

# The Interstitial Cystitis/ Bladder Pain Syndrome (IC/BPS) Patient Journey: How Can We Improve?

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# Disclosures

- Abbvie Pharmaceuticals, Consultant
- Alivio Pharmaceuticals, Consultant
- Spero Therapeutics, Consultant
- Ironwood Pharmaceuticals

# The Patient Journey: Let's Talk Definitions

## Interstitial Cystitis Bladder Pain Syndrome

“An unpleasant sensation (pain, pressure, discomfort) *perceived* to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes.”

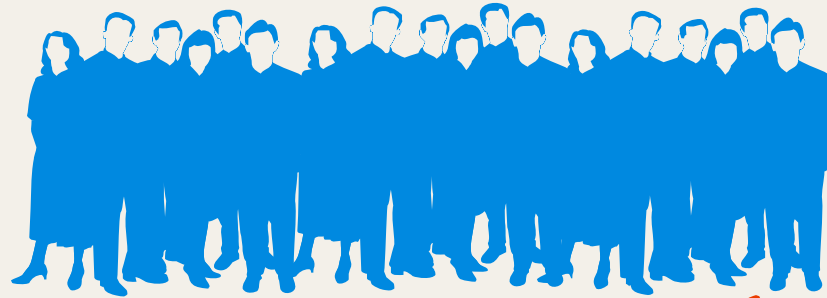


Hanno P and Dmochowski R: Status of international consensus on interstitial cystitis/bladder pain syndrome/painful bladder syndrome: 2008 snapshot. *Neurourology and Urodynamics* 2009; **28**: 274.

# IC Diagnosis Rule

The stricter the criteria...

the more homogeneous the patient population  
but...



...the more patients left untreated.



Hanno PM, Landis JR, Matthews-Cook Y, *et al*: The diagnosis of interstitial cystitis revisited: lessons learned from the National Institutes of Health Interstitial Cystitis Database study. *J Urol* , 1999,161: 553–557.

Warren JW, Meyer WA, Greenberg P, Horne L, Diggs C, Tracy JK. Using the international continence society's Definition of painful bladder syndrome. *Urology*, 2006, 67:1138–1143.

# Varied Pathologies: Varied Therapeutic Targets

- Bladder wall structural defects
- Bladder wall inflammation (cellular and/or humoral)
- Systemic inflammation (cellular and/or humoral)
- Nerve upregulation (central versus peripheral)
- Central processing alterations
- Viscero-viscero convergence (bowel-bladder)
- Viscero-somatic convergence (bladder-pelvic floor)

# The Ideal Patient Journey

Bladder Pain + LUTS + Negative Urine studies



Empiric Therapy for IC/BPS

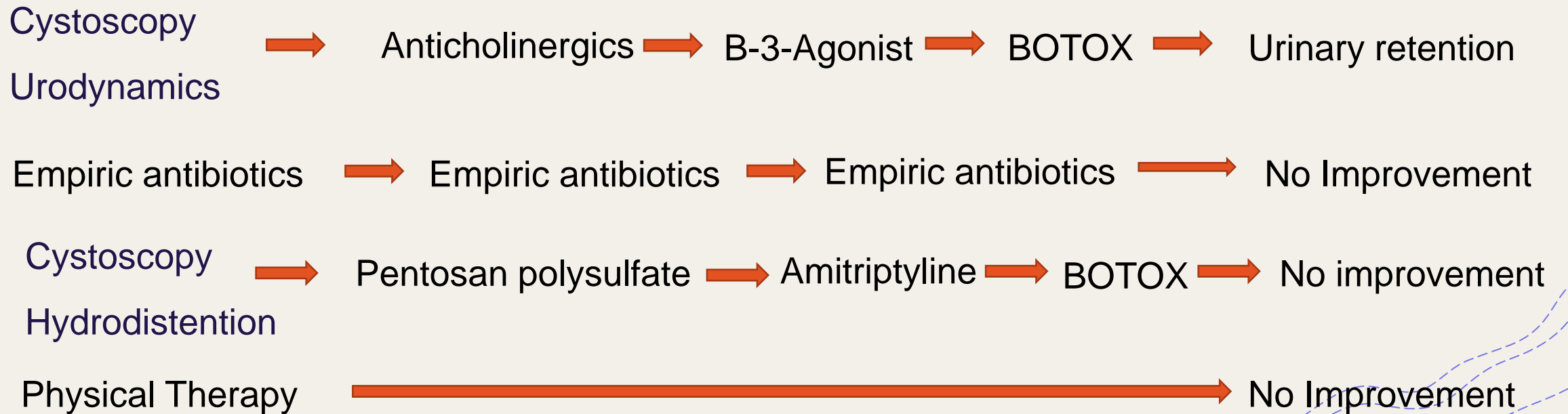


Symptom Improvement

LUTS: Lower Urinary Tract Symptoms

# The REAL Patient Journey

Bladder Pain + LUTS + Negative Urine studies ...



LUTS: Lower Urinary Tract Symptoms

# The Patient Experience

- Descriptive study 20 female IC/BPS patients (21-69 yoa, mean 46)
  - Diagnostic uncertainty
  - Restrictions and limitations on life
  - Self-management
  - Interpersonal relationships and social support



# The Patient Experience

- Depression in up to 70% of cases
- Anxiety symptoms ranged between 14 and 52%
- Panic disorder, low self-esteem common<sup>1</sup>
- Compared to 6% in healthy controls, 23% of patients endorsed Suicidal Ideation in the past two weeks.<sup>2</sup>

1. McKernan LC, Walsh CG, Reynolds WS, et al: Psychosocial co-morbidities in Interstitial Cystitis/Bladder Pain syndrome (IC/BPS): A systematic review. *Neurourol Urodynam* 2018; **37**: 926–941.

2. Tripp DA, Nickel JC, Krsmanovic A, et al: Depression and catastrophizing predict suicidal ideation in tertiary care patients with interstitial cystitis/bladder pain syndrome. *Can Urological Assoc J* 2016; **10**: 383–8.

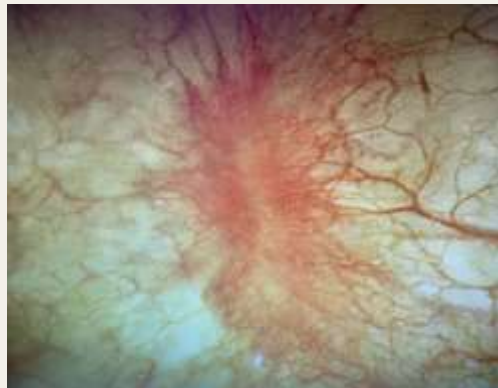
# The REAL Patient Journey (Hunner lesion)

Bladder Pain + LUTS + Negative Urine studies + Cystoscopy with Hunner Lesion (HL)

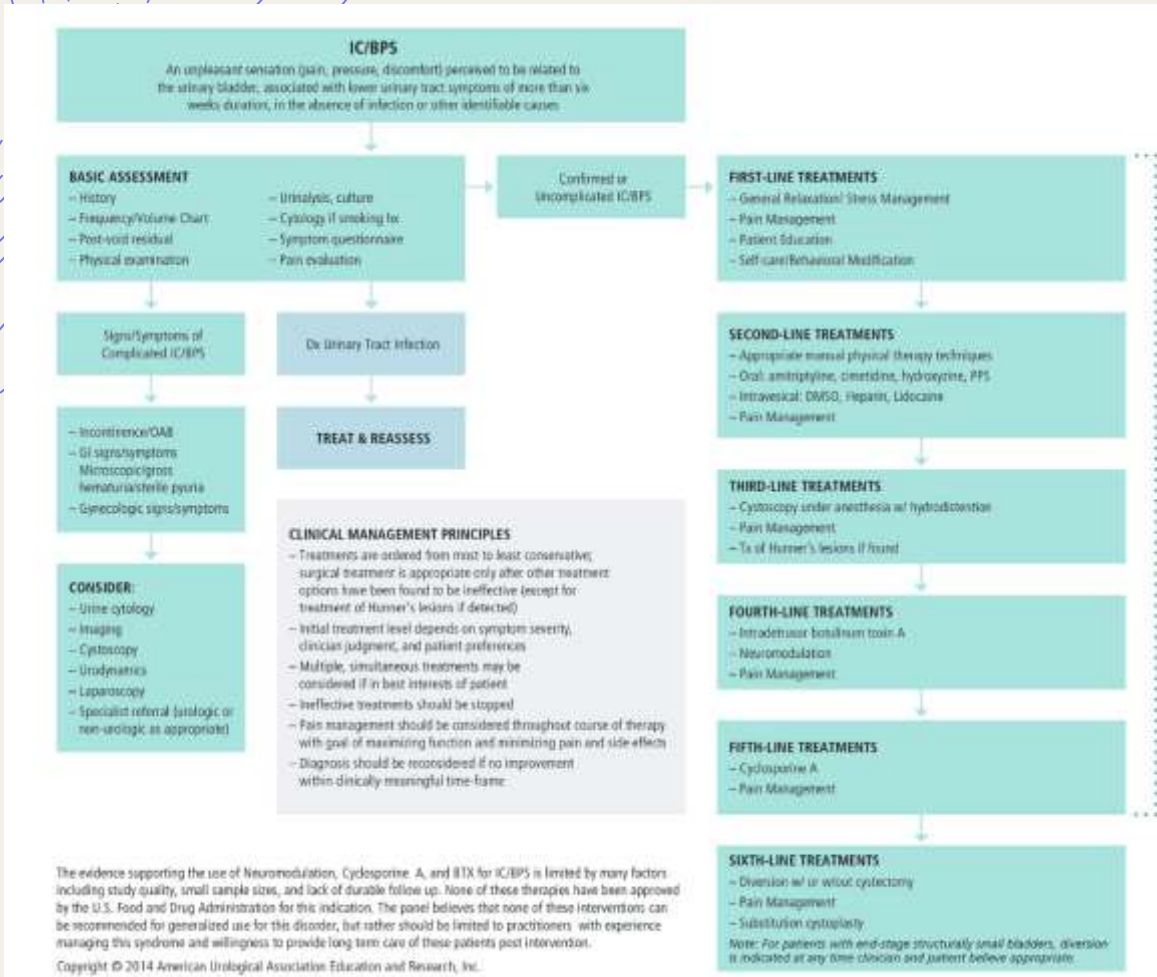
Cystoscopy/ Bx/ fulguration



Symptom Improvement



# Guidelines : The Good, The Bad, and The Ugly



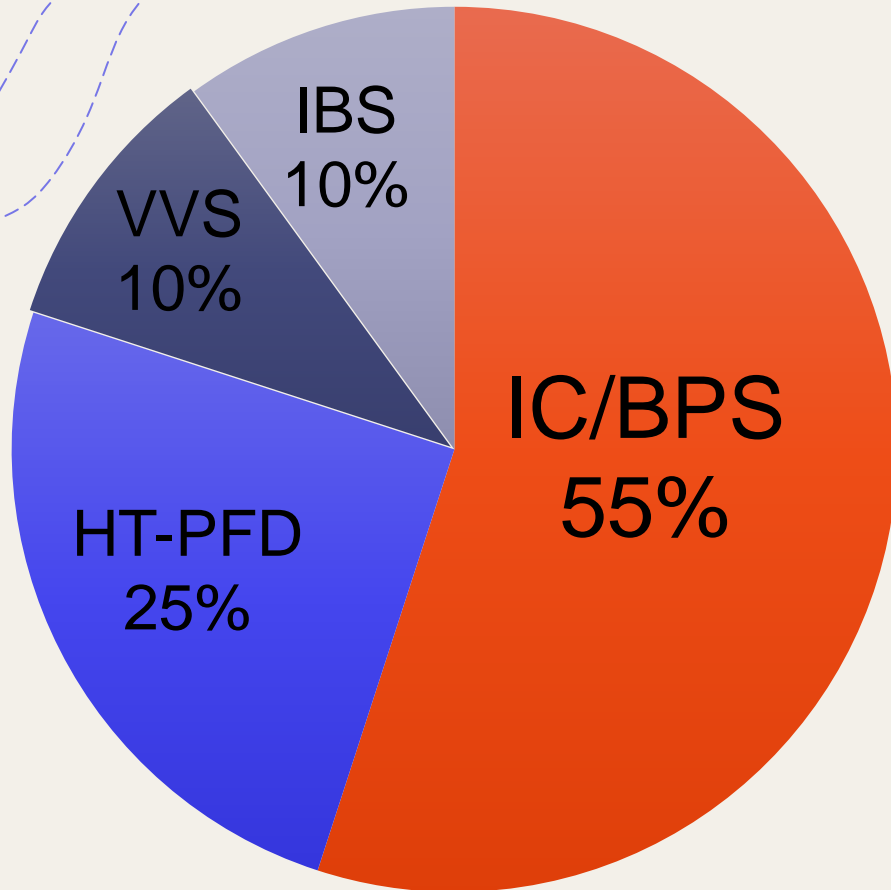
## GOOD:

- Simplified evaluation
- Conservative to invasive management
- Endorses use of “Off-label” therapies (expert opinion)
- Multidisciplinary care

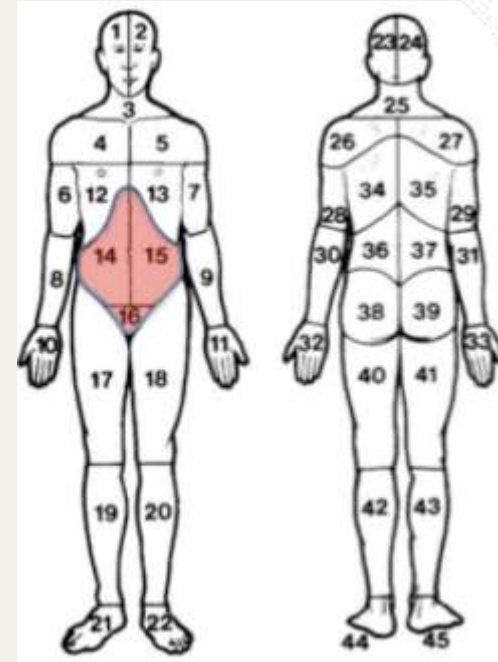
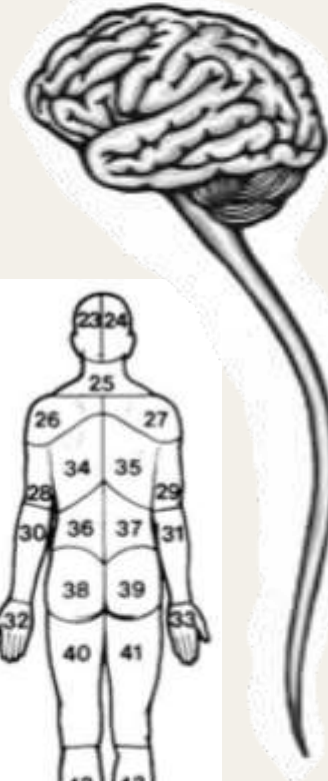
## BAD AND UGLY:

- Do clinicians care about guidelines?
- Definitions blur with other disorders
- Poor ability to phenotype
- Co-morbid pain generators
- Only 2 FDA approved meds
  - Questionable efficacy/ legal concerns
- “Off-label” meds side effects
- Multidisciplinary care

# The Pie of Pain



HT-PFD, High-tone pelvic floor dysfunction  
IBS, Irritable Bowel Syndrome  
VVS, Vulvodynia



## Pelvic Pain and Beyond

- 74%
- “Centralized” phenotype

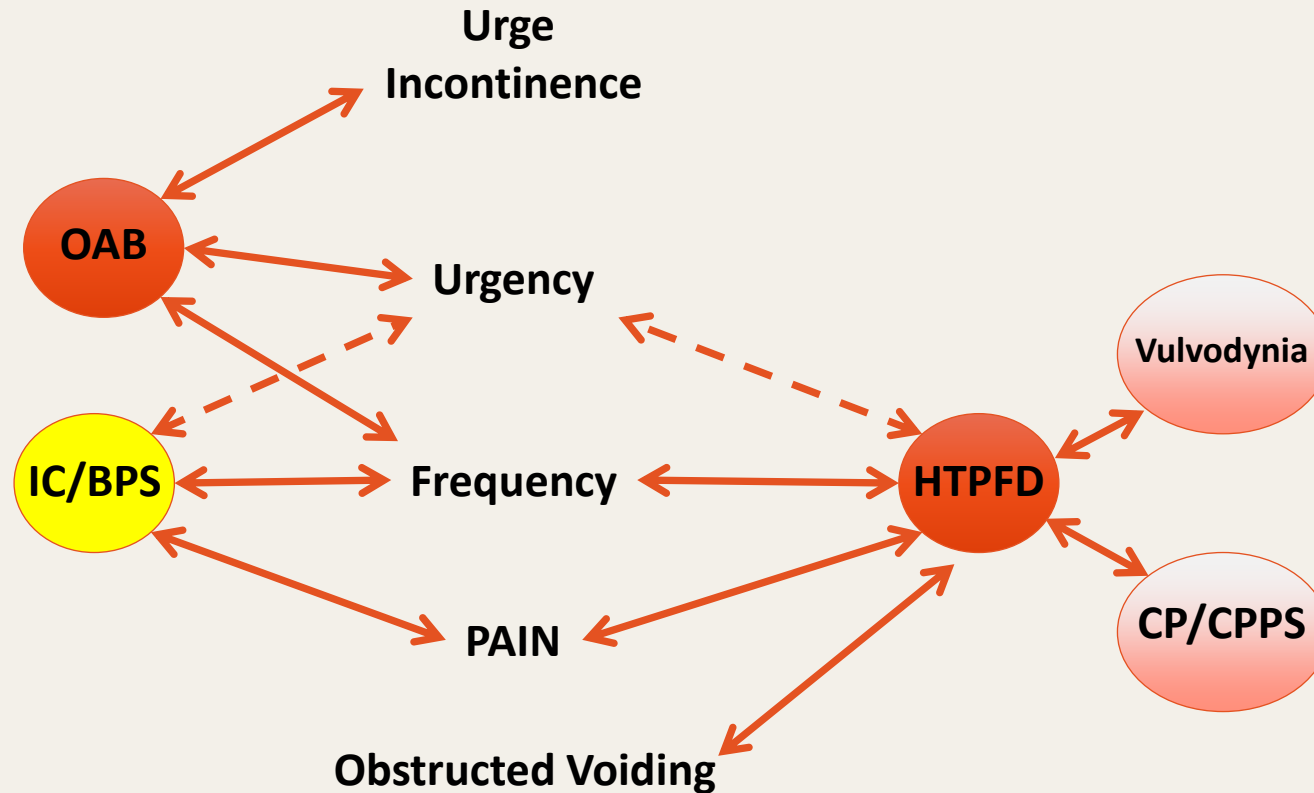
# Self-Reported Diagnoses

| <b>Diagnosis</b>         | <b>IC/BPS<br/>N=205</b> | <b>Control<br/>N=117</b> | <b><i>p</i></b> |
|--------------------------|-------------------------|--------------------------|-----------------|
| Irritable Bowel Syndrome | 38.6%                   | 5.2%                     | <0.001          |
| Fibromyalgia             | 17.7%                   | 2.6%                     | <0.001          |
| Chronic Fatigue Syndrome | 9.5%                    | 1.7%                     | 0.008           |
| Vulvodynia               | 17%                     | 0.9%                     | <0.001          |
| Migraine Headache        | 29.9%                   | 11.2%                    | <0.001          |
| Tension Headache         | 25.6%                   | 10.3%                    | <0.001          |
| TMJD                     | 12%                     | 5.2%                     | 0.048           |
| Low Back Pain            | 46.6%                   | 18.8%                    | <0.001          |
| Psychiatric Condition    | 38.7%                   | 16.2%                    | <0.001          |

Nickel JC, Tripp DA, Pontari MA, Moldwin RM, Mayer R, Carr LK, Doggweiler R, Yang CC, Whitcomb D, Mishra N, Nordling J. Interstitial Cystitis/Painful Bladder Syndrome and Associated Medical Conditions with an Emphasis on Irritable Bowel Syndrome, Fibromyalgia and Chronic Fatigue Syndrome, J Urol, 2010, 184, 1358-1363.

# Future /Present Diagnostic

## Sorting out the symptoms...



OAB, overactive bladder

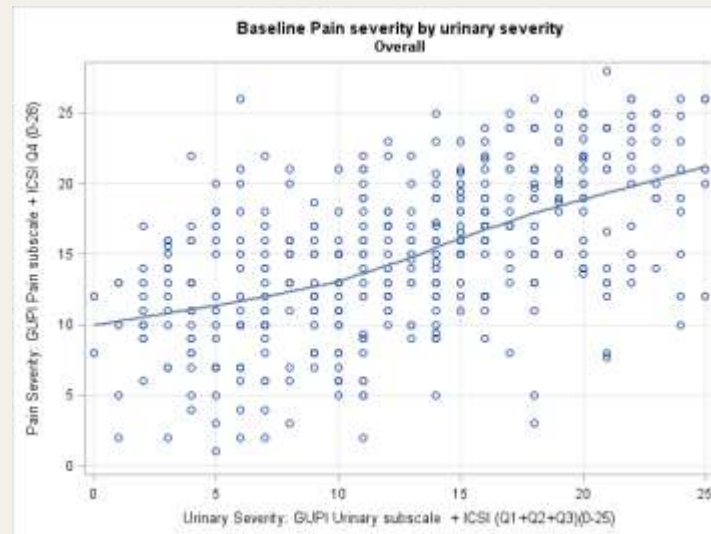
IC/BPS, interstitial cystitis/bladder pain syndrome

HTPFD, High-tone pelvic floor dysfunction

CP/CPPS, chronic prostatitis-chronic pelvic pain syndrome

# Urinary Symptoms and Pain

- Urologic Chronic Pelvic Pain Syndrome (UCPPS) patient cohort (n=424)
- Multiple frequently employed instruments for patient assessment
- Principle components analysis and factor analysis
- **Urinary symptoms** and **pain**: the two most meaningful factors to characterize and clinically follow UCPPS.
- These parameters independently correlate to comorbid conditions.



Pearson Correlation  
Coefficient = 0.56 (p value < .0001)

Griffith J, et. al. A psychometric analysis of pain and urinary symptoms in patients with interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome: findings from MAPP research network. J. Urol. 2015; 193:e303.

# The Patient Experience

“There appears to be a disconnect between what health care providers believe is important to address in treating interstitial cystitis/bladder pain syndrome and the real-world perspective of patients”

## The Biopsychosocial Approach

| Coping with and attitudes toward experience with IC/BPS       |                   |
|---|-------------------|
| Management of IC Symptoms                                     | No./Total No. (%) |
| Coping and support:   |                   |
| Ability to cope with symptoms:                                |                   |
| Excellent   | 2/28 (7.1)        |
| Good  | 19/28 (67.9)      |
| Poor  | 5/28 (17.9)       |
| Very poor   | 2/28 (7.1)        |
| Use of coping mechanisms                                      | 23/28 (82.1)      |
| Support system available                                      | 19/26 (73.1)      |
| Attitude toward IC/BPS:                                       |                   |
| Feel it controls me   | 9/32 (28.1)       |
| Have techniques/methods to cope but at times they do not work | 22/32 (68.8)      |
| At times question if this is all in my head                   | 2/32 (6.3)        |
| I do not allow it to take over my life                        | 17/32 (53.1)      |
| I have come to realize that IC is a chronic disease           | 18/32 (56.3)      |
| I am made to feel dismissed                                   | 4/32 (12.5)       |
| Other   | 3/32 (9.4)        |

Nickel JC, Tripp DA, Beiko D, et al: The Interstitial Cystitis/Bladder Pain Syndrome Clinical Picture: A Perspective from Patient Life Experience. Urology Pract 2018; 5: 286–292.



# Current (we hope) Treatment Landscape

## UPOINT

|                       | Examples of Directed Therapies  |
|-----------------------|---|
| Urinary               | Alpha-blockers, Beta-3-agonists, neuromodulation,                                 |
| Psychosocial          | Mental Health support, patient support groups                                     |
| Organ-specific        | Pentosan polysulfate, bladder instillations, hydrodistention                      |
| Infectious            | Antimicrobials  |
| Neurological/Systemic | Tricyclic antidepressants, neuroleptics, neuromodulation                          |
| Tenderness of Muscles | Skeletal muscle relaxants, specialized physical therapy, Trigger point injections |
| Sexual                | 5-PDE inhibitors, sexual counseling   |

# Future Treatment Landscape

| Bladder Centric Pain   | Centralized /Widespread Pain |
|--|------------------------------|
| Tricyclic antidepressants (TCA)                              | TCA's                        |
| Neuroleptics   | Neuroleptics                 |
| selective 5-HT and noradrenaline re-uptake inhibitors (SNRI) | SNRIs                        |
| Antihistamines   | Neuromodulation              |
| Pentosan polysulfate   | Cannabis?                    |
| Urinary anesthetics  |                              |
| Intravesical agents  |                              |
| Hydrodistention/ fulguration                                 |                              |
| Neuromodulation  |                              |
| Intratriganal Botulinum toxin A                              |                              |
| Cyclosporine   |                              |
| Urinary diversion  |                              |

# In Conclusion...

- Lots of patients, lots of suffering
- Guidelines helpful but not perfect
- Heterogeneous population (except Hunner lesion?)
- The patient experience is important!
- A phenotypic approach is best for patient care and clinical trials