Development, Validation and Testing of an Epidemiological Case Definition of Interstitial Cystitis/Painful Bladder Syndrome

Supplementary Tables

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Table 1. Final Median and Agreement Ratings of IC/PBS Case Definition Panel

<table>
<thead>
<tr>
<th>Criteria with Strong Evidence</th>
<th>IC/PBS</th>
<th>OAB</th>
<th>ENDO</th>
<th>VULVO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient reports pain by location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of pain somewhere in pelvic area (suprapubic to upper thighs)</td>
<td>4A*</td>
<td>-5A*</td>
<td>4A*</td>
<td>5U</td>
</tr>
<tr>
<td>Bladder pain</td>
<td>5A*</td>
<td>-5A*</td>
<td>1A</td>
<td>0U</td>
</tr>
<tr>
<td>Suprapubic pain</td>
<td>5A*</td>
<td>-5A*</td>
<td>2A</td>
<td>0U</td>
</tr>
<tr>
<td>Urethral pain</td>
<td>2A</td>
<td>-5U</td>
<td>0A</td>
<td>1A</td>
</tr>
<tr>
<td>Vulvar pain</td>
<td>0U</td>
<td>-5U</td>
<td>0U</td>
<td>5A*</td>
</tr>
<tr>
<td>Vaginal pain</td>
<td>1A</td>
<td>-5U</td>
<td>2U</td>
<td>4A</td>
</tr>
<tr>
<td>Rectal pain</td>
<td>0A</td>
<td>-5U</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>Pain in lower back</td>
<td>0A</td>
<td>0U</td>
<td>1A</td>
<td>0A</td>
</tr>
<tr>
<td>Pain in inner thighs</td>
<td>0A</td>
<td>-2U</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>Pain awakening at night</td>
<td>5A</td>
<td>-4A</td>
<td>0U</td>
<td>0U</td>
</tr>
<tr>
<td>Localized pain below waist (always same area)</td>
<td>4A</td>
<td>-5U</td>
<td>3U</td>
<td>4A</td>
</tr>
<tr>
<td>Migratory pain (location varies over time)</td>
<td>0U</td>
<td>-5U</td>
<td>1A</td>
<td>-1U</td>
</tr>
<tr>
<td><strong>Patient reports type of pain</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cramping/Bladder spasms</td>
<td>3A</td>
<td>3U</td>
<td>-3U</td>
<td>0U</td>
</tr>
<tr>
<td>Pain, pressure &amp; discomfort</td>
<td>5A*</td>
<td>0U</td>
<td>4A*</td>
<td>3A</td>
</tr>
<tr>
<td>Varies from mild/moderate-severe/excruciating</td>
<td>3U</td>
<td>-4U</td>
<td>4A</td>
<td>3U</td>
</tr>
<tr>
<td><strong>Patient reports pain worsens</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>When bladder is full</td>
<td>5A*</td>
<td>0U</td>
<td>-3U</td>
<td>-3U</td>
</tr>
<tr>
<td>During urination (burning)</td>
<td>1A</td>
<td>-4U</td>
<td>-3U</td>
<td>-2U</td>
</tr>
<tr>
<td>After bladder is emptied</td>
<td>-2U</td>
<td>-4U</td>
<td>-2U</td>
<td>0U</td>
</tr>
<tr>
<td>With vaginal intercourse, on entry</td>
<td>2U</td>
<td>0U</td>
<td>2U</td>
<td>5A</td>
</tr>
<tr>
<td>During vaginal intercourse, deep penetration</td>
<td>3A</td>
<td>0U</td>
<td>4A</td>
<td>4A</td>
</tr>
<tr>
<td>When vulvar area is touched</td>
<td>-3U</td>
<td>0U</td>
<td>0U</td>
<td>5A*</td>
</tr>
<tr>
<td>During tampon insertion</td>
<td>0U</td>
<td>0U</td>
<td>1A</td>
<td>4A</td>
</tr>
<tr>
<td>Just before menstruation begins</td>
<td>2U</td>
<td>0U</td>
<td>1U</td>
<td>0A</td>
</tr>
<tr>
<td>During menstruation</td>
<td>-2U</td>
<td>0U</td>
<td>5A*</td>
<td>0A</td>
</tr>
<tr>
<td>When bowels are full</td>
<td>0A</td>
<td>0U</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>Soon after consuming acidic or spicy foods, caffeine, or alcohol</td>
<td>4A</td>
<td>0U</td>
<td>0U</td>
<td>0U</td>
</tr>
<tr>
<td>When patient is under stress</td>
<td>4A</td>
<td>3A</td>
<td>1A</td>
<td>2A</td>
</tr>
<tr>
<td>When wearing constrictive clothing</td>
<td>0U</td>
<td>0U</td>
<td>0A</td>
<td>4U</td>
</tr>
<tr>
<td><strong>Patient reports pain improves</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After menstrual period</td>
<td>0U</td>
<td>0U</td>
<td>3A</td>
<td>0</td>
</tr>
<tr>
<td>After bladder is emptied (within 5 - 30 minutes)</td>
<td>5U*</td>
<td>0U</td>
<td>0A</td>
<td>0U</td>
</tr>
<tr>
<td><strong>Patient reports urgent need to urinate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>To relieve pain</td>
<td>5A*</td>
<td>-5A*</td>
<td>-3U</td>
<td>-2U</td>
</tr>
<tr>
<td>To avoid incontinence</td>
<td>-5U*</td>
<td>5A</td>
<td>-3U</td>
<td>0U</td>
</tr>
</tbody>
</table>
Patient reports frequent need to urinate

<table>
<thead>
<tr>
<th></th>
<th>5A*</th>
<th>4A*</th>
<th>0U</th>
<th>0A</th>
</tr>
</thead>
<tbody>
<tr>
<td>During the daytime</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waking her up from sleep at night</td>
<td>5A*</td>
<td>4A</td>
<td>0U</td>
<td>0A</td>
</tr>
</tbody>
</table>

Patient reports other symptoms

<table>
<thead>
<tr>
<th></th>
<th>0A</th>
<th>0A</th>
<th>2U</th>
<th>0A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unable to become pregnant after 1 yr of trying</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urge incontinence</td>
<td>-3U</td>
<td>5A</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>Difficulty starting urine flow</td>
<td>0U</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>Difficulty emptying bladder</td>
<td>2U</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
</tr>
</tbody>
</table>

Patient reports events preceded onset

<table>
<thead>
<tr>
<th></th>
<th>0A</th>
<th>0A</th>
<th>4A*</th>
<th>0A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysmenorrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UTI treated with no improvement</td>
<td>4A</td>
<td>0U</td>
<td>0A</td>
<td>0U</td>
</tr>
<tr>
<td>Incident of holding urine for a long period (e.g. airplane flight)</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>Pelvic surgery</td>
<td>0A</td>
<td>0U</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>Blunt trauma to the abdomen</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
</tr>
<tr>
<td>STD, PID</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
<td>0A</td>
</tr>
</tbody>
</table>

Notes:
Median values of +4 and +5 are strong evidence for the disease, and values of −4 and −5 are strong evidence against the disease
A = agreement among panelists and U = undetermined
* = rated as necessary for diagnosis
IC/PBS = interstitial cystitis/painful bladder syndrome; OAB = overactive bladder; ENDO = endometriosis; VULV = vulvodynia.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Necessary Symptoms</th>
<th>Evidence Against</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interstitial Cystitis/Painful</td>
<td>1. Pain, pressure, and/or discomfort</td>
<td>1. Pain pressure, and/or discomfort only occurs during menstruation</td>
</tr>
<tr>
<td>Bladder Syndrome</td>
<td>a. In pelvic area (suprapubic to upper thighs)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Worsens as bladder fills and/or is diminished by emptying the bladder</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Frequent urination (over 24-hours, includes daytime and nighttime)</td>
<td>2. Urge incontinence/concern about urge incontinence</td>
</tr>
<tr>
<td>Overactive Bladder</td>
<td>1. Urgency</td>
<td>1. Urgency to relieve pain</td>
</tr>
<tr>
<td></td>
<td>2. Pain in pelvic area (suprapubic to upper thighs, including bladder/suprapubic pain)</td>
<td></td>
</tr>
<tr>
<td>Endometriosis</td>
<td>1. Pain, pressure, and/or discomfort</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. In pelvic area (suprapubic to upper thighs)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. during menstruation (dysmenorrhea)</td>
<td></td>
</tr>
<tr>
<td>Vulvodynia</td>
<td>1. Vulvar pain not related to bladder filling</td>
<td></td>
</tr>
</tbody>
</table>
Table 3 RICE Case Definition Questionnaire Items

1. In the past 3 months, have you ever had a feeling of pain, pressure, or discomfort in your lower abdomen or pelvic area -- that is, the part of your body that is above your legs and below your belly button?
   <1> YES
   <2> NO

2. In the past 3 months, have you had a feeling of a strong urge or feeling that you had to urinate or "pee" that made it difficult for you to wait to go to the bathroom?
   <1> YES
   <2> NO [goto Q4]

3. Would you say this urge to urinate is mainly because of pain, pressure or discomfort or mainly because you are afraid you will not make it to the toilet in time to avoid wetting?
   <1> PAIN, PRESSURE, DISCOMFORT, OR
   <2> FEAR OF WETTING

4. In the past 3 months, before you urinate, as your bladder starts to fill, does your feeling of pain, pressure, or discomfort usually:
   <1> Get worse,
   <2> Get better, or
   <3> Stay the same?

5. In the past 3 months (when you were having symptoms), how many times on average have you had to go to the bathroom to urinate during the day when you are awake?

   ENTER NUMBER OF TIMES: _______

6. In the past 3 months, have you had one or more urinary tract or bladder infections that were diagnosed by a doctor or nurse?
   <1> Yes-- One
   <2> Yes-- More Than One
   <3> No [goto Q9]

7. Were you treated with antibiotics for urinary tract or bladder infection(s)?
   <1> YES
   <2> NO [goto Q9]
8. Did all of your symptoms disappear (each time) after you took antibiotics?

   <1> YES
   <2> NO

9. Have you ever been diagnosed with a medical condition called endometriosis?

   <1> YES
   <2> NO - END

10. Were you diagnosed (with endometriosis) with a laparoscopy under anesthesia, that is, a scope that allowed your doctor to look inside your abdomen, after you were put to sleep?

    <1> YES
    <2> NO - END

11. Did you ever have hormone injection to treat endometriosis, such as depolupron?

    <1> YES
    <2> NO
<table>
<thead>
<tr>
<th>Definition</th>
<th>Source</th>
<th>IC/PBS cases identified as IC/PBS (sensitivity) (%)</th>
<th>Non-IC/PBS cases correctly excluded from the definition (specificity) (%)</th>
<th>Non-IC/PBS cases incorrectly identified as IC/PBS (false positives) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain, pressure or discomfort in the pelvic area</td>
<td>RICE Study</td>
<td>91</td>
<td>42</td>
<td>58</td>
</tr>
<tr>
<td>Daytime frequency 10+ OR urgency due to the pain, pressure or discomfort</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain, pressure or discomfort in the pelvic area which worsens as the bladder fills</td>
<td>RICE Study</td>
<td>56</td>
<td>79</td>
<td>21</td>
</tr>
<tr>
<td>Daytime frequency 10+ OR urgency due to pain, pressure discomfort</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms do not resolve with antibiotics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Lupron treatment for endometriosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain, pressure or discomfort in the pelvic area which worsens as the bladder fills and/or is relieved by urination</td>
<td>International Continence Society</td>
<td>65</td>
<td>72</td>
<td>28</td>
</tr>
<tr>
<td>Daytime frequency 10+ OR Nocturia 2+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interstitial Cystitis Symptoms Index 7+</td>
<td>Boston Area Community Health Study</td>
<td>81</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>Interstitial Cystitis Symptoms Index 12+</td>
<td>Boston Area Community Health Study</td>
<td>48</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>Symptom</td>
<td>Frequency</td>
<td>Leppilahti et al</td>
<td>Interstitial Cystitis Symptoms Index</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-----------</td>
<td>-----------------</td>
<td>--------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Burning, pain, discomfort or pressure in pubic or bladder area - fairly often, usually, almost always</td>
<td>Duration 3+ months</td>
<td>Pain increasing as the bladder fills OR pain relieved by urination— fairly often, usually, almost always</td>
<td>Duration 3+ months</td>
<td></td>
</tr>
<tr>
<td>Pain increasing as the bladder fills OR pain relieved by urination— fairly often, usually, almost always</td>
<td>Frequency (urinating again &lt; 2 hours after you finished urinating – fairly often, usually or almost always OR frequent urination - fairly often, usually or almost always OR daytime frequency 8+)</td>
<td>Urgency (difficulty postponing urination – fairly often, usually, almost always OR strong urge or pressure to urinate immediately with little warning – fairly often, usually or almost always</td>
<td>Nocturia 2+</td>
<td></td>
</tr>
<tr>
<td>Burning, pain, discomfort or pressure in the pubic or bladder area – a few times, fairly often, usually, almost always</td>
<td>Interstitial Cystitis Symptoms Index 7+</td>
<td>Burning, pain, discomfort or pressure in the pubic or bladder area – a few times, fairly often, usually, almost always</td>
<td>Interstitial Cystitis Symptoms Index 12+</td>
<td></td>
</tr>
</tbody>
</table>