Management of Symptom Flares and Patient-reported Flare Triggers in Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS)—Findings From One Site of the MAPP Research Network

H. Henry Lai, Joel Vetter, Joseph Song, Gerald L. Andriole, Graham A. Colditz, and Siobhan Sutcliffe

OBJECTIVE To document patient-reported interstitial cystitis/bladder pain syndrome (IC/BPS) flare management strategies and triggers.

MATERIALS AND METHODS Twenty-four male and 29 female participants enrolled at the Washington University site of the MAPP Research Network completed a questionnaire on strategies they utilized to manage flares and factors they believed triggered their flares (eg, specific food items, physical activities, sexual activities, infections, and stress). Participants were also asked about the diurnal timing of their flares.

RESULTS A total of 96.2% of participants reported having ever experienced a symptom flare. Participants treated or managed their flares using a wide variety of strategies, ranging from common strategies, such as drinking additional water or fluid (74.5%), to less common strategies, such as acupuncture/acupressure (5.9% of participants). Participants also reported a wide range of perceived flare triggers, including previously reported factors (citrus fruits, tomatoes, spicy food, alcoholic and caffeinated beverages, driving/sitting in forms of transportation, urinary tract infections, stress, and tight clothing), as well as some less common, previously undocumented factors (eg, certain foods, nongenitourinary infections, wearing high-heeled shoes/boots or perfume, hair dye, and toothpaste). In general, female participants and those with somatic sensory hypersensitivity reported greater numbers of therapies and triggers. Finally, flares were reported most commonly in the afternoon or evening.

CONCLUSION IC/BPS participants reported diverse flare management strategies and numerous perceived triggers. These findings, together with those from the small body of literature to date, provide a wide array of candidates and hypotheses for future global and tailored flare management and prevention interventions. UROLOGY 126: 24–33, 2019. © 2019 Published by Elsevier Inc.

Symptom exacerbations ("flares") occur commonly among patients with interstitial cystitis/bladder pain syndrome (IC/BPS) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).[1-3] Despite their common occurrence and negative impact on quality of life,[3] little is known about the best ways in which to treat or prevent flares. To date, only one small study—a 7-patient single-arm trial of oral prednisolone[4]—has investigated therapies specifically for flares. In addition, only a few previous studies have examined flare triggers empirically to inform flare prevention,[5-7] and none, to our knowledge, has tested flare prevention strategies.

Given this paucity of data on flare management and prevention, additional studies testing promising strategies are needed. To support this research, we queried participants at one site of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Epidemiology and Phenotyping Study about strategies they use to manage

Funding Support: *This study was supported by the NIDDK MAPP (Multidisciplinary Approach to the Study of Pelvic Pain) Research Network grant U01-DK082315 (HHL, GLA, GAC, SS).*

From the Division of Urologic Surgery, Washington University School of Medicine, St Louis, MO; the Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St Louis, MO; and the Department of Anesthesiology, Washington University School of Medicine, St Louis, MO

Address correspondence to: *H. Henry Lai, M.D., Division of Urologic Surgery, Washington University School of Medicine, 4960 Children's Place, Campus Box 8242, St Louis, MO 63110. E-mail: laih@wustl.edu*

Submitted: November 21, 2018, accepted (with revisions): January 16, 2019

https://doi.org/10.1016/j.urology.2019.01.012
0090-4295

their flares and factors they believe trigger their flares to inform the full scope of possible flare therapies and triggers, and to generate hypotheses for future empirical research. By querying men in addition to women, and by assessing a broad range of therapies, self-management strategies, and triggers, our study complements and expands previous investigations in this area that were limited predominantly to women[3,8-12] and/or a much narrower range of therapies and triggers.[12-17]

MATERIALS AND METHODS

Study Population and Design

The MAPP Epidemiology and Phenotyping Study was designed to identify subgroups of IC/BPS and CP/CPPS patients with possible differing etiology and clinical course.[18] The inclusion and exclusion criteria have been described previously.[18] Participants enrolled at the Washington University site were asked to complete an additional questionnaire at their final 12-month research visit that inquired about their flare management strategies and perceived triggers. All participants provided written informed consent following an IRB-approved protocol.

Of the 60 UCPPS participants enrolled at the Washington University site, 57 completed their 12-month research visit and were thus eligible for the present analysis. We further restricted this sample to the 53 participants with IC/BPS symptoms (ie, removing participants with CP/CPPS symptoms only) to allow for more homogeneous comparisons.

Assessment of Flare Management Strategies and Perceived Triggers

On the 12-month questionnaire, participants were asked whether they had ever experienced a flare, which we defined as "urologic or pelvic pain symptoms that are much worse than usual," consistent with previous studies.[1-3] Participants who responded affirmatively were asked about strategies they used to treat or manage their flares, and factors they believed triggered their flares. Treatment and self-management response options were derived from clinical expertise. Trigger response options were derived from the Brief Flare Risk Factor Questionnaire, a questionnaire developed specifically for the MAPP flare trigger case-crossover study,[5,18] as well as from clinical and epidemiologic expertise. Open-ended response options were also included throughout the questionnaire. Finally, as the "empirical induction period"[19] (ie, the length of time it takes for an exposure to trigger a flare) is unknown, we asked participants about their diurnal timing of flares to begin to inform this question. For instance, if most participants experienced the onset of their flares in the morning, this might imply that factors, such as food, take at least 8 hours to trigger a flare (ie, the time between eating the previous night and experiencing a flare the next morning), whereas if participants experienced flares in the evening, this might imply a shorter induction period.

UCPPS is generally believed to comprise multiple subgroups of participants with possibly differing response to therapy, and underlying etiology and clinical course.[20] Likewise, flare triggers are also believed to affect subgroups of UCPPS patients differently.[3,5] Therefore, to begin to explore this possible heterogeneity of treatment effects and flare trigger susceptibility, we performed several stratified analyses, taking advantage of the extensive "phenotyping" performed in the MAPP study. These analyses included stratified investigations by: (1) sex; (2) symptoms of irritable bowel syndrome (IBS), as patients have reported that dietary factors trigger their IBS, which in turn trigger their UCPPS symptoms[3]; (3) symptoms of other chronic overlapping pain conditions (COPCs, fibromyalgia, and chronic fatigue syndrome), as UCPPS patients with COPCs may represent a "centralized pain" subgroup[21]; (4) symptoms of bladder hypersensitivity (ie, painful bladder filling and painful urgency), as patients with these symptoms may represent a "peripheral pain" subgroup[22]; (5) a history of allergies; and (6) symptoms of somatic sensory hypersensitivity, as these patients might also be more sensitive to potential flare triggers. We used modules from the Complex Medical Symptoms Inventory (CMSI)[23] to assess IBS, other COPC symptoms, and somatic sensory hypersensitivity, and the RICE instrument to assess bladder hypersensitivity.[24] Participants were considered to have sensory hypersensitivity if they reported sensitivity to chemicals (eg, perfumes, laundry detergents, gasoline), sound, odor, or bright lights on the CMSI.[23] In performing this last stratified analysis, we recognized that participants might be classified as having sensory hypersensitivity simply because of their perceived triggers, for instance, if perfume triggered their flares, this would classify them as having both sensory hypersensitivity and perfume as a perceived flare trigger.

Statistical Analysis

Participants' responses to flare management and trigger questions were summarized by percentages for individual items and by means for the sum of multiple items. These values were compared by phenotypic characteristic status (eg, sex) using logistic and linear regression, respectively. In the few situations in which 0% of participants reported a particular therapy or trigger, Firth's method of bias-reduction logistic regression models was used.[25] Statistical analyses were performed using R (v 3.3.1). P values $<.05$ were considered statistically significant in this largely, exploratory analysis.

RESULTS

Of the 53 participants eligible for the present analysis, just over half were female (54.7%) and most were Caucasian (84.9%), with a mean age of 47.6 years and a mean duration of symptoms of 10.3 years (Appendix Table 1). Approximately, one-third of the sample (34.0%) reported sensory hypersensitivity and almost all (96.2%) had experienced a flare at least once since their condition began. The 2 participants (1 male and 1 female) who had never experienced a flare were excluded from further analysis.

Patient-reported Management Strategies During UCPPS Flares

When asked how they treated or managed their flares, participants reported multiple strategies of various different modalities (Table 1). A total of 35.3%-41.2% contacted or visited their healthcare provider during flares, whereas relatively few (9.8%) visited an emergency room or urgent care center. A total of 27.5% changed the dose or started a new prescription medication *with* approval from their healthcare provider, and 15.7% changed the dose/started a new medication *without* approval. Medications used during flares included over-the-counter analgesics (52.9%), prescription analgesics (37.3%), dietary supplements (41.2%), and sleeping pills (19.6%). A small percentage of participants (15.7%) also reported performing self-bladder instillations. Female participants were more likely to take

Table 1. Flare treatment and self-management strategies reported by urologic chronic pelvic pain syndrome participants at the Washington University site of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network

		Stratified by Sex				Stratified by Somatic Sensory Hypersensitivity Feature[†]			
	All Participants ($n = 51$)	Male ($n = 23$)	Female ($n = 28$)	*P* Value	*P* Value[‡]	Without Feature ($n = 33$)	With Feature ($n = 18$)	*P* Value	*P* Value[‡]
Healthcare provider-related strategies (%):									
Contact providers by phone or e-mail	41.2	26.1	53.6	*	*	36.4	50.0		
See providers in their office	35.3	26.1	42.9			33.3	38.9		
Visit the emergency department or an urgent care center	9.8	8.7	10.7			6.1	16.7		
Medication/medical procedure-related self-management strategies (%):									
Change dose/start a new prescription medication *with* approval from a healthcare provider	27.5	26.1	28.6			21.2	38.9		
Change dose/start a new prescription medication *without* approval from a healthcare provider	15.7	8.7	21.4			12.1	22.2		
Take over the counter analgesics	52.9	39.1	64.3	*		45.5	66.7		
Take prescription analgesics (eg, narcotics)	37.3	34.8	39.3			30.3	50.0		
Take dietary supplements, herbs, and other plant products (eg, prelief, aloe vera, cystoprotek, cysta-Q, and prosta-Q)	41.2	26.1	53.6	*		30.3	61.1	**	
Take sleeping pills	19.6	4.3	32.1	**	**	15.2	27.8		
Do a bladder instillation yourself at home	15.7	0.0	28.6**	***	**	9.1	27.8		
Nonmedication-related self-management strategies (%):[§]									
Drink additional water or fluid	74.5	69.6	78.6			72.7	77.8		
Drink water mixed with baking soda	21.6	8.7	32.1	*		9.1	44.4	**	**
Go back to a "strict diet"	41.2	26.1	53.6	*		27.3	66.7	***	**
Place a cold pack, heating pad, or hot water bottle on your abdomen/pelvis, or take a sitz bath	47.1	30.4	60.7	**		30.3	77.8	***	**
Stop and rest	56.9	39.1	71.4	**	*	48.5	72.2		
Do tai-chi, yoga, light exercise, or low impact aerobics	15.7	4.3	25.0	*		9.1	27.8		
Get a body massage	13.7	0.0	25.0	**	*	3.0	33.3	***	*
Get acupuncture or acupressure	5.9	4.3	7.1			0.0	16.7	**	**
Use relaxation techniques (eg, meditation, visualization, or hypnosis)	25.5	21.7	28.6			15.2	44.4	**	**
Place knees against your chest, reclining with spread legs or adopting a squatting position	21.6	8.7	32.1	*		9.1	44.4	**	**

Continued

Table 1. Continued

	All Participants ($n = 51$)	Stratified by Sex				Stratified by Somatic Sensory Hypersensitivity Feature†			
		Male ($n = 23$)	Female ($n = 28$)	*P* Value	*P* Value‡	Without Feature ($n = 33$)	With Feature ($n = 18$)	*P* Value	*P* Value‡
Test yourself for a urinary tract infection using a home kit	11.8	4.3	17.9			6.1	22.2		
Social support strategies (%):									
Reach out to family members	39.2	17.4	57.1	***	**	33.3	50.0		
Reach out to other patients (eg, support groups, internet forums, and national organizations)	15.7	8.7	21.4			9.1	27.8		
Deal with the flare yourself without reaching out to others	66.7	73.9	60.7			69.7	61.1		
Total no. of management strategies used (mean ± standard deviation)	7.5 ± 0.7	5.2 ± 0.7	9.5 ± 1.0	***	**	5.8 ± 0.6	10.7 ± 1.5	***	**

* .1> $P \geq .05$; ** .05 > $P \geq .01$; *** $P < .01$.

† Defined as reported sensitivity to chemicals (eg, perfumes, laundry detergents, and gasoline), sound, odor, or bright lights on the Complex Medical Symptoms Inventory.

‡ Adjusted for sex or somatic sensory hypersensitivity feature, as appropriate.

§ An additional strategy reported by 1 participant in an open-ended text field was: massaging the tip of his penis. Note that the sum of percentages may exceed 100% since participants may respond affirmatively to multiple questions.

sleeping pills and perform self-bladder instillations than male participants, independent of somatic sensory hypersensitivity status.

With respect to nonmedication-related flare management strategies, the most commonly reported were drinking additional water or fluid (74.5%), "stopping and resting" (56.9%), using heat or cold therapy (47.1%), going back to a "strict diet" (41.2%), and using relaxation techniques, such as meditation, visualization, and hypnosis (25.5%). Less commonly reported strategies were drinking water with baking soda; doing light exercise; getting a massage, acupuncture, or acupressure; placing their knees against their chest; and testing themselves for a urinary tract infection (UTI). An additional strategy reported in an open-ended field was "massaging the tip of the penis." In general, female participants and those with somatic sensory hypersensitivity were more likely to manage their flares by various nonmedication-related strategies than male participants and those without hypersensitivity. These differences were largely explained by somatic sensory hypersensitivity, with significant differences persisting for those with hypersensitivity after adjustment for sex.

Finally, with respect to social support, 39.2% of participants reached out to family members during flares; 15.7% reached out to other patients, support groups, internet forums, or national organizations; and 66.7% did not reach out to others and managed their flares alone. Female participants were significantly more likely to reach out to others than male participants, whereas significant differences were not observed by somatic sensory hypersensitivity status. Note that sum of percentages may exceed 100% since participants may respond affirmatively to multiple questions.

When all strategies were considered together, participants reported an average of 7.5 flare strategies, 5.2 for men vs 9.5 for women (adjusted $P < .01$), and 5.8 for participants without somatic sensory hypersensitivity vs 10.7 for those with hypersensitivity (adjusted $P < .01$). Flare management and treatment strategies did not vary by any other participant characteristics examined (ie, IBS, other COPCs, bladder hypersensitivity, and history of allergies).

Patient-reported Triggers of UCPPS Flares

Dietary Factors. When asked what they believed triggered their flares, participants reported numerous dietary factors (Table 2). The most common of these were citrus fruits, tomatoes, spicy food, alcohol, and caffeinated beverages, all of which were reported by over half of participants. Approximately one-third of participants reported that consumption of pineapples, cranberries, onions, yogurt, vinegar, chocolate, and noncaffeinated, carbonated beverages triggered their flares. Less commonly reported triggers were pears, asparagus, beans, nuts, aged cheese, sour cream, and shrimp. Foods not included in our survey, but reported by participants in open-ended fields were potassium-rich foods, mango, milk, and barbecue sauce. When information on all dietary factors assessed was combined, 94.1% of participants reported at least 1 dietary trigger, with an average of 7.5 reported triggers per participant.

Although reported beverage triggers were fairly similar by sex and somatic sensory hypersensitivity status, female participants and those with somatic sensory hypersensitivity were almost always more likely to report foods as triggers than male participants and those without hypersensitivity. These differences were largely explained by somatic sensory hypersensitivity, as most sex-specific differences attenuated after adjustment for hypersensitivity, whereas those for hypersensitivity persisted for onions, beans, yogurt, and chocolate after adjustment for sex.

Table 2. Dietary flare triggers[†] reported by urologic chronic pelvic pain syndrome participants at the Washington University site of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network

		Stratified by Sex				Stratified by Somatic Sensory Hypersensitivity Feature[‡]			
Patient-reported Dietary Flare Triggers (%):	All Participants ($n = 51$)	Male ($n = 23$)	Female ($n = 28$)	*P* Value	*P* Value[§]	Without Feature ($n = 33$)	With Feature ($n = 18$)	*P* Value	*P* Value[§]
Fruit (including juice):									
Citrus	56.9	34.8	75.0	***	*	42.4	83.3	***	*
Pineapple	35.3	21.7	46.4	*		24.2	55.6	**	
Cranberry	33.3	17.4	46.4	**		24.2	50.0		
Pear	23.5	13.0	32.1			15.2	38.9	*	
Vegetables and legumes (raw, cooked, or juice):									
Tomato	56.9	43.5	67.9	*		45.5	77.8	**	*
Onion	35.3	17.4	50.0	**		18.2	66.7	***	***
Asparagus	19.6	8.7	28.6	*		15.2	27.8		
Beans	19.6	13.0	25.0			9.1	38.9	**	**
Nuts	25.5	17.4	32.1			15.2	44.4	**	*
Dairy products:									
Aged cheese	23.5	13.0	32.1			18.2	33.3		
Sour cream	23.5	17.4	28.6			15.2	38.9	*	
Yogurt	31.4	21.7	39.3			18.2	55.6	**	**
Other foods and condiments:									
Shrimp	15.7	13.0	17.9			12.1	22.2		
Spicy food	60.8	47.8	71.4			48.5	83.3	**	*
Vinegar	35.3	21.7	46.4	*		24.2	55.6	**	
Chocolate	43.1	30.4	53.6			27.3	72.2	***	**
Other beverages:									
Alcohol	54.9	56.5	53.6			54.5	55.6		
Caffeinated tea and coffee	56.9	56.5	57.1			54.5	61.1		
Caffeinated carbonated drinks	62.7	60.9	64.3			54.5	77.8		*
Noncaffeinated carbonated drinks	31.4	30.4	32.1			24.2	44.4		
Any dietary item	94.1	91.3	96.4			90.9	100.0		
No. of dietary items (mean ± standard deviation)	7.5 ± 0.9	5.6 ± 1.2	9.0 ± 1.2	**		5.6 ± 1.0	10.8 ± 1.4	***	**

*.1> $P \geq .05$; **.05> $P \geq .01$; ***$P < .01$.

[†] Additional dietary flare triggers reported by participants in an open-ended text field were: foods rich in potassium (eg, bananas, certain milks), mango, milk (for flares lasting <1 hour), and BBQ sauces (for flares lasting >1 day).

[‡] Defined as reported sensitivity to chemicals (eg, perfumes, laundry detergents, and gasoline), sound, odor, or bright lights on the Complex Medical Symptoms Inventory.

[§] Adjusted for sex or somatic sensory hypersensitivity feature, as appropriate.Note that the sum of percentages may exceed 100% since participants may respond affirmatively to multiple questions.

Nondietary Factors. With respect to nondietary factors, large percentages of participants (~30%-50%) reported that performing exercises that work their abdominal muscles, physical overexertion, sitting in forms of active and sedentary transportation, and sitting, in general, triggered their flares (Table 3). Activities not included in our survey, but reported by participants in open-ended fields were standing for long periods of time and "working." One participant also reported that physical activities triggered flares only when they did not drink enough water. Over one-third of participants (39.2%) reported that vaginal intercourse triggered their flares, over half (58.8%) reported that UTIs triggered their flares, and over one-third of female participants (39.3%) reported that vaginal infections triggered their flares. Other types of infections, such as gastroenteritis, were reported much less commonly as flare triggers. Kidney infection was also reported by one participant in an open-ended field.

Finally, with respect to other potential triggers, over three-quarters of participants (78.4%) reported that stress triggered their flares, approximately half (54.9%) reported that wearing tight clothing triggered their flares, and one-quarter (25.5%) reported that a change in the weather triggered their flares. In female participants, menstrual cycle (28.6%), ovulation (21.4%), and wearing shoes/boots with high heels (28.6%) were also fairly commonly reported triggers. Less commonly reported triggers were perfume, hair dye, and toothpaste, and other possible triggers not included in our survey, but reported by participants in open-ended fields, were jostling or constant vibration/oscillation, cleaning supplies, back muscle spasm/strain, pudendal nerve area aggravation, tampons, constipation, using a mouthguard with bisphenol A, and humidity.

In general, female participants and those with somatic sensory hypersensitivity were more likely to report various nondietary factors as triggers than male participants and those without hypersensitivity. Similar to findings for dietary factors, these nondietary findings were driven by sensory hypersensitivity, with several significant differences persisting for sensory hypersensitivity after adjustment by sex.

Diurnal Timing of UCPPS Flares

When asked about their typical diurnal timing of flares, only 5 participants (9.8%; 3 male and 2 female) reported 1 typical time; 1 in the morning, 1 in the afternoon, and 3 in the evening. The remaining participants reported that their flares could occur anytime during the day or night, or provided multiple responses, indicating variability in their diurnal timing of flares. Considering all responses together, the most commonly reported times were in the afternoon (45.7%) and evening (47.8%), followed by the morning (37.0%), waking up with a flare (21.7%), and during the night (21.7%; Table 4). A total of 52.2% of participants also reported that their flares could occur at any time.

DISCUSSION

In our sample of UCPPS patients, almost all participants reported experiencing a flare at some time in their condition. Participants treated or managed their flares using a wide variety of strategies, ranging from drinking additional water or fluid (74.5% of participants) to acupuncture/acupressure (5.9%). Participants also reported a wide range of perceived flare triggers, including more commonly reported triggers (citrus fruits, tomatoes, spicy food, alcoholic and caffeinated beverages, driving/sitting in forms of transportation, UTIs, stress, and tight clothing), as well as some less common, previously undocumented factors (eg, certain foods, nongenitourinary infections, wearing high-heeled shoes/boots or perfume, coloring their hair, or using a new toothpaste). In general, female participants and those with somatic sensory hypersensitivity reported a greater number of therapies and triggers. Finally, although flares were reported at any time during the day or night, they were experienced most commonly in the afternoon or evening.

Flare Treatment and Management

Our findings for flare treatment and self-management strategies are similar to those from most previous surveys and interviews/focus groups conducted to date.[2,3,8-11,17,26,27] However, we also observed a few additional strategies not previously documented in other studies, including acupuncture or acupressure, placing their knees against their chest and reclining with spread legs or adopting a squatting position to relax their pelvic muscles, and testing themselves for a UTI.

While we cannot comment on the efficacy of patient-reported flare treatments and self-care strategies, our findings, together with those from previous studies, provide several candidates for future treatment and complementary alternative medicine flare interventions, as well as possible insight into flare pathogenesis. For instance, participants' use of sleeping pills during flares may indicate sleep disruption, a consequence of flares that has received little attention to date and that could be addressed with future flare management strategies. Participants may also use sleeping pills for anxiolytic properties, as anxiety is common in IC/BPS. In addition, participants' frequent intake of additional water or fluid during flares may indicate that forced fluid diuresis and passive bladder distension is therapeutic for flares, an inference consistent with the short-term improvement in pain observed for some IC/BPS patients following bladder hydrodistention under anesthesia.[28] Alternatively, it may indicate that "flushing out" or "diluting" dietary irritants in the bladder or urine is therapeutic.[3] A better understanding of these mechanisms might inform both flare triggers and additional flare therapies.

Discrepancies between reported flare triggers and flare management strategies also highlight opportunities for flare management. For instance, although a large proportion of participants reported stress as a flare trigger, many fewer used recommended stress-management or relaxation techniques[29] to manage their flares. A similar discrepancy was observed for perceived UTI triggers and use of home UTI urine kits. If participants' flares are indeed triggered by UTIs, earlier identification of infection through home testing could allow for earlier UTI management while their culture is still pending. Finally, although depression and coping difficulties are common in UCPPS patients,[30] a large proportion of participants,

Table 3. Nondietary flare triggers reported by urologic chronic pelvic pain syndrome participants at the Washington University site of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network

		Stratified by Sex				Stratified by Somatic Sensory Hypersensitivity Feature[†]			
Patient-reported Flare Triggers (%):	All Participants ($n = 51$)	Male ($n = 23$)	Female ($n = 28$)	*P* Value	*P* Value[‡]	Without Feature ($n = 33$)	With Feature ($n = 18$)	*P* Value	*P* Value[‡]
Physical activities and sedentary behaviors:[§]									
Exercises that work abdominal muscles (eg, sit-up, crunch)	35.3	17.4	50.0	**		21.2	61.1	***	**
Roller skating, roller blading, or ice skating	15.7	8.7	21.4			9.1	27.8		
Physical overexertion, irrespective of activity	49.0	34.8	60.7	*		33.3	77.8	***	**
Driving/sitting in a car, bus, train, or plane, etc.	51.0	52.2	50.0			45.5	61.1		
Riding a bicycle, exercise bicycle, horse, etc.	39.2	39.1	39.3			33.3	50.0		
Sitting (eg, at work, watching TV, reading)	43.1	43.5	42.9			30.3	66.7	**	***
Sexual activities:									
Engaging in vaginal intercourse	39.2	30.4	46.4			33.3	50.0		
Receiving oral intercourse	19.6	13.0	25.0			12.1	33.3		
Receiving anal intercourse	7.8	4.3	10.7			0.0	22.2	**	**
Performing anal intercourse (males only)	N/A	0.0	N/A			0.0	0.0		
Any sexual activities	43.1	30.4	53.6			36.4	55.6		
Infections/allergies:[‖]									
Urinary tract infection (UTI)	58.8	47.8	67.9			54.5	66.7		
Gastroenteritis or “the stomach flu”	25.5	21.7	28.6			18.2	38.9		
Vaginal infection	N/A	N/A	39.3			12.1	44.4	**	
Respiratory infection (eg cold, flu, sinus infection, pneumonia, bronchitis)	21.6	13.0	28.6			12.1	38.9	**	*
Hay fever or allergic reaction	13.7	0.0	25.0	**	**	6.1	27.8	*	
Eye infection	7.8	0.0	14.3			0.0	22.2	**	*
Ear infection	5.9	0.0	10.7			0.0	16.7	**	
Fever	9.8	8.7	10.7			6.1	16.7		
Any infection/allergy	72.5	65.2	78.6			75.8	66.7		
No. of infections/allergies (mean ± standard deviation)	1.7 ± 0.3	1.0 ± 0.2	2.3 ± 0.5	*		1.1 ± 0.2	2.7 ± 0.7		**
Other reported triggers:[¶]									
Stress	78.4	69.6	85.7			69.7	94.4	*	
Wearing tight clothing	54.9	47.8	60.7			45.5	72.2	*	
Change in the weather	25.5	4.3	42.9	***	*	9.1	55.6	***	**
Start of allergy season	17.6	4.3	28.6	**		12.1	27.8		
Starting new medications	15.7	4.3	25.0	*		3.0	38.9	***	**
Menstrual cycle	N/A	N/A	28.6			15.2	16.7		
Ovulation	N/A	N/A	21.4			3.0	27.8	**	
Wearing shoes/boots with high heels	N/A	N/A	28.6			0.0	44.4	***	***

Continued

Table 3. Continued

	All Participants ($n = 51$)	Stratified by Sex				Stratified by Somatic Sensory Hypersensitivity Feature†			
		Male ($n = 23$)	Female ($n = 28$)	*P* Value	*P* Value‡	Without Feature ($n = 33$)	With Feature ($n = 18$)	*P* Value	*P* Value‡
Patient-reported Flare Triggers (%):									
Wearing perfume or being near someone wearing perfume	7.8	0.0	14.3			0.0	22.2	***	*
Coloring or dying your hair	5.9	0.0	10.7			0.0	16.7	**	
Using a new toothpaste	7.8	0.0	14.3			3.0	16.7		
Total no. of flare triggers reported (mean ± standard deviation)	15.1 ± 1.6	10.4 ± 1.6	18.9 ± 2.5	***	**	10.8 ± 1.4	23.1 ± 3.1	***	***

* .1> $P \geq .05$; ** .05> $P \geq .01$; *** $P < .01$.
† Defined as reported sensitivity to chemicals (eg, perfumes, laundry detergents, and gasoline), sound, odor, or bright lights on the Complex Medical Symptoms Inventory.
‡ Adjusted for sex or somatic sensory hypersensitivity feature, as appropriate.
§ Additional physical activity/sedentary behavior triggers or comments reported by participants were: only when not drinking enough water, standing on their feet for a long time, and working.
‖ Additional infection triggers reported by participants were: kidney infection.
¶ Additional triggers reported by participants were: jostling or constant vibration/oscillation, cleaning supplies, back muscle spasm/strain, pudendal nerve area aggravation, tampons, constipation, using a mouthguard with bisphenol A, and humidity. Note that the sum of percentages may exceed 100% since participants may respond affirmatively to multiple questions.

particularly male participants, did not reach out to others during flares, and instead coped with their flares themselves. Therefore, increasing male participants' use of family and social support may serve as another possible strategy to reduce the negative impact of flares.

Patient-reported Flare Triggers

Similar to previous surveys and focus groups, participants in our study reported a wide variety of triggers related to diet, physical and sexual activities, infections, and other factors. Perceived triggers reported in our survey that have not yet been reported, to our knowledge, in the literature were certain foods (pears, bananas, mango, asparagus, shrimp, and milk); physical activities (physical overexertion, abdominal muscle exercises); nongenitourinary infections, such as ear, eye, and respiratory tract infections; and a few additional factors, such as wearing shoes or boots with high heels (women only), wearing perfume/being near someone wearing perfume, cleaning supplies, coloring or dying their hair, and using a new toothpaste. While many of these perceived triggers were not reported by a large proportion of participants, they still add to the body of potential flare candidates that can be tested in future flare prevention studies. To help tailor these strategies, we also found that participants with somatic sensory hypersensitivity were more likely to report foods/activities as triggers and a larger overall number of triggers than those without hypersensitivity, possibly identifying a subgroup (or "phenotype") of participants that might benefit most from flare prevention strategies. Interestingly, our findings were not modified by a history of allergies, similar to previous null findings by Shorter et al.[10] Finally, to help inform the empirical induction period of flares, we investigated the diurnal timing of flares and found that participants reported flares most commonly in the afternoon and evening, possibly implying that triggers, such as diet and stress, take at least several hours to contribute to a flare. Newer technologies, such as mobile phone "apps" and wearable activity trackers, may shed additional light on this question.

Similar to almost all previous studies on this topic, our study is limited by the fact that we asked participants how they treated/managed their flares and what they believed triggered their flares rather than testing these therapies and perceived triggers directly. Additional limitations include our relatively low sample size and the possible influence of the interstitial cystitis lays literature on sex-based comparisons. Strengths of our study include our investigation of flare treatments and self-management strategies, which have not been studied in detail in the past; and our inclusion of male participants, who have not been studied extensively or compared directly to female participants. In addition, our detailed characterization of participants allowed us to perform stratified analyses to inform the potential for future tailored strategies.

Table 4. Usual diurnal timing of flares reported by urologic chronic pelvic pain syndrome participants at the Washington University site of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network

Usual Diurnal Timing of Flares (%[†]):	All Participants ($n = 51$)	Stratified by Sex				Stratified by Somatic Sensory Hypersensitivity Feature[†]			
		Male ($n = 23$)	Female ($n = 28$)	*P* Value	*P* Value[‡]	Without Feature ($n = 33$)	With Feature ($n = 18$)	*P* Value	*P* Value[‡]
Wake up with a flare	21.7	5.0	34.6	**	*	16.1	33.3		
In the morning (after you wake up)	37.0	35.0	38.5			29.0	53.3		
In the afternoon	45.7	25.0	61.5	**	*	35.5	66.7	*	
In the evening (until you go to bed)	47.8	25.0	65.4	***	*	32.3	80.0	***	**
During the night (while you are asleep)	21.7	10.0	30.8			19.4	26.7		
Anytime	52.2	50.0	53.8			54.8	46.7		

* .1> $P \geq .05$; ** .05> $P \geq .01$; *** $P < .01$.
[†] The total percentage exceeds 100% because participants could report multiple diurnal intervals on the questionnaire.
[‡] Adjusted for sex or somatic sensory hypersensitivity feature, as appropriate.

CONCLUSION

We identified a wide range of flare treatments, self-management strategies, and perceived triggers, including some previously undocumented therapies/triggers. Together with the small body of literature on this topic, these findings provide a wide array of candidates for global and tailored flare management and prevention efforts.

Acknowledgment. The authors would like to thank Vivien Gardner and Rebecca Bristol for recruitment of participants at our site.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.01.012.

References

1. Sutcliffe S, Colditz GA, Goodman MS, et al. Urological chronic pelvic pain syndrome symptom flares: characterisation of the full range of flares at two sites in the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network. *BJU Int.* 2014;114:916–925.
2. Sutcliffe S, Colditz GA, Pakpahan R, et al. Changes in symptoms during urologic chronic pelvic pain syndrome symptom flares: findings from one site of the MAPP Research Network. *Neurourol Urodyn.* 2015;34:188–195.
3. Sutcliffe S, Bradley CS, Clemens JQ, et al. Urological chronic pelvic pain syndrome flares and their impact: qualitative analysis in the MAPP network. *Int Urogynecol J.* 2015;26:1047–1060.
4. Jeong HJ. Effects of a short course of oral prednisolone in patients with bladder pain syndrome with fluctuating, worsening pain despite low-dose triple therapy. *Int Neurourol J.* 2012;16:175–180.
5. Sutcliffe S, Jemielita T, Lai HH, et al. A case-crossover study of urologic chronic pelvic pain syndrome flare triggers in the MAPP research network. *J Urol.* 2018;199:1245–1251.
6. Powell-Boone T, Ness TJ, Cannon R, Lloyd LK, Weigent DA, Fillingim RB. Menstrual cycle affects bladder pain sensation in subjects with interstitial cystitis. *J Urol.* 2005;174:1832–1836.
7. Lutgendorf SK, Kreder KJ, Rothrock NE, Ratliff TL, Zimmerman B. Stress and symptomatology in patients with interstitial cystitis: a laboratory stress model. *J Urol.* 2000;164:1265–1269.
8. Koziol JA. Epidemiology of interstitial cystitis. *Urol Clin North Am.* 1994;21:7–20.
9. Webster DC, Brennan T. Self-care strategies used for acute attack of interstitial cystitis. *Urol Nurs.* 1995;15:86–93.
10. Shorter B, Lesser M, Moldwin RM, Kushner L. Effect of comestibles on symptoms of interstitial cystitis. *J Urol.* 2007;178:145–152.
11. Bassaly R, Downes K, Hart S. Dietary consumption triggers in interstitial cystitis/bladder pain syndrome patients. *Female Pelvic Med Reconstr Surg.* 2011;17:36–39.
12. Parsons CL. How does interstitial cystitis begin? *Transl Androl Urol.* 2015;4:605–610.
13. Alexander RB, Trissel D. Chronic prostatitis: results of an internet survey. *Urology.* 1996;48:568–574.
14. Moon TD. Questionnaire survey of urologists and primary care physicians' diagnostic and treatment practices for prostatitis. *Urology.* 1997;50:543–547.
15. Mehik A, Hellstrom P, Lukkarinen O, Sarpola A, Jarvelin M. Epidemiology of prostatitis in Finnish men: a population-based cross-sectional study. *BJU Int.* 2000;86:443–448.
16. Hedelin H, Jonsson K. Chronic abacterial prostatitis and cold exposure: an explorative study. *Scand J Urol Nephrol.* 2007;41:430–435.

17. Hedelin H, Jonsson K. Chronic prostatitis/chronic pelvic pain syndrome: symptoms are aggravated by cold and become less distressing with age and time. *Scand J Urol Nephrol*. 2007;41:516–520.
18. Landis JR, Williams DA, Lucia MS, et al. The MAPP research network: design, patient characterization and operations. *BMC Urol*. 2014;14:58.
19. Rothman KJ. Induction and latent periods. *Am J Epidemiol*. 1981;114:253–259.
20. Clemens JQ, Mullins C, Kusek JW, et al. The MAPP research network: a novel study of urologic chronic pelvic pain syndromes. *BMC Urol*. 2014;14:57.
21. Lai HH, Jemielita T, Sutcliffe S, et al. Characterization of whole body pain in urologic chronic pelvic pain syndrome at baseline—a MAPP research network study. *J Urol*. 2017;198:622–631.
22. Lai HH, Krieger JN, Pontari MA, et al. Painful bladder filling and painful urgency are distinct characteristics in men and women with urological chronic pelvic pain syndromes: a MAPP research network study. *J Urol*. 2015;194:1634–1641.
23. Williams DA, Schilling S. Advances in the assessment of fibromyalgia. *Rheum Dis Clin North Am*. 2009;35:339–357.
24. Berry SH, Bogart LM, Pham C, et al. Development, validation and testing of an epidemiological case definition of interstitial cystitis/painful bladder syndrome. *J Urol*. 2010;183:1848–1852.
25. Firth D. Bias reduction of maximum likelihood estimates. *Biometrika*. 1993;80:27–38.
26. Hedelin H, Jonsson K, Lundh D. Pain associated with the chronic pelvic pain syndrome is strongly related to the ambient temperature. *Scand J Urol Nephrol*. 2012;46:279–283.
27. Herati AS, Shorter B, Srinivasan AK, et al. Effects of foods and beverages on the symptoms of chronic prostatitis/chronic pelvic pain syndrome. *Urology*. 2013;82:1376–1380.
28. Erickson DR, Kunselman AR, Bentley CM, et al. Changes in urine markers and symptoms after bladder distention for interstitial cystitis. *J Urol*. 2007;177:556–560.
29. Hanno PM, Erickson D, Moldwin R, Faraday MM. American Urological Association. Diagnosis and treatment of interstitial cystitis/bladder pain syndrome: AUA guideline amendment. *J Urol*. 2015;193:1545–1553.
30. Naliboff BD, Stephens AJ, Afari N, et al. Widespread psychosocial difficulties in men and women with urologic chronic pelvic pain syndromes: case-control findings from the multidisciplinary approach to the study of chronic pelvic pain research network. *Urology*. 2015;85:1319–1327.