# Conducting network meta-analysis of treatments for bladder pain syndrome in adults: benefits and challenges

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## BACKGROUND

- Bladder pain syndrome (BPS) is a poorly understood clinical condition. There is no universally accepted diagnosis and diverse causative factors have been proposed. This diversity is reflected in wide-ranging treatment options with limited evidence.
- We conducted a network meta-analysis (NMA) to evaluate the clinical effectiveness of available treatments for BPS, which have been assessed in randomised controlled trials (RCTs).
- Primary outcomes were cure or improvement of symptoms; secondary outcomes were pain, urinary frequency and nocturia.

## OBJECTIVES

- To describe the main methodological issues encountered in the conduct of the NMA for treatments of BPS.

## METHODS

### *Literature search*

- We searched the Cochrane Incontinence Specialised Register, which contains trials identified from CENTRAL, MEDLINE, MEDLINE In-Process, MEDLINE Epub Ahead of Print, ClinicalTrials.gov, WHO ICTRP and from hand searching of journals and conference proceedings (last search date: 5 June 2019). We also perused reference lists of relevant identified articles.
- No language or other restrictions were applied to the literature searches.

### *Inclusion criteria*

- RCT and quasi-RCT (alternate allocation) of treatments for BPS in adults.

### *Interventions for BPS*

All types of interventions were eligible, used either alone or in combination.
These fell into three main categories:

- Conservative (e.g. behavioural, psychological, complementary, physical).
- Pharmacological (any route of administration, e.g. oral, intravesical, subcutaneous).
- Surgical (e.g. injection, hydrodistension).

### *Analysis*

- Random effects NMA models were fitted using WinBUGS 1.4.
- The results for each treatment versus control were compared with direct evidence from pairwise meta-analyses (PMA).

## RESULTS

- We included 81 RCTs with a median of 38 participants (range 10 to 369). There were 65 different active treatments which were grouped into 31 treatment categories by mode of action.
- Overall, credible intervals (CrIs) from the NMA excluded the null value for six (proportion cured/improved), one (pain), one (frequency) and zero (nocturia) treatment categories, respectively.
- Certainty of evidence (GRADE) was mainly defined as very low, but occasionally low or moderate.
- Figures 1 and 2 show the network diagram and results of the NMA and PMA meta-analyses, respectively, for the proportion of people cured or improved.

### *Benefits and challenges of NMA*

- NMA was successfully conducted for both binary and continuous outcomes.
- The NMA approach can incorporate data from multi-arm studies and a mixture of change score and final score data for continuous outcomes (Dias 2011).
- Due to the heterogeneity in treatment and outcome definitions, a large amount of work was required to prepare the data in a suitable format.
- Is it sensible to "cancel" treatments from "A+B vs A" to "B vs control" if treatment A is a standard intervention that most patients would get anyway? A possible alternative is to conduct a component NMA (Freeman 2018).
- For most outcomes, the network was almost "star-shaped" (most trials compared an active treatment against control). The benefit of NMA may be relatively low in these situations.
- Multiple small trials meant that CrIs from NMA were often very wide.
- NMA and PMA results were similar but CrIs from NMA were often wider than CIs from PMA because of the star-shaped network, contrary to what might be expected with a well-connected network.
- We used the CINeMA approach (CINeMA 2017) to inform GRADE.
- There is a lack of guidance on the best way to report NMAs within a Cochrane review.

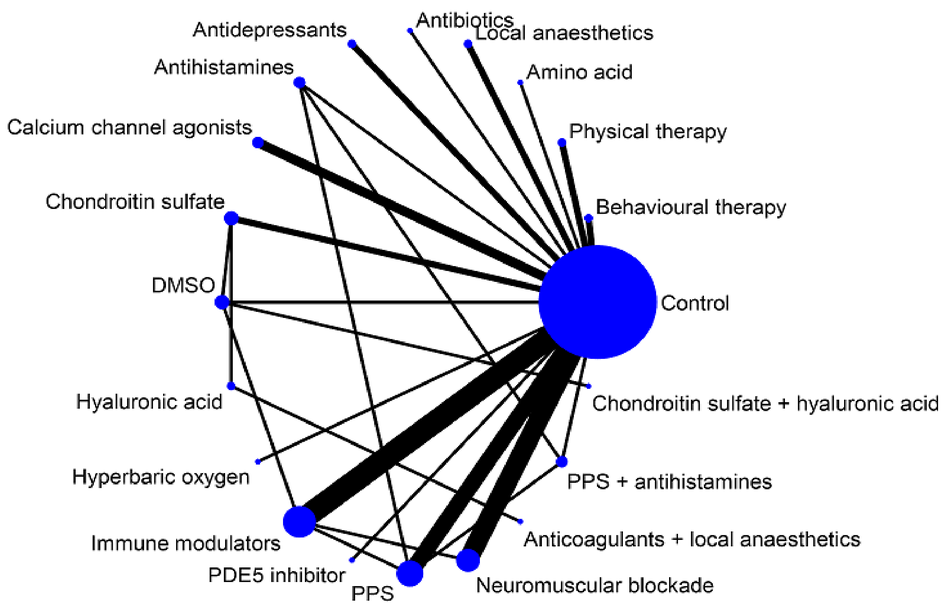
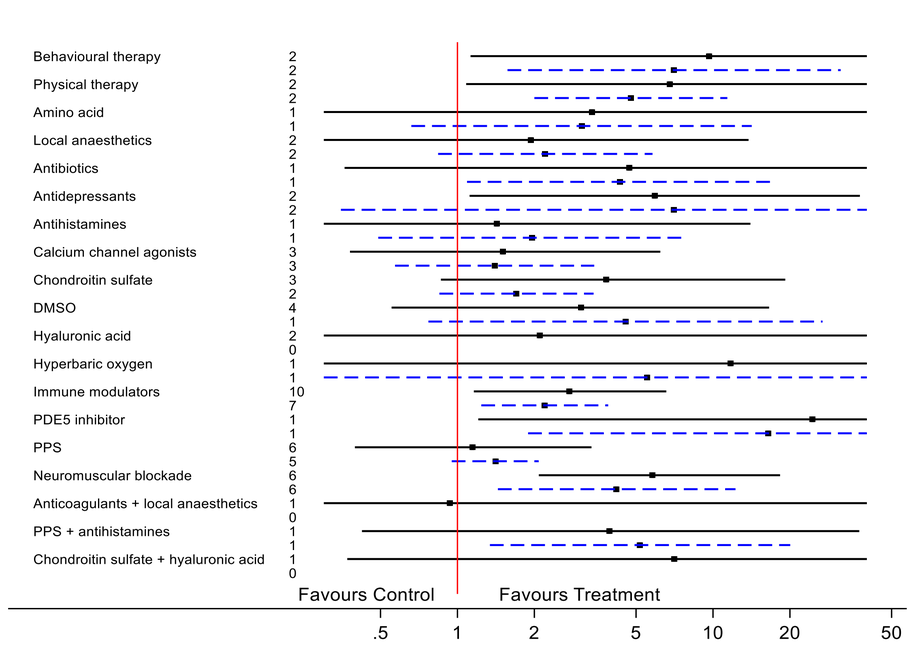



**Figure 1 Network diagram for proportion cured/improved**




For each treatment category the unbroken horizontal line represents the odds ratio (95% CrI) versus control from the NMA and the dotted line represents the odds ratio (95% CI) versus control from the PMA (if applicable). The number of studies included in each analysis is also shown.

**Figure 2 NMA/PMA Results for proportion cured/improved**

## CONCLUSIONS

- A NMA approach can be used successfully in a large complex systematic review with wide variation in treatment and outcome definitions; however, it is time-consuming and its added benefit over PMA may be relatively small especially in the presence of star-shaped networks.
- In our NMA, the small sample size of included studies hindered the interpretation of the results. Larger, more robust trials are needed to address this clinical problem.

## REFERENCES

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