruitment of a minimum of 400 subjects.

Statistical Methods

We designed a complex sample file plan using the Complex Sample Module of SPSS 19.0 (IBM SPSS, Armonk, New York, USA). Descriptive and inferential statistics were determined using the Complex Sample Module yielding point estimates with 95% CI. For categorical variables, an adjusted F statistic was

calculated. General linear models were used to estimate the association of continuous predictor variables with categorical outcomes. P -values were calculated based on the Wald statistic. A multivariable logistic regression was performed to identify variables independently associated with the prevalence of IBS. Odds ratios (OR) along with their corresponding 95% CI were calculated for variables included in the model. All hypothesis testing was 2-tailed with $\alpha = 0.05$.

Results

We recruited 419 subjects from unique households in the targeted zip code tabulation area. After weighting and scaling of the surveyed sample this corresponded to 21,264 (95% CI, 19,777-22,751) citizens. The overall weighted prevalence of IBS was 8.2%. Table 1 highlights the characteristics of the population stratified by IBS status. The number of females in the group with IBS was substantially higher than in the group without 81.8% (95% CI, 66.4-99.1) vs. 54.5% (95% CI, 48.3-60.6). IBS subjects were more obese and more likely to have undergone divorce. Those with IBS had a higher level of educational attainment but minimal difference in annual income. Not surprisingly, those with IBS were more likely to have been investigated with colonoscopy (35.1% [95% CI, 17.7-57.5] vs. 23.1% [95% CI, 17.7-29.7]), however the percent of individuals visiting a doctor at least once in the previous year was similar. By univariate analysis the prevalence of PTSD (score ≥ 3) and harmful alcohol use was far higher in those with IBS than those without.

Table 2 demonstrates that the majority of individuals with IBS suffered from moderate-severe depression (73%), and 17.3% had severe depression (95% CI, 7.3-35.5). More patients with IBS than without reported taking a prescription or herbal antidepressant (13.5% vs. 8.3%). Although less common than depression, 51% of individuals with IBS had some anxiety which is substantially higher than individuals without IBS (34.1%). Figure demonstrates that IBS has a negative impact on every domain of QOL as measured by the SF-36. Table 3 shows the results of a multivariable regression model. Female gender, age > 40 , higher educational attainment and divorce were independently associated with IBS. Those with IBS were 4.5 times more likely to suffer from PTSD (OR, 4.54; 95% CI, 4.07-5.06).

We further explored the impact of PTSD on our study population. As shown in Table 4, the majority of subjects who met criteria for PTSD were female (70.4%). The negative impact of PTSD was associated with depression, anxiety, harmful drinking

Table 1. Characteristics of Study Subjects Stratified by Irritable Bowel Syndrome Status

	Total Weighted (N = 21,264) (95% CI: 19,777-22,751)	No IBS Weighted (n = 19,516) (95% CI: 17,974-21,058)	IBS Weighted (n = 1,748) (95% CI: 1,065-2,431)
Age (yr)	44.2 (42.0-46.4)	44.0 (41.7-46.3)	46.3 (39.9-52.8)
% Female	56.8 (50.8-62.5)	54.5 (48.3-60.6)	81.8 (66.4-99.1)
Body mass index	29.1 (28.2-30.0)	28.2 (28.0-29.8)	30.9 (26.5-35.2)
Educational level (%)			
< High school graduate	31.6 (26.4-37.3)	33.0 (27.4-39.0)	16.5 (8.0-31.0)
High school graduate	61.8 (55.9-67.4)	60.9 (54.6-66.7)	72.7 (53.2-86.2)
College graduate	6.6 (4.1-10.4)	6.2 (3.7-10.1)	10.8 (2.7-34.7)
Marital status (%)			
Single, never married	73.4 (67.2-78.9)	73.8 (67.1-79.5)	69.7 (51.7-83.2)
Divorced	14.1 (9.7-20.1)	13.6 (9.0-20.2)	19.3 (9.0-36.7)
Separated	4.0 (2.2-7.3)	4.1 (2.1-7.8)	2.9 (0.9-9.1)
Married	8.4 (5.7-12.4)	8.5 (5.5-12.7)	8.0 (2.9-20.4)
Annual home employment income (%)			
Unemployed	35.5 (30.3-41.1)	35.5 (30.0-41.4)	35.9 (20.7-54.5)
< \$20,000	48.2 (42.3-54.2)	48.1 (41.9-54.4)	49.3 (30.2-68.6)
\$20,000-\$50,000	14.7 (10.9-19.6)	14.9 (10.9-20.1)	12.6 (4.6-30.2)
> \$50,000	1.5 (0.9-2.8)	1.5 (0.8-2.7)	2.2 (0.3-14.6)
Visit PCP at least yearly (%)	79.6 (74.5-83.8)	79.3 (74.0-83.8)	81.9 (65.0-91.7)
Colonoscopy in past 5 years (%)	24.1 (18.8-30.4)	23.1 (17.7-29.7)	35.1 (17.7-57.5)
Comorbidities			
Hypertension	38.9 (33.1-45.1)	39.0 (32.9-45.4)	38.6 (20.5-60.5)
Obstructive airways disease	26.3 (21.2-32.1)	25.4 (20.1-31.6)	35.9 (19.9-55.8)
Diabetes	15.0 (10.9-20.2)	15.1 (10.8-20.6)	13.8 (5.3-31.3)
Elevated cholesterol	20.4 (15.8-25.8)	20.8 (15.9-26.6)	15.7 (6.9-31.8)
Coronary artery disease	4.0 (2.0-7.9)	4.0 (1.9-8.3)	4.0 (1.0-15.2)
Viral hepatitis	4.1 (2.2-7.5)	4.2 (2.2-7.9)	2.9 (0.4-18.1)
PTSD screener score (%)			
0	59.1 (53.2-64.7)	61.2 (55.1-67.0)	35.2 (17.7-57.7)
1	9.0 (6.0-13.2)	9.2 (6.1-13.6)	6.5 (0.9-34)
2	9.7 (6.7-13.9)	10.1 (6.8-14.5)	5.7 (1.4-21.1)
3	8.0 (5.6-11.4)	7.7 (5.2-11.2)	12.6 (4.7-29.7)
4	14.2 (10.7-18.5)	11.8 (8.5-16.2)	40.0 (23.6-59.1)
Harmful drinking habits (%)	12.1 (9.1-15.8)	11.4 (8.4-15.3)	19.9 (9.2-37.7)
High nicotine dependence (%)	5.1 (3.1-8.3)	5.4 (3.3-8.8)	2.0 (0.3-13.5)
Prescription or illicit substance abuse (%)	11.1 (8.1-14.9)	11.2 (8.1-15.4)	9.0 (3.4-21.7)

PCP, primary care physician.

and substance abuse. The component QOL summary scores from the SF-36 were significantly reduced for the mental (39.2 ± 11.1 vs. 54.6 ± 9.9) and physical (42.9 ± 10.2 vs. 47.6 ± 10.2) domains in those with PTSD.

Discussion

In this study we found the prevalence of IBS among urban AA to be 8.2% with the majority (81.8%) female. PTSD had a

strong independent association with IBS among AA (OR, 4.54; 95% CI, 4.07-5.06). Similarly, we found a strong association between PTSD and moderately severe to severe depression as well as anti-depressant use. In distinction from previous reports, we found age ≥ 40 years to be associated with greater than twice the risk of IBS. Previous studies reported a higher prevalence of IBS in those less than 45 years old^{2,5} and only 9.4% in those older than 45 years.¹ The prevalence of women with IBS is higher in our study 81.8% (95% CI, 66.4-99.1) compared to the commonly re-

Table 2. Depression and Anxiety Prevalence Stratified by Irritable Bowel Syndrome Status

	Total weighted (N = 21,264) (95% CI, 19,777-22,751)	No IBS weighted (n = 19,516) (95% CI, 17,974-21,058)	IBS weighted (n = 1,748) (95% CI, 1,065-2,431)
Depression level			
None-mild	62.3 (56.5-67.8)	65.3 (59.3-70.9)	26.8 (10.4-53.7)
Moderate	18.9 (14.7-24.0)	19.1 (14.7-24.5)	17.0 (8.1-42.2)
Moderately severe	12.5 (9.3-16.7)	10.3 (7.3-14.3)	38.9 (21.7-59.5)
Severe	6.2 (4.2-9.3)	5.3 (3.3-8.4)	17.3 (7.3-35.5)
Prescribed an antidepressant	8.7 (6.3-12.0)	8.3 (5.8-11.8)	13.5 (6.0-27.8)
Anxiety disability			
None	64.5 (58.8-69.9)	65.9 (59.9-71.4)	49.2 (30.1-68.5)
Some amount	28.1 (23.2-33.6)	26.9 (21.8-32.7)	41.7 (24.6-60.9)
Moderate amount	5.5 (3.5-8.4)	5.1 (3.2-8.3)	9.1 (3.5-21.8)
Severe amount	1.9 (0.9-4.1)	2.1 (0.9-4.4)	0.0 (0.0-41.9)

IBS, irritable bowel syndrome.

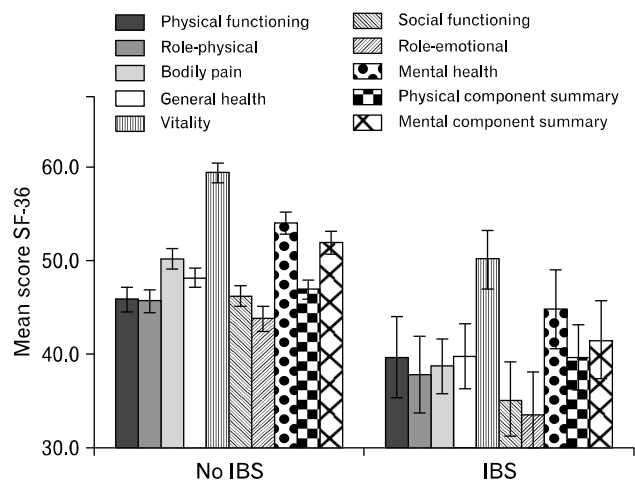


Figure. Comparison of 36-item short-form health survey (SF-36) scores in patients with and without irritable bowel syndrome (IBS).

ported 2:1 ratio.^{2,5}

To our knowledge, no prior studies have evaluated PTSD and its association with IBS among AA. In a survey of 990 subjects (670 AA and 320 Caucasian) Minocha et al¹⁰ found no difference in history of abuse (physical or sexual) among AA subjects with IBS. They found an overall increased frequency of abuse history among subjects with IBS as well as more suicidal thoughts, loss of interest, anxiety or depression.¹⁰ Drossman¹⁴ hypothesized that higher abuse rates correlated with more severe symptoms.

Alcohol abuse is strongly linked to various emotional, psychological and physical illnesses. We found an increased prevalence of harmful alcohol abuse among subjects with IBS and a

Table 3. Regression Model - Independent Factors Associated With Irritable Bowel Syndrome

	Adjusted ^a OR	95% CI for OR
Male	Reference	
Female	3.28	2.88-3.74
Age < 40	Reference	
Age ≥ 40	2.21	1.95-2.50
Education		
< High school graduate	Reference	
High school graduate	3.25	2.82-3.73
College graduate	4.97	3.99-6.19
Marital status		
Single, never married	Reference	
Divorced	1.38	1.19-1.60
Married	0.67	0.54-0.82
Annual home employment income		
Unemployed	Reference	
< \$20,000	0.86	0.76-0.97
> \$50,000	1.26	0.87-1.82
Screen for PTSD		
Negative	Reference	
Positive	4.54	4.07-5.06

^aAdjusted for all other variables in model.
PTSD, post-traumatic stress disorder.

more than 2-fold risk among subjects with PTSD (20.0% vs. 9.8%; OR, 2.29; 95% CI, 2.10-2.50). Similarly, there was a higher rate of substance abuse among subjects with PTSD (22.3% vs. 8.0%), but only a slightly higher rate comparing IBS vs. non-IBS (11.2% vs. 9%). In a prospective community-based study of women (88% non-Hispanic White) aged 18-48 years

Table 4. Univariate Relationship Between Select Variables and Post-traumatic Stress Disorder Status

	PTSD Status		OR ^a (95% CI)	P-value
	Positive Weighted (n = 4,729)	Negative Weighted (n = 16,535)		
Categorical variables (%)				
Female	70.4	52.9	2.12 (1.98-2.27)	
Divorce rate	11.9	14.7	0.78 (0.71-0.86)	
Anxiety disability	18.0	4.3	4.86 (4.38-5.30)	
Depression	55.2	8.9	12.61 (11.65-13.66)	
Harmful alcohol use	20.0	9.8	2.29 (2.10-2.50)	
Substance abuse	22.3	8.0	3.32 (3.02-3.64)	
Unemployment	37.8	34.9	1.14 (1.06-1.21)	
Continuous variables mean (SD)				
PCS	42.9 (10.2)	47.6 (10.2)		< 0.001
MCS	39.2 (11.1)	54.6 (9.9)		< 0.001

^aUsing the Cochran's Mantel-Haenszel test of conditional independence.

PTSD, post-traumatic stress disorder; Depression, individuals self-assessed as moderately to severely depressed; Anxiety disability, individuals self-assessed as moderate to severe; PCS, physical component summary; MCS, mental component summary.

with and without IBS, Reding et al²⁴ studied the relationship between alcohol consumption and GI symptoms and found no difference in the quantity of alcohol consumption between women with and without IBS. However, those that reported binge drinking were twice as likely to experience diarrhea (OR, 2.1; 95% CI, 1.2-3.5), nausea (OR, 2.4; 95% CI, 1.2-4.8), abdominal pain (OR, 2.1; 95% CI, 1.2-3.7) and indigestion (OR, 2.0; 95% CI, 1.1-3.6) the following day. However, Halder et al²⁵ found no significant association between IBS and alcohol consumption when accounting for other variables such as gender, smoking, education, age, and somatization.

There are several avenues by which IBS could be linked to PTSD. The pathogenesis of IBS is multifactorial with psychosocial, genetic, nervous system (central and enteric), hormonal, visceral hypersensitivity and infectious/inflammatory components.^{3,11,15} This concept is presented in the "biopsychosocial" model of IBS by Tanaka et al.¹² They divide the factors that influence IBS development into early life (genetics, social learning), psychosocial (stress, abuse and psychological state) and abnormal physiology (including abnormalities of motility and sensitivity, brain-gut interaction, regional brain activation, hypothalamic-pituitary-adrenal axis [HPAA] and post-infectious). Videlock et al²⁶ studied the HPAA response to a visceral stressor (sigmoidoscopy) in patients with IBS vs. healthy controls and those exposed to early adverse life events (EALs) using salivary cortisol levels. They found higher mean cortisol levels in those who experienced EALs regardless of whether or not they

had IBS.²⁶ However, for patients with cortisol levels that returned to baseline more quickly the investigators noted decreased symptom severity ($r = -0.36$, $P < 0.05$) and better disease-specific QOL ($r = 0.33$, $P < 0.05$)²⁶ suggesting that perhaps the HPAA has a symptom-modulating effect.

Hormones released in response to stress, such as corticotropin-releasing hormone (CRH), regulate changes in gut motility, visceral perception and autonomic function.²⁷ CRH is released by the hypothalamus and stimulates adrenocorticotropic hormone (ACTH) release by the pituitary gland which in turn stimulates cortisol release from the adrenal cortex.²⁸ Exogenous administration of CRH has been shown to increase colonic motility and stimulate serum ACTH with an exaggerated response found in patients with IBS.²⁹ In a study by Fukudo,²⁷ 10 IBS patients and 10 control subjects underwent pressure transducer placement in the colon and were then injected with CRH. While there was no difference in motility at baseline, the IBS group developed significantly greater colonic motor activity and longer duration of abdominal symptoms in response to CRH administration compared with controls ($P < 0.05$). CRH induced a rise in serum ACTH in both groups, although a significantly higher increase in the IBS group ($P < 0.01$). There was no difference in serum cortisol response in the 2 groups.²⁹

Ringel et al³⁰ used PET scan to compare cerebral blood flow in patients with IBS and controls with *post-hoc* analyses comparing patients with a history of physical or sexual abuse and patients without abuse.³⁰ They found a greater increase in anterior cingu-

late cortex activity in non-IBS subjects and those without a history of abuse. IBS patients showed higher activity in the thalamus, an area previously shown to be associated with pain response.

The main strength of this study is the novel study population. There is a lack of previous investigation into differences among IBS patients of various races in the US. Our structured survey relied on standardized questionnaires including Rome III and therefore misclassification was minimized.³¹ Another strength is that our study group appeared to represent the target population after weighting and scaling. For example, our prevalence estimate for the proportion of adult AA in the ZTCA that are female was 56.8 (50.8-62.5) while the actual proportion is 58.8% (<https://www.census.gov/regions/philadelphia>). The mean weighted age of our adult AA sample is 44.2 (42.0-46.4) years, similar to census results (ranging from 40.7 to 46.6 years). The study group had a low rate of college education. A recent survey found that only 9% of adults (not stratified by race) over the age of 25 had a college degree in the ZCTA; very close to the weighted prevalence found in our survey of 6.6 (4.1-10.4).

There are several limitations to our study which should be stressed. First, this study took place in an urban, low-income population with a relatively small sample size. The generalizability to other AA populations with different social and economic demographics must be considered with caution. Secondly, this study specifically addressed AA and cannot be extrapolated to other races or ethnicities. Additionally, data was obtained from self-reported questionnaires and lacks objective findings. Subjects were not required to have a colonoscopy, imaging, or other investigation to rule out organic causes for symptoms. A final potential weakness relates to our stratified sampling methodology and our failure to estimate the impact of the design effect on our prevalence estimates and sample size calculation. Estimating the design effect requires comparing the variance of the prevalence estimate under different sampling methods. While the variability of the prevalence estimate under simple random sampling can be derived from basic probability theory, multiple simulations to discover the variability under respondent-driven sampling such as our survey are required.³² Generally, but not always, the design effects from respondent-driven sampling are less precise than estimates from simple random sampling.

In conclusions, as with Caucasian subjects with IBS, the prevalence of previous emotional and/or physical trauma is substantial in the AA community. After adjustment for other important confounders, AA with IBS were twice as likely to suffer from PTSD. PTSD was associated with adverse lifestyle choices

(drug and alcohol misuse) and had a substantial impact on QOL, both in the physical and particularly psychological domains. Our study highlights the need to screen for PTSD in AA with IBS.

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