

THE JOURNAL *of* UROLOGY[®]

- Peer Review Report -

Original Submission:

Reviewer #1:

This manuscript reviews a large amount of literature on the topic of flare in patients with urological chronic pelvic pain syndrome, including interstitial cystitis/bladder pain syndrome (IC/BPS) and chronic prostatitis/chronic prostatic pain syndrome (CP/CPPS). The authors reported the detail of their research, but did not make analysis of the data. Therefore, the reader might not catch the messages the authors tried to express.

- 1) I do hope the authors can put all the tables in the appendix, and briefly tabulate the data in each section to address the most important findings regarding the manifestation, factors associated with flare burden, therapy, quality of life impact, and pathophysiology related with the flare of UCPPS.
- 2) The review did not separately report flare issues of IC/BPS and CP/CPPS, if possible, in the new developed tables, please separately report the flare issues in each UCPPS.
- 3) In fact, most of the reported literature did not address the association between clinical phenotype and flare, or the treatment and flare. The authors might comment on this important point.
- 4) Although this review article is prepared in detail, there are many redundant sections. Please shorten the text and use clearly presented tables for readers to understand the content of flare in UCPPS.

Reviewer #2:

This is a review of peer reviewed literature on flares. The purpose is to add to a foundation for future empirical research.

1. Under eligibility criteria- what was the rationale for excluding studies focused exclusively on pain associated with sexual activity or urination? Although they are incorporated into some outcome measures such as GUPI, these surveys do not include all possible items, and also isn't the purpose to see what the impact of these factors are on flares?
2. Under factors associated with flare burden, the statement "Only IC/BPS symptoms (versus CP/CPPS in men)..." - men can also get symptoms of IC/BPS. These symptoms are not exclusive of each other.
3. In the discussion, bottom of page 16- the flares that last during urination only could also be from pelvic floor spasm, i.e. lack of relaxation. The pelvic floor symptoms do not necessarily last minutes long. I think this is speculative.
4. This is a lengthy review. It would helpful to end up with some recommendations based on the findings rather than just listing the findings. This could be for clinical practice, or for research methods.

Revision 1:

Reviewer #3 (Statistician):

Guidelines for Reporting of Figures and Tables for Clinical Research in Urology:
<https://www.auajournals.org/doi/10.1097/JU.0000000000001096>

Guidelines for Reporting of Statistics for Clinical Research in Urology: <https://www.auajournals.org/doi/pdf/10.1097/JU.0000000000000001>

1. "Data extraction was performed in duplicate." What does this mean?

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2. What type of random effects model are you fitting? For prevalence I would assume a generalized linear mixed model with logit link?
3. "mean/median" this is hard to interpret, maybe report the range for both means and medians separately
4. If referring to findings from a single study please make that clear throughout
5. In all tables
 - a. please present each cell as counts and percentages N (%)
 - b. Please provide SD rather than adding and subtracting it from mean
6. Appendix table 2 - I don't see this referenced anywhere in the manuscript?
7. Appendix table 3 - I am having a very hard time interpreting this table
8. Table 2 is extremely dense - consider presenting this table graphically
9. Could you provide forest plots for the larger categories in table 2 (fruits+juices, dairy, spicy food, caffeinated drinks)- this will help readers appreciate the amount of between-study variation in prevalence.

Chief Statistician comments:

In addition to the comments from the statistical reviewer, please address the following:
- See Guideline 4.1 and apply appropriate levels of precision throughout all text and tables.

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Consultants and Editors contributing to the peer review process for this article were Toby C. Chai, Maria Masotti, Michel A Pontari, D. Robert Siemens, Emily Zabor, and one anonymous reviewer.