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Is Abuse Causally Related to Urologic Symptoms? Results from the Boston Area Community Heath (BACH) Survey

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Abstract

Objectives: We investigated (1) whether sexual, physical, or emotional abuse experienced either as a child or as an adolescent/adult is associated with symptoms of urinary frequency, urgency, and nocturia, and (2) the extent to which the observed association between abuse and urologic symptoms may be causal.

Methods: Analyses are based on data from the Boston Area Community Health (BACH) survey, a community-based epidemiologic study of many different urologic symptoms and risk factors. BACH used a multistage stratified cluster sample to recruit 5506 adults, aged 30[en]79 yr (2301 men, 3205 women; 1770 black [African American], 1877 Hispanic, and 1859 white respondents).

Results: The symptoms considered are common, with 33% of BACH respondents reporting urinary frequency, 12% reporting urgency, and 28% reporting nocturia. All three symptoms are positively associated with childhood and adolescent/adult sexual, physical, and emotional abuse (p < 0.05), with abuse significantly increasing the odds of urinary frequency by a factor ranging from 1.6 to 1.9, the odds of urgency by a factor from 2.0 to 2.3, and the odds of nocturia by a factor from 1.3 to 1.5.

Conclusions: Our analyses extend previous work. First, we show a strong association between abuse and urinary frequency, urgency, and nocturia in a community-based random sample. Second, we move beyond discussion of statistical association and find considerable evidence to suggest that the relationship between abuse and these symptoms may be causal.

Keywords

Abuse; Corticotrophin-releasing factor (CRF); Epidemiology; Nocturia; Stress; Symptom research; Urgency; Urinary frequency

1. Introduction

Abuse has been identified as a major public health issue, with national probability and community-based samples conservatively estimating that well over one quarter of the United States adult population report either physical or sexual lifetime abuse [1[en]4]. Medically,

Physical, sexual, and emotional abuses experienced as a child or as an adolescent/adult are positively associated with urinary frequency, urgency, and nocturia. This association meets many criteria to suggest causation in a diverse community-based random sample of adults.

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Take-home message

abuse is strongly associated with a range of gastroenterologic and genitourinary symptoms [5 [en]13].

This linkage is not surprising because anxiety and fear may manifest as physical symptoms, especially urinary and sexual complaints, even years after the abuse has occurred [14]. Previous studies have focused on women or children who have been abused [7[en]10]. Conversely, examination of women and children with voiding complaints have found that a substantial portion were victims of abuse or severe psychological trauma [6]. This association between abuse and urinary complaints has been attributed to an underlying psychological issue rather than a physiologic abnormality [16]. However, contemporary studies of the neurobiologic basis for stress and anxiety offer a plausible mechanism whereby physical or psychological abuse can sensitize micturition pathways, leading to an overactive bladder characterized by urinary urgency, usually with frequency or nocturia [17[en]19]. Urologic symptoms are not uncommon in the population [20,21].

We extend existing literature in this area in two ways. First, we investigated the association of different types of abuse and the urologic symptoms of frequency, urgency, and nocturia in a diverse community-based random sample. Second, and moving beyond previous work, we considered whether the relationship between abuse and these symptoms may be said to be causal. To do this we drew from Sir Austin Bradford Hill's classic discussion of criteria for determining whether an association can be considered causal [22]. Although there is continuing debate on the subject of causality [23[en]25], Hills criteria provide a useful starting point when considering this question.

2. Methods

The Boston Area Community Health (BACH) survey is a community-based epidemiologic study of urologic symptoms and risk factors conducted from 2002 to 2005. BACH is a cross-sectional random sample of community-dwelling adults, not a convenience sample. Detailed methods are given in a previous paper in this issue [26]. In brief, BACH used a multistage stratified random sample to recruit 5506 adults aged 30[en]79 yr in three racial/ethnic groups from the city of Boston (2301 men, 3205 women, 1770 black [African American], 1877 Hispanic, 1859 white respondents). Information about urologic symptoms, comorbidities, lifestyle, anthropometrics, and psychosocial attributes was collected via an interviewer-administered questionnaire; respondents used a self-administered questionnaire to answer questions about sexual function and abuse.

The BACH survey asked several questions about urinary frequency, urgency, and nocturia (Table 1). Respondents were said to have: (a) *urinary frequency* if they needed to urinate again < 2 h after urinating (fairly often, usually, almost always) and/or had frequent urination during the day (fairly often, usually, almost always) and/or had (on average) eight or more urinations during the day; (b) *urgency* if they had difficulty postponing urination (fairly often, usually, almost always) and/or had a strong urge or pressure to urinate immediately with no or little warning (fairly often, usually, almost always) and/or had a strong urge or pressure to urinate immediately whether or not they urinated or leaked urine (several times, many times, every day); and (c) *nocturia* if they had to get up to urinate more than once during the night (fairly often, usually, almost always) and/or had (on average) two or more urinations during the night after falling asleep. Composite measures were created as we found that the different questions for frequency, urgency, and nocturia did not give similar responses. These composite measures are different from the current International Continence Society definitions [27].

Three types of abuse (sexual, physical, and emotional) were assessed over two life stages (childhood [age 13 or younger], adolescence/adulthood [age 14 or older]) using a validated

self-administered questionnaire [28] (Table 1). Sexual abuse was defined as present if the respondent reported any of the following (unwanted) experiences (and the perpetuator was an adult): exposed sex organs of their body (only included in the definition of childhood sexual abuse), threatened to have sex, touched respondents sex organs, made respondent touch their sex organs, forced respondent to have sex, or other sexual experiences. Physical abuse was defined as present if the respondent reported being hit, kicked, or beaten by an adult (occasionally or often) or having his/her life seriously threatened (seldom, occasionally, or often). Emotional abuse was defined as present if an adult had emotionally abused, humiliated, or insulted the respondent (occasionally or often).

We used a $\rm X^2$ test of independence and logistic regression to determine if the urologic symptoms of frequency, urgency, and nocturia were associated with different types of abuse. A linear test for trend was performed for data on frequency of abuse and frequency of the urologic symptoms. Information on urologic symptoms from the interviewer-administered questionnaire was seldom missing (< 1%), but information about abuse from the self-administered questionnaire was more frequently missing (about 10%). Missing data were replaced by plausible values using 25 multiple imputations [29]. To be representative of the city of Boston, observations were weighted inversely proportional to their probability of selection [30]. Weights were then post-stratified to the Boston population according to the 2000 census. Analyses were conducted in version 9.1 of SAS (SAS Institute, Cary, NC, USA) and version 9.0.1 of SUDAAN (Research Triangle Institute, Research Triangle Park, NC, USA).

3. Results

The prevalence of various types of abuse are comparable (Table 2) to the limited available information from other population-based US surveys [1[en]3]. The prevalence of urinary frequency, urgency, and nocturia was significantly (p < 0.05) higher in the group that had experienced abuse (Table 3). This was consistent for each urologic symptom and for each type of abuse. Moreover, these patterns hold if we look at various subgroups, gender and race/ethnicity (Fig. 1). In results not presented here, we used logistic regression to consider interactions between abuse and gender, abuse and race/ethnicity, and three-way interactions between abuse and gender and race/ethnicity. The only interactions that were significant (p < 0.05) were of emotional abuse (childhood and adult) and gender with urinary frequency. However, the association of emotional abuse and frequency is significant for both genders; therefore on examination of the interaction, we conclude that the effect is smaller for women compared to men.

We sought to determine whether there is evidence of a dose-response relationship between abuse and urologic symptoms. If abuse is more frequent, does the prevalence of urinary frequency, urgency, and nocturia also increase? To examine this question, we compared the frequency of the urologic symptoms with increasing frequency of abuse (Fig. 2). (The prevalence of urologic symptoms for the group reporting that they have occasionally and often had someone seriously threaten their life are combined due to low numbers in these cells.) We found that the prevalence of all three urologic symptoms increases with the frequency of each type of abuse. A linear test for trend is significant (p < 0.05) for each plot.

4. Discussion

We drew from Hill's [22] criteria for determining causation to more systematically examine characteristics of the associations observed in BACH and to assess the extent to which these results constitute evidence of a causal relationship between abuse and urinary frequency, urgency, and nocturia. We also considered which kinds of evidence should be sought in future

work to continue to move the field beyond documenting association and toward the identification of causal mechanisms. Table 4 summarizes our results.

4.1. Strength

The overall strength of the association is large. The prevalence of urinary frequency increases by 33[en]50%, the prevalence of urgency doubles, and the prevalence of nocturia increases by 25% in those that report experiencing abuse compared to those who do not. Any relationship producing an odds ratio (OR) indicating at least a 2-fold difference (OR \geq 2.0 or \leq 0.5) is unlikely to be due to chance. Conversely, any odds ratio in the interval 0.8[en]1.25 is at high risk to alternative explanation. All odds ratios reported here are outside that range and one was 2.0.

4.2. Consistency

The consistency of the results across both gender and race/ethnicity adds support to the case for a causal relationship. Although much previous work has focused on women and children, we report a consistent pattern among both men and women, across black (African American), Hispanic, and white respondents, and also across the life course. With respect to emotional abuse, evidence suggests that its effect on urinary frequency may be greater in men than its effect in women. That the integrity of the result holds across different gender and race/ethnic groups adds support for the causal argument.

4.3. Specificity

Specificity has two components. In the first, Hill [22] was concerned with occupational hazards and whether an association was present among a specific group of workers. This criterion is not directly applicable here because all respondents are potentially subject to abuse. The second consideration of specificity is the question of whether the association of abuse is restricted to a specific set of complaints. This is obviously false because abuse has been found to be associated with a number of ailments [5,12,13,31].

4.4 Temporality

The temporal ordering of abuse and these urologic symptoms will be the subject of future longitudinal work in the BACH study. On one hand, there is a strong association between childhood abuse and current urologic symptoms. Here the reported abuse (at least for the majority who have experienced symptoms < 6 yr) has preceded the current symptoms, thereby strengthening the causal hypothesis. As BACH transitions to a longitudinal cohort study, we should be able to determine if respondents who did not report symptoms at baseline are more likely to develop these urologic symptoms if they have reported abuse at baseline.

4.5. Biologic gradient (dose-response)

As discussed above, we find evidence of a biologic gradient or dose-response curve (Fig. 2), which further supports the possibility of a causal relationship. The increased prevalence of these urologic symptoms with increased frequency of abuse suggests a much more specific association than one of general association.

4.6. Biologic plausibility

Recent research has reported that anxiety and behavioral responses to stress involve complex neural circuits and multiple neurochemical components. Acute and chronic stress due to abuse can alter these circuits, their neurochemical components, and bladder function [15,32].

Most of the evidence for biologic plausibility comes from animal experiments. Stress induced by water immersion, cold, or restraint alters bladder histology and pharmacology [17,18,33,

34]. Stress increases muscarinic-induced contractile responses in the bladder [19]. These alterations have been hypothesized to derive from mediators of stress and involve the hypothalamic-pituitary-adrenal axis (HPA) with an effector system relying on peripheral humoral factors.

An alternative explanation to a purely peripheral effector system for mediating traumatic experiences on urinary function relies on central neural mechanisms involved in the stress response. A primary neurotransmitter expressed by neurons within the central stress network is corticotrophin-releasing factor (CRF). CRF is expressed by neurons within a pontine micturition center found in Barringtons nucleus and within regions in the spinal cord that form part of the micturition reflex pathway [35,36].

Exogenous administration of CRF has variable effects on bladder function. For example, intracerebroventricular administration of CRF has been reported to decrease, increase, or have no effect on bladder activity [37]. In contrast, intrathecal CRF induces urinary frequency and lowers micturition volumes [38]. In animals subjected to stress, CRF is up-regulated in Barringtons nucleus, the amygdala, and paraventricular nucleus [35]. Mice overexpressing CRF exhibit behaviors associated with anxiety and increased urinary frequency [32,38]. Thus, experimental data suggest that increased CRF release by neurons in the central nervous system may heighten bladder activity.

The case for CRF being a link between abuse and increased bladder activity is made more robust by a large body of literature demonstrating neural plasticity within the HPA and amygdala in the pathogenesis of anxiety in victims of sexual abuse or posttraumatic stress [15,39[en]42]. Abused subjects demonstrate increased levels of CRF in the cerebrospinal fluid and heightened responses of the HPA to exogenous CRF than controls [15,41,43[en]45]. Investigators postulate that the neuroendocrine stress response is permanently altered in abuse victims [15]. The working hypothesis is that CRF is involved in a positive feed-forward system that becomes supersensitive to stress responses. Compelling evidence for a link between stress, CRF, and bladder function is the finding that systemic CRF-1 antagonists reduce urinary frequency and micturition volumes either due to exogenous CRF or in rats exhibiting anxiety [32,38]. It is relevant that CRF antagonists are currently under development to treat stress-induced depression and irritable bowel syndrome [32].

4.7. Coherence

Hill [22] suggested "the cause-and effect interpretation of our data should not seriously conflict with the generally known facts of the natural history and biology of the disease." We know of nothing in the literature that would contradict the argument for a causal relationship.

4.8. Experiment (reversibility)

This criterion focuses on evidence that if the cause is removed, then the purportedly associated symptom will be ameliorated. Although previously experienced abuse cannot be removed, psychotherapy may relieve its deleterious effects. Frewan reported improvement in urinary symptoms after psychotherapy plus bladder training [46]. Corroborative support for potential reversibility is provided by Macaulay and coworkers [47] who reported that sensory urgency, detrusor overactivity, and incontinence can be cured by intense psychotherapy even without bladder training.

4.9. Analogy

This criterion proposes that the case for causation is strengthened if other comparable phenomena are also associated with a similar effect. With respect to abuse for example, somewhat comparable traumatic phenomena could be natural disasters (Tsunami), warfare

(Iraq), and posttraumatic stress disorder (PTSD). Although a search of PubMed for PTSD and urinary symptoms did not yield any useful citations, an alternate search of PTSD and CRF did. CRF appears to play a significant role in many anxiety disorders including PTSD [48].

4.10. Summary

Although sexual and physical abuse has been reported to be associated with urologic symptoms in small numbers of female or juvenile patients [6[en]11], this research extends these results and reports that this association is also evident in a large (n = 5506) diverse community-based random sample of both men and women and across three different race/ethnic groups. We also report an association of emotional abuse and urologic symptoms and find that the association of emotional abuse and urinary frequency may be even more evident in men than in women.

Attention has tended to focus on the association of abuse and pelvic pain [31], but our research suggests that attention needs to be broadened to include the symptoms of urinary frequency, urgency, and nocturia, especially because these symptoms are much more common in the population.

We also show that our data fulfill many of Hill's [22] criteria to suggest causation including strength, consistency, dose-response, biologic plausibility, coherence, experiment, and analogy. We do not claim that abuse is the only cause of urologic symptoms, which may have many causes. This research is an attempt to move the field of urologic epidemiology from statistical association to causation and eventually the identification of physiologic pathways that are amenable to treatment.

4.11. Strengths and limitations

BACH has many strengths. BACH is a random sample of community-dwelling adults not a convenience sample of patients. BACH includes men and women, covers a broad age range, and includes adequate representation of the US primary racial/ethnic groups. BACH used validated instruments whenever possible and included questions on many urologic symptoms and confounders. BACH has some limitations. It was conducted in one geographic area. However, when comparing results from some national surveys to BACH, the health characteristics of Boston residents are similar (details at www.neriscience.com) suggesting that, with appropriate adjustments, results could be generalized to the US population. BACH does not include some other important race/ethnic groups such as Asians or Native Americans due to logistical challenges (many languages) or insufficient numbers. Definitions pose a serious challenge for abuse research and, particularly in a cross-national context, we would expect cultural differences and expectations on abuse to limit the extent to which prevalence rates and odds ratios can be compared directly across studies.

5. Conclusion

We show that current symptoms of urinary frequency, urgency, and nocturia are associated with previously experienced sexual, physical, and emotional abuse for both men and women and for three race/ethnic groups. We show that this association meets several criteria that suggest a causal relationship. Our results suggest that clinicians (both urologists and primary care providers) should consider the possible contribution of abuse when managing patients who present with the symptoms of urinary frequency, urgency, and nocturia.

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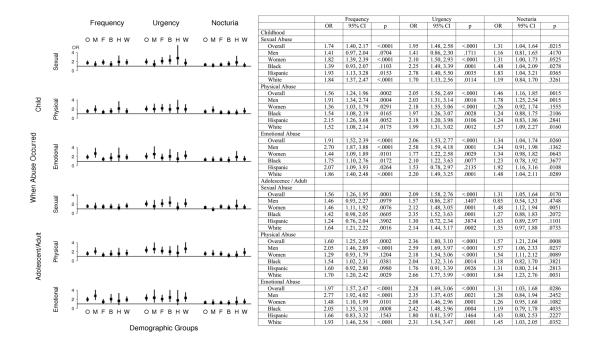
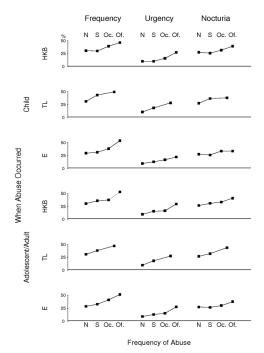


Fig. 1. Odds ratios (OR) and 95 percent confidence intervals (CI) for the association of frequency, urgency, and nocturia with different kinds of abuse, overall, by gender, and by race/ethnicity Odds ratios and 95% confidence intervals of frequency, urgency, and nocturia for each type of abuse. Line at 1 = no effect; O = overall; M = men; F = women; B = black (African American); H = Hispanic; W = white.



	Frequency	Urgency	Nocturia
Childhood			
Hit, kick, or beat			
never	30.7	10.2	27.6
seldom	30.1	10.4	25.9
occasionally	39.3	16.0	31.8
often	46.4	27.4	39.3
Seriously threaten life			
never	31.2	10.8	27.5
seldom	43.4	18.6	36.8
occasionally or often	49.5	28.3	38.0
Emotionally abuse			
never	29.4	9.7	27.5
seldom	31.3	12.9	26.1
occasionally	38.1	16.7	33.6
often	53.7	22.1	33.4
Adult			
Hit, kick, or beat			
never	30.4	9.8	26.8
seldom	35.9	15.6	31.0
occasionally	37.5	16.6	33.5
often	53.1	29.7	40.9
Seriously threaten life			
never	31.0	10.1	27.0
seldom	38.2	18.4	32.2
occasionally or often	47.2	27.6	43.7
Emotionally abuse			
never	28.8	9.1	27.4
seldom	32.8	13.0	26.8
occasionally	41.2	15.3	30.2
often	51.8	27.7	37.8

Fig. 2. Prevalence (percent) of frequency, urgency, and nocturia by frequency and type of abuse Prevalence (percent) of frequency, urgency, and nocturia with increasing frequency of abuse. HKB = hit, kick, or beat; TL = seriously threaten life; E = emotionally abused; N = never, S = seldom; Oc = occasionally; Of = often.

Table 1
Questions (and source used) to determine urologic symptoms and presence of abuse

Measure	Question	Possible	Reference/sour
	C	responses	
Frequency	During the last month,	I do not have	49
	how often have you	symptom,	
	had to urinate again <	rarely, a few	
	2 h after you finished	times, fairly	
	urinating?	often,	
		usually,	
		almost	
		always	
	Description of the allocations and the		50
	During the last month,	I do not have	50
	how often have you	symptom,	
	had frequent urination	rarely, a few	
	during the day?	times, fairly	
		often,	
		usually,	
		almost	
		always	
	T. d. 1. 4.7.1		51
	In the last 7 d, on	Number [en]	51
	average, how many	8+	
	times have you had to		
	go to the bathroom to		
	empty your bladder		
	during the day?		İ
Urganay		I do not have	49
Urgency	During the last month,		H ²
	how often have you	symptom,	
	had difficulty	rarely, a few	
	postponing urination?	times, fairly	
		often,	
		usually,	
		almost	
		always	
	D 1 d 1 d		50
	During the last month,	I do not have	50
	how often have you	symptom,	
	had a strong urge or	rarely, a few	
	pressure to urinate	times, fairly	
	immediately, with no,	often,	
	or little warning?	usually,	
	of fittle warming:		
		almost	
		always	
	Some people	Not at all,	51
	experience a strong	once, a few	
	urge to urinate or a	times	
	pressure to urinate	(2[en]3),	
	that signals the need	Several	
	to urinate. In the last 7	times	
	d, how many times did		
	you feel a strong urge	many times	
	or pressure that	(≥ 7), every	
	signaled the need to	day	l
	urinate immediately,		İ
	whether or not you		
	urinated or leaked		
	urine?		
Nootunio		I do not have	
Nocturia	During the last month,	I do not have	
	how often have you	symptom,	I
	had to get up to	rarely, a few	I
	urinate more than	times, fairly	İ
	once dung the night?	often.	
		usually,	İ
		almost	
		always	İ
	7 4 1 17 7		40
	In the last 7 d, on	Number [en]	49
	average, how many	2+	
	times have you had to		I
			I
			1
	go to the bathroom to		
	go to the bathroom to empty your bladder		
	go to the bathroom to empty your bladder during the night after		
	go to the bathroom to empty your bladder during the night after falling asleep?		
Sexual	go to the bathroom to empty your bladder during the night after falling asleep? During your		28
Sexual abuse	go to the bathroom to empty your bladder during the night after falling asleep?		28
	go to the bathroom to empty your bladder during the night after falling asleep? During your		28
	go to the bathroom to empty your bladder during the night after falling asleep? During your childhood/adolescence or adulthood has any		28
	go to the bathroom to empty your bladder during the night after falling asleep? During your childhood/adolescence		28

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Measure	Question	Possible responses	Reference/source
	organs of their body to you when you did not want it?		
	Threatened to have sex with you when you did not want this?	Yes, no	
	Touched the sex organs of your body when you did not want this?	Yes, no	
	Made you touch the sex organs of their body when you did not want this?	Yes, no	
	Forced you to have sex when you did not want this?	Yes, no	
	Have you had any other unwanted sexual experiences not mentioned above?	Yes, no	
Physical abuse	When you were a child/adolescent or adult, has any (other) adult done the following?		28
	Hit, kicked, or beaten you?	Never, seldom, occasionally, often	
	Seriously threaten your life?	Never, seldom, occasionally, often	
Emotional abuse	When you were a child/adolescent or adult, has any (other) adult emotionally abused, humiliated, or insulted you?	Never, seldom, occasionally, often	

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Highlighted/boldface responses are indicative of the urologic symptom.

 Table 2

 Prevalence of frequency, urgency, nocturia, and different types of abuse overall and by gender

Variable	Overall, %	Men, %	Women, %
Frequency	32.6	27.8	36.9
Urgency	11.9	9.3	14.2
Nocturia	28.4	25.3	31.3
Childhood			
Sexual abuse	21.6	16.2	26.5
Physical abuse	22.7	24.5	21.1
Emotional abuse	18.7	18.4	19.0
Adolescence/adulthood			
Sexual abuse	19.5	12.6	25.7
Physical abuse	19.4	17.9	20.7
Emotional abuse	19.0	14.8	22.9

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Prevalence of urologic symptoms for those who have or have not experienced different kinds of abuse and odds ratios for the association of different types

of abuse and urologic symptoms (p values in parentheses)

, ,			,			
	Free	Frequency	Ur	Urgency	Noct	Nocturia
	Prevalence,	Odds	Prevalence,	Odds	Prevalence,	Odds
Childhood						
Sexual abuse	(<.0001)	(<.0001)	(<.0001)	(<.0001)	(.0227)	(.0215)
Yes	42.6	1.74	18.1	1.95	32.8	1.31
No	29.8		10.1		27.2	
d	(<.0001)	(<.0001)	(<.0001)	(<.0001)	(.0227)	(.0215)
Physical abuse						
Yes	40.4	1.56	18.4	2.05	34.7	1.46
$N_{\rm O}$	30.3		6.6		26.6	
p	(.0004)	(.0002)	(<.0001)	(<.0001)	(.0034)	(.0015)
Emotional abuse						
Yes	40.8	1.91	19.0	2.06	33.5	1.34
No	30.6		10.1		27.3	
p	(<.0001)	(<:0001)	.0001	(<.0001)	(.0344)	(.0260)
Adolescent/adult Sexual abuse						
Yes	40.8	1.56	19.0	2.09	33.0	1.31
No	30.6		10.1		27.3	
p	(.0001)	(.0001)	(<.0001)	(<.0001)	(.0224)	(.0170)
Physical abuse						
Yes	41.2	1.60	20.4	2.36	36.2	1.57
No	30.5		8.6		26.6	
p	(.0006)	(.0002)	(<.0001)	(<.0001)	(0016)	(.0008)
Emotional abuse						
Yes	45.3	1.97	20.0	2.28	33.1	1.31
No	29.6		6.6		27.4	
p	(<.0001)	(<.0001)	(<.0001)	(<.0001)	(.0354)	(.0286)
		7		7 = 0 0 0 1	1	

Table 4

The extent to which the relationship between abuse and urologic symptoms can be considered causal: summary of criteria proposed by Hill in 1965

Criteria for establishing causation	Data meet this criterion	Comment
1. Strength	Yes	The prevalence of (a) urinary frequency increases by 33[en]50%, (b) urgency doubles, and (c) nocturia increases by 25% in the group that has experienced abuse compared to those who have not.
2. Consistency	Yes	The relationship holds for both men and women, also for black (African American), Hispanic, and white respondents.
3. Specificity	Not applicable No	The association is not restricted to specific people. Abuse is associated with other symptoms other than urinary frequency, urgency, and nocturia.
4. Temporality	Potentially	Childhood abuse precedes (in the aggregate) current urologic symptoms. Longitudinal data not yet available.
5. Biologic gradient (dose-response)	Yes	Increasing frequency of abuse leads to increased prevalence of symptoms.
6. Biologic plausibility	Yes	Animal models suggest a biologic pathway.
7. Coherence	Yes	No known evidence to contradict this causal relationship.
8. Experiment (reversibility)	Yes	Intensive psychotherapy may ameliorate urologic symptoms.
9. Analogy	Potentially	Data on comparable phenomena (PTSD) not presently available, although CRF appears to play a role in many anxiety disorders (including PTSD).

PTSD = posttraumatic stress disorder; CRF = corticotropin-releasing factor.