Research Review Disposition of Peer and Public Comments

Research Review Title:
Nonsurgical Treatments for Urinary Incontinence in Adult Women: A Systematic Review Update

Draft review available for public comment from December 20, 2017 to February 10, 2018.

Research Review Citation: Balk E, Adam GP, Kimmel H, Rofeberg V, Saeed I, Jeppson P, Trikalinos T. Nonsurgical Treatments for Urinary Incontinence in Women: A Systematic Review Update. Comparative Effectiveness Review No. 212. (Prepared by the Brown Evidence-based Practice Center under Contract No. 290-2015-00002-I for AHRQ and PCORI.) AHRQ Publication No. 18-EHC016-EF. PCORI Publication No. 2018-SR-03. Rockville, MD: Agency for Healthcare Research and Quality; August 2018. Posted final reports are located on the Effective Health Care Program search page. https://doi.org/10.23970/AHRQEPCCER212.

Response to Peer and Public Comments on this Research Review

The Evidence-based Practice Center (EPC) Program encourages the public to participate in the development of its research projects. A draft form of each research review is posted to the AHRQ Web site for public comment. Comments can be submitted via the Web site, mail or email. At the conclusion of the 3-4-week public comment period, authors use these comments to revise the draft research review.

In addition to public comments, each draft research review is independently evaluated by peer reviewers before it is finalized. Because they are chosen for their expertise in the subject matter and research methods, and freedom from conflict of interest, peer reviewers help to assure that the final report is accurate and free from bias.

The table below includes the original comments by peer reviewers and the public, as well as the authors' response for each comment that was submitted for the draft research review. Comments are not edited for spelling, grammar, or other content errors. Each public comment is listed with the name and affiliation of the commentator, if this information is provided. Peer reviewers are listed by number. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the AHRQ.

Research Review Section	Reviewer	Comment	Response
Introduction	Peer Reviewer #2	IIne 20 --Really don't understand the categories. To implant the battery for interstim You have to make a 5 cm incision. TO implant a midurethral sling you make a 1 cm incision. Why is the former considered nonsurgical and the latter surgical? Interstim should be considered a surgical therapy.	We agree that some of the categorizations of interventions is somewhat arbitrary, but decisions had to be made. We acknowledge this in the Methods. Clearly Interstim, other neuromodulators, onabotulinum toxin, and periurethral bulking require incisions or injections, but since the surgery and for most of these the mainteneance is nonsurgical, we have maintained them as nonsurgical interventions. We believe these are mostly similar to pacemakers, which are commonly deemed to be nonsurgical interventions (eg, compared with ablation surgery) despite their surgical implantation.
Introduction	Peer Reviewer #3	No problems	Thank you
Introduction	Peer Reviewer #4	The introduction is appropriate and justifies the need for the updated review.	Thank you
Introduction	Peer Reviewer #6	No major criticism of the Intro-overall informative and lays the groundwork for the Results.	Thank you
Methods	Peer Reviewer #1	Data: First, the authors' effort to conduct this update and include many appendix tables (which are very informative to understand the literature search strategy, study selection, design details etc. are highly applauded.	Thank you
Methods	Peer Reviewer #1	Second, as this update basically deal with multiple interventions (i.e., 51 specific interventions and 14 categories of	We have added an appendix with the technical description of the NMA

Research Review Section	Reviewer	Comment	Response
		interventions) and multiple outcomes (UI outcomes, QoL and adverse events) --- which is an area with active statistical methodology research, a Table with the final raw data with final computer code used in the analysis is suggested for three reasons: 1) to facilitate future update (particularly if done by other groups); 2) to enhance reproducibility; and 3) to facilitate alternative statistical methods development. For example the 2013 AHRQ report on A Bayesian Missing Data Framework for Multiple Continuous Outcome Mixed Treatment Comparisons give a good example.	
Methods	Peer Reviewer #1	Statistical Methods: as indicated in the above, the statistical methods for network meta-analysis with multiple outcomes is an active research area, there are two main approaches: arm-based (AB) and contrast-based (CB) approaches. In addition, there are Bayesian and frequentist procedures to estimate the AB and CB network meta-analysis models. It would be great, if the authors can provide appendix with the specific statistical models used and computer code implemented, with appropriate	We did not perform a joint NMA for multiple outcomes. This is now clearly described in the methodological appendix that describes the analysis. We added in the text of the methods section of the report that "Analyses were performed separately for each outcome."

Research Review Section	Reviewer	Comment	Response
		references. Did the authors analyze the outcome variables separately or jointly?	
Methods	Peer Reviewer #1	As the report has presented both relative effect size in terms of odds ratio, and absolute effects size in terms of the mean and forecasted improvement rates (it is not clear how they are estimated), it seems that the authors might have considered both approaches, but it is unclear which approaches have been implemented. Furthermore, assumptions and limitations need to be discussed for the specific methods implemented (e.g., if a CB approach is used, do the authors make homogeneous or heterogeneous variance assumption?). If a Bayesian approach is implemented, are the authors interested in the probabilities for being the best or top X treatments? Are the authors interested in combing different interventions and categories of interventions? Have the authors considered network meta-regression to adjust the difference in study population and followup times etc.? Are the results from high versus low quality studies different?	Too detailed for report, but described in full in the new appendix.
Methods	Peer Reviewer #1	As it is unclear which specific network meta-analysis method was used and how it is	Too detailed for report, but described in full in the new appendix.

Research Review Section	Reviewer	Comment	Response
		implemented, it is difficult to assess whether the methods used are appropriate. So I answered "no" to most questions related to methods, consistency/inconsistency etc. However, I suspect that the methods used might be appropriate, but I am not sure.	
Methods	Peer Reviewer #2	See comments above about inclusion and exclusion. IS PTNS = TENS?	Tes, PTNS is a form of TENS
Methods	Peer Reviewer #3	Inclusions and exclusions are fine.	Thank you
Methods	Peer Reviewer #3	I prefer to see definitions of 'meaningful clinical differences' discussed when outcomes are measured in scales. Statistical differences may have little to no impact on patient perceptions. I saw no discussion of this in any table.	We agree with the concept of MCID, particularly for clinicians. However, in practice we have found, as is the case for UI in women, that there is little to no good evidence or concensus about what an MCID means. Furthermore, it can be highly heterogeneous differing for each individual outcome and scale. For death, a reasonable MCID would be 0. For "cure", improvement, and satisfaction, there is no evidence to suggest what policymakers, clinicians, or patients would be consider to be an adequate response. Nevertheless, we have taken three major approaches: 1) for all UI outcomes, we consider all statistically signficant differences to be important. 2) We highlight likely differences based on a not statistically significant OR of at least 2.0 where the lower bound of the 95% CI is >=0.8. This is somewhat equivalent to an MCID of 20-25% (4/5 or 5/4). 3) For quality of life we maintained using conclusions based on what was reported in the studies, which for the most part was simple statistical significance. While this might not be

Research Review Section	Reviewer	Comment	Response
			ideal, for practical purposes it would be very resource- and time-intensive to find evidence for MCIDs for all QoL measures used, find consensus among stakeholders for those without evidence, and then implement those uniformly.
Methods	Peer Reviewer #3	On the other hand, I did like the grouping of results into "cure", "Improvement" and "satisfaction". I would have appreciated more mention of the challenges in even these parameters, and perhaps more discussion in the methods of how results were sorted into these categories. For instance, in neither the exec summary or the report itself is this issue discussed.	We have added cure, improvement, and satisfaction more explicitly into the PICOTS table.
Methods	Peer Reviewer #4	The inclusion and exclusion criteria are clearly stated and justifiable. In the appendix, the reasons for that individual studies were excluded are presented in table format. An overview of the search strategy was presented in review and the detailed strategies for each database are in the appendix. The authors defined their outcomes of cure or improvement in UI. I believe that the other outcomes- satisfaction, quality of life, and adverse events - were also adequately defined and operationalized based on the review.The addition of network meta-analysis to compare interventions not	Thank you

Research Review Section	Reviewer	Comment	Response
		directly compared in the included studies is, in my opinion, a positive addition to this update.	
Methods	Peer Reviewer #4	In the methods section of the full report, there are two sections that I think need some clarification(the page numbers listed correspond to the numbers in the upper left corner of each page): - Page 44, lines 41-44: The examples (D1 and D2) used to explain evidence graphs do not actually appear in the graph in Figure 2 (referred to in the sentence). I recommend using differ nodes that appear in the graph to help readers understand how to interpret these graphs. Will the use of "shading" to describe the graphs be confusing to readers when there is no shading in the graphs? The only evidence graph where I saw shading was Figure 5.	We have updated the figures and the text regarding them. We swapped out the example figure but didn't update the text. The text and figures now align. We have also replaced shading with colored bubbles.
Methods	Peer Reviewer #4	Page 46, lines 44-48: I think this explanation of shading could be confusing to some readers. The authors state that, "The cell shading indicates whether there were direct (head-to-head) comparisons of the row and column interventions among the eligible trials. Grey shading indicates that the estimate of OR is derived from indirect evidence (i.e., that no trials directly compared	Thank you. We have reworded for better clarity.

Research Review Section	Reviewer	Comment	Response
		the interventions)." I think readers will typically think of shading as some cell color other that white. I would consider saying something like, "Cell shading was used to differentiation between comparisons based on direct (head-to-head) comparisons of the row and column interventions in eligible trials from comparisons based on indirect evidence. Cells with no shading report the results from direct comparisons of the intervention categories while grey shading indicates that the estimate of OR is derived from indirect evidence (i.e., that no trials directly compared the interventions)."	
Methods	Peer Reviewer #6	The Methods were well described and understandable. Not sure why pessaries were not included (device) when vaginal cones were included.As noted above, phenylpropanolamine should be under alpha agonist. Inclusion/exclusion criteria well described. Search strategies and definitions well described. Statistical methods seemed robust.	We have clarified that pessaries are a form of bladder support. As noted in response to the comment specific to phenylpropanoloamine, we have kept this as an anticholinergic. Thank you for your other comments.
Results	Peer Reviewer #1	Evidence graphs: the author should consider using standard network metaanalysis plots, which use node size and line width to refer the number of subjects and trials etc.	We determined the "standard" approach (with edges and nodes proportionate in size to numbers of stkudies and their sample sizes) would be too difficult to read and would make

Research Review Section	Reviewer	Comment	Response
			the organzation of each plot unique. Our approach is cleaner and allows standard placemt of all interventions.
Results	Peer Reviewer #1	Presentation of the assessment of risk of bias: the authors might consider using a heatmap type graph to present the results of each item of the risk of bias assessment tool for each trial (if different outcomes have different assessment scores, can consider separate heatmaps).	Thank you for this suggestion. We have added more graphical representations of the risk of bias across studies.
Results	Peer Reviewer #2	I think the evidence graphs are helpful.	Thank you
Results	Peer Reviewer #3	I found a consistent problem of reporting results that were not statistically significant. For example, on page ES-5, three bullets include information that treatments that produced statistically insignificant results were 'better' than other treatments. This is inappropriate in an evidence review. "Better" by what criteria? You have already defined statistical significance levels, which these treatments did not meet. Nothing further should be said.	We respectfully disagree that the review's findings and summaries should be dictated by statistical significance. The lack of significance often relates more to power as opposed to lack of difference. The choice of a P value of 0.05 is standard, but arbitrary. We have added a description of our criteria for describing NS findings as possible a difference between intervention OR >=2.0 with a minimum lower bound of the 95% CI of 0.8).
Results	Peer Reviewer #3	Similarly, on ES 17, the authors state that there is insignificant evidence to report on subgroups, then proceed to do just that. Nothing further should be said in an evidence review paper.	We respectfully disagree. As noted by other reviewers, there is a strong interest in understanding the evidence pertinent to specific populations based on UI type (urge vs. stress). We believe this is important information to highlight, even if the evidence is not fully adequate to make strong statements.

Research Review Section	Reviewer	Comment	Response
Results	Peer Reviewer #4	In my opinion, the amount of detail presented in the results section was appropriate and is supplemented by the tables of studies in the appendices. Figures and tables in the body of the review are clear and summarize the results. I am unaware of any additional studies that should have been included and it appears that studies that were include met the stated eligibility criteria.	Thank you
Results	Peer Reviewer #4	In the results section of the Evidence Summary or the full report, there are a couple of areas that need clarification/editing (the page numbers listed correspond to the numbers in the upper left corner of each page): - On page 13, lines 34-39, (Evidence Summary) the authors state that, "In surveys and focus groups, people with UI generally ranked adverse events among important outcomes, in contrast with clinicians." Were these focus groups and surveys part of the review process or were they conducted as part of other studies? I recommend clarifying the source of this information and adding references if this came from other studies. In the next sentence in this section, the authors state that, "In one study in particular,	We have clarified that the surveys and focus groups were conducted by the studies we summarize. We did not do any new surveys or focus groups. As per AHRQ format, we do not reference the reviewed studies in the Evidence Summary. The references are in the main report.

Research Review Section	Reviewer	Comment	Response
		women……." There should be a reference for the study.	
Results	Peer Reviewer #4	Page 16, lines 6-9 (in Evidence Summary): I found this section unclear. In the first sentence, the authors seem to state that most studies examining interventions is women with only stress UI and those that focused exclusively on women with urge UI examined different interventions. In the next sentence, however, they state that both sets of studies evaluated behavioral therapy and/or neuromodulation. These two sentences seem to contradict each other.	We've clarified the language. We meant "However" they both evaluated behavioral therapy and neuromodulation.
Results	Peer Reviewer #4	Page 109, lines 35-37: The reader is referred back to Table 7. The table presenting these results is Table 8 not Table 7. On page 110, lines 19-21 the reader is also referred to an earlier table of results, "Table 10". The results referred to are reported in Table 11 not table 10. Renumbering of tables is common during the revision process and I would recommend checking all table referred to in the text to make sure they refer to the correct table.	Thank you for noting this error. We have renumbered tables and confirmed text.
Results	Peer Reviewer #6	As noted above, perhaps as a personal preference, I would have liked to see the results presented with respect to UI type.	Given the poor state of the evidence in terms of whether studied women with urgency or stress (or mixed) UI, we have maintained as our preliminary analyses all studies and

Research Review Section	Reviewer	Comment	Response
			all interventions. However, we have added better sections of subgroup analyses regarding urge vs. stress, which in part separates out interventions commonly used only for urgency or only for stress UI. The Evidence Summary and the specific sections for KQ 1 to KQ 4 now focus more on four groups of analyses: Stress UI 1st and 2nd line vs 1st and 2nd line comparisons, Stress UI 3rd line vs. 3rd line comparisons; Urgency UI 1st and 2nd line vs 1st and 2nd line comparisons, Urgency UI 3rd line vs. 3rd line comparisons
Results	Peer Reviewer #6	There were no concerns regarding key messages and the figures, tables and appendices were well presented.	Thank you
Results	Peer Reviewer #6	One outcome that is reflected in the literature more than cure, is 50% reduction in measured outcome ie incontinence episodes, urgency, frequency and that was not explored here.	This outcome is included as improvement.
Results	Peer Reviewer #6	Conclusions made clinical sense.	Thank you
Discussion and Conclusions	Peer Reviewer #2	Yes , Future research needs to look at subpopulations - Urgency incontinence and Stress incontinence.	Thank you. We have expanded our discussion about the need for cleaner subpopulation studies in the Future Research section.
Discussion and Conclusions	Peer Reviewer #3	I found the inclusion of guideline information from the Am Urol Society on anticholinergic medications inappropriate in an evidence review. This document should not be a	We believe that this is an important statement on anticholinergics to include in the Discussion. The language makes clear that a) we are summarizing an existing recommendation, not providing guidance; and b) the body of literature from which the concerns is drawn looks at the use

Research Review Section	Reviewer	Comment	Response
		guideline statement itself, but rather a review of literature. (Page ES 17)	of anticholinergics for purposes other than the treatment of UI. We have added some language to suggest that we quote the guideline only as a point of information.
Discussion and Conclusions	Peer Reviewer #3	I feel the lines on ES-16 that BTX is more effective than behavioral treatment for cure and improvement is not supported by their data. BTX is better than other pharmacologic treatments, not better than behavioral Stated as in current draft, this could represent an author bias.	We agree that this is not the best choice of comparisons to make the point about patient preferences. We chose the two because they were at the opposite ends of the spectrum regarding invasiveness. Also we chose BTX for this example based on what we had read in regards to the Contextual Question. We have changed the example to BTX vs. anticholinergics.
Discussion and Conclusions	Peer Reviewer #4	The major findings are summarized clearly. The limitations of the review are clearly reported and there are recommendations for future research.	Thank you
Discussion and Conclusions	Peer Reviewer #6	The Conclusions and Limitations are well presented, but just as in the Cochrane review, perhaps a more "lay" oriented or a "clinician not involved in research" summary should be considered.	We have a Key Messages box which gives a very brief lay summary.
Clarity and Usability	Peer Reviewer #2	I really think this needs to be 2 reports. One on Urgency incontinence and the other on Stress urinary incontinence.Urgency incontinence is a bladder broblem. Stress incontinence is a urethral problem. It makes no biological sense to combine them. As it stands the conclusions are not helpful. Patients who get interstim, botox , or	We agree that it would be ideal to cleanly separate stress from urge UI, and also to evaluate mixed incontinence separately. Unfortunately, as we believe the report makes clear, the published studies have not separated these populations cleanly so we are unable to do so. We have, however, more clearly discussed the evidence pertinent to the specific populations, as subanalyses.

Research Review Section	Reviewer	Comment	Response
		periurethral injections are severe patients who have already failed conservative treatment. It makes no sense to say add behavioral therapy to that treatment.	
Clarity and Usability	Peer Reviewer #3	I liked the inclusion of information on patient preferences, and the documentation of differences between patients and researchers in outcome preference.	Thank you
Clarity and Usability	Peer Reviewer #3	I found the language clear.	Thank you
Clarity and Usability	Peer Reviewer #4	I believe that the report is well structured and that main points are clearly organized. Detailed materials are presented in the appendices to supplement and expand on what is included in the report. The conclusions are relevant to practice and to research.	Thank you
Clarity and Usability	Peer Reviewer #6	I think that I noted some overall thoughts addressing this section above. Readers may wish the content in the context of UI type and mixed UI addressed.	We now more clearly discuss findings related specifically to urgency, stress, and mixed UI.
Clarity and Usability	Peer Reviewer #6	Urge incontinence should be referred to as "urgency" incontinence.	We agree and have made the change throughout the report.
Clarity and Usability	Peer Reviewer #6	A summary directed toward interested parties that are not active in research.	We have a Key Messages box which gives a very brief lay summary.

Research Review Section	Reviewer	Comment	Response
Clarity and Usability	Peer Reviewer #6	Overall the Conclusions are relevant to policy and practice and the main points reasonably clearly written	Thank you
General comments	Peer Reviewer #1	First, I would like to congratulate the authors for their extensive and thorough work on this systematic review update. The update has addressed several important evidence gaps on the evaluation of UI outcomes, quality of life and adverse events	Thank you
General comments	Peer Reviewer #1	Title: as the report has included extensive (network) meta-analyses, it might be better to call it "nonsurgical treatments for urinary incontinence in adult women: a systematic review and network meta-analysis update".	To maintain consistency across AHRQ and PCORI-sponsored reviews, we have maintained the title. The NMA is part of the systematic review process.
General comments	Peer Reviewer #2	It is just not a very helpful report, mostly because it lumps stress and urge incontinence together and tries to compare third line therapies with first line therapies.	Given the poor state of the evidence in terms of whether studied women with urgency or stress (or mixed) UI, we have maintained as our preliminary analyses all studies and all interventions. However, we have added better sections of subgroup analyses regarding urge vs. stress, which in part separates out interventions commonly used only for urgency or only for stress UI. The Evidence Summary and the specific sections for KQ 1 to KQ 4 now focus more on four groups of analyses: Stress UI 1st and 2nd line vs 1st and 2nd line comparisons, Stress UI 3rd line vs. 3rd line comparisons; Urgency UI 1st and 2nd line vs 1st and 2nd line comparisons, Urgency UI 3rd line vs. 3rd line comparisons

Research Review Section	Reviewer	Comment	Response
General comments	Peer Reviewer #2	It is not clear what neuromodulation is. In table b in includes Interstim, but then in the next line when they compare neuromodulation and behavioral therapy, Interstim is not included. What is TENS? We don't even use TENS. We use percutaneous (PTNS) not transcutaneous stimulation. .So the Key Question conclusions are dumb.	Interstim not studied in combination with behavioral; therefore, this combination is not shown in Table B which lists "Interventions evaluated by eligible studies" . PTNS is a form of TENS. The term is used in the literature. We have clarified that it includes transvaginal, surface, and related electric stimulation. Neuromodulation is now defined in the Methods section.
General comments	Peer Reviewer #2	#1- You don't add behavioral therapy to neuromodulation. Everyone who gets neuromodulation should have have already failed behavioral therapy.	This statement may be true in clinical practice, but the studies comparing the combination to another treatment did not have both (or either) behavioral therapy and neuromodulation in the compartor arms.
General comments	Peer Reviewer #2	#2. - WHy are you comparing Botox (an urge incontinence treatment) to alpha agonists, hormomes and periurethral bulking agents which are all SUI treatments. These are 2 non-overlapping patient groups.	Given the poor state of the evidence in terms of whether studied women with urgency or stress (or mixed) UI, we have maintained as our preliminary analyses all studies and all interventions. However, we have added better sections of subgroup analyses regarding urge vs. stress, which in part separates out interventions commonly used only for urgency or only for stress UI. The Evidence Summary and the specific sections for KQ 1 to KQ 4 now focus more on four groups of analyses: Stress UI 1st and 2nd line vs 1st and 2nd line comparisons, Stress UI 3rd line vs. 3rd line comparisons; Urgency UI 1st and 2nd line vs 1st and 2nd line comparisons, Urgency UI 3rd line vs. 3rd line comparisons
General comments	Peer Reviewer #2	#3 Again why are you comparing urge incontinence treaments with alpha agonists.	Given the poor state of the evidence in terms of whether studied women with urgency or stress (or mixed) UI, we

Research Review Section	Reviewer	Comment	Response
			have maintained as our preliminary analyses all studies and all interventions. However, we have added better sections of subgroup analyses regarding urge vs. stress, which in part separates out interventions commonly used only for urgency or only for stress UI. The Evidence Summary and the specific sections for KQ 1 to KQ 4 now focus more on four groups of analyses: Stress UI 1st and 2nd line vs 1st and 2nd line comparisons, Stress UI 3rd line vs. 3rd line comparisons; Urgency UI 1st and 2nd line vs 1st and 2nd line comparisons, Urgency UI 3rd line vs. 3rd line comparisons
General comments	Peer Reviewer #2	#4 A lot of patients who get behavioral therapy will have satisfaction (but not cure or improvement). THey receive a lot of attention.	Our findings regarding behavioral therapy are based on the comparisons of this intervention with others. There is evidence regarding cure, improvement, and satisfaction. In theory, at least, the satisfaction patients garner from the attention they get should cancel out. If they are more satisfied because of more attention from behavioral therapies, then this is a good outcome of the intervention, regardless of its cause.
General comments	Peer Reviewer #2	This report is very behavioral therapy biased.	We respectfully disagree. Behavioral therapy was extracted, analyzed, and summarized equivalently to all other interventions.
General comments	Peer Reviewer #3	Urinary Incontinence is an import and overlooked area of primary care practice. This review updates and expands the evidence available to guide practice.	Thank you

Research Review Section	Reviewer	Comment	Response
General comments	Peer Reviewer #3	The target population and audience are well defined.	Thank you
General comments	Peer Reviewer #3	The key questions are comprehensive and clear.	Thank you
General comments	Peer Reviewer #3	Limiting the review to non surgical treatments is a fair limitation of scope, as most of the techniques discussed are office based. Some (botox injections) are not routinely available in primary care.	Thank you
General comments	Peer Reviewer #4	This updated review will be a valuable contribution to current knowledge about the non-surgical treatment of urinary incontinence in adult women. It will be a helpful resource for both clinicians and researchers. The key questions are appropriate and explicitly stated.	Thank you
General comments	Peer Reviewer #5	The authors are to be congratulated on a well conducted review of this very complex literature. That said, I doubt this research will have any impact on clinical care. The nonsurgical treatments included have different risk benefit profiles. While all subjects may have had similar measures for UI, women choosing to participate in each study may have been quite different making comparison across studies even more challenging.	Thank you. However, we remain more optimistic about the value of the report, particularly if it gets used by policymaking organizations.

Research Review Section	Reviewer	Comment	Response
		Women who elect to participate in a pelvic floor muscle exercise study may be fundamentally different from women who choose to participate study of botulinum toxin or women who elect placement of an Interstim for neuromodulation.	
General comments	Peer Reviewer #5	I think the authors did a great job of bring contextual issues forward: women have different goals than clinicians and preferences for treatment approach may have impacts that are not measured. From my perspective this was the most interesting part of the report.	Thank you
General comments	Peer Reviewer #5	The pragmatic approach as outlined in the discussion will be hard to displace from clinical practice no matter what the efficacy data shows. This is a condition where the women's willingness to engage in a therapy overrides efficacy. The efficacy data for a drug for urgency incontinence may be quite good but this doesn't matter if the woman does not want to take a pill for her bladder problem. Pelvic floor muscle exercises may be quite effective but many are not willing to do them. The pragmatic approach is start with the least invasive treatment the women is willing to try and work from there. For some women "shot gun" approaches work –	We are hopeful that this review will provide additional evidence to help clinicians and their patients make the most appropriate choices for each woman.

Research Review Section	Reviewer	Comment	Response
		multiple behavioral strategies and drug to demonstrate success and then let her decide what she is willing to do long term. For some women, the impact is so severe and their willingness/ability to engage in less invasive treatment is so limited that you are just wasting time recommending the least "invasive" option because she is not going to engage with it.	
General comments	Peer Reviewer #5	I would not recommend repeating this exercise in another few years, even if another nonsurgical treatment becomes available. Future efficacy studies need to not only assess efficacy but measure a broader array of factors that might help identify responders to each of the therapies.	A next update will be a decision for a future date. It is reasonable to think that a future update will have similar conclusions unless better research studies become available.
General comments	Peer Reviewer #6	In general, the rationale and Methods utilized are well-explained. With regard to the Results, I would have liked them presented in the context of UI subtype. That is, results for UUI, SUI and mixed UI-in fact, the treatment of mixed UI was not addressed and should be	Unfortunately, no study reported specifically on mixed UI. We have stated this more clearly and that, thus, we cannot make specific conclusions for this population. We have better emphasized the comparisons of the different interventions for UUI and SUI.
General comments	Peer Reviewer #6	Target populations are well outlined and the KQs are well written.	Thank you
General comments	Peer Reviewer #6	The more accepted way to characterize urge incontinence is now "urgency" incontinence and that should be included here.	We agree and have made the change throughout the report.

Research Review Section	Reviewer	Comment	Response
General comments	Peer Reviewer #6	Although clinically meaningful, unless the reader is a researcher, the general clinician would find this intimidating to tackle and go through.	Certainly the full report is aimed more at a dedicated reader, but we believe the Executive Summary is easily accessible by the interested clinician.
General comments	Peer Reviewer #6	In the structured abstract, the table lists phenylpropanolamine as an anticholinergic-it is actually a fairly potent alpha and beta adrenergic agonist. Not sure if classifying as such would impact on any of the outcomes as is not generally available.	Although originally thought to act as a direct adrenergic agonist, it has been shown to have only a weak affinity for these receptors. It acts as an indirect sympathomimetic. We have not changed the category of this drug.
General comments	Peer Reviewer #6	The topography/evidence graphs were quite interesting.	Thank you
General comments	Public Reviewer #1 Gwendolyn Hooper, Society of Urologic Nurses and Associates	Overall, a good generalized review of Non-surgical Treatments for Urinary Incontinence in Adult Women.	Thank you
General comments	Public Reviewer #1 Gwendolyn Hooper, Society of Urologic Nurses and Associates	It would be wise to mention in the key messages section that there does exist certain contraindications with neuromodulation. Safety and efficacy have not been determined for various patient populations such as pregnant women and patients with neurological conditions. Some patients may not be candidates for this non-surgical treatment.	We considered implementing this suggestion but this concern is true for several of the pharmacological interentions also. We discuss the safety concerns about anticholinergics; however, the concerns are about a subpopulation of interest to the review. The concerns for neuromodulation are for pregnant women and those with neurological conditions, the two populations who were excluded from analysis.

Research Review Section	Reviewer	Comment	Response
General comments	Public Reviewer #2 Emily Lukacz	I find it rather confusing to be lumping SUI and UUI therapies together given mechanism of disease and treatment are vary very different....I am strongly opposed to publishing this as a systematic review in it's current format. Need to separate out treatments for SUI vs. UUI and be sure that the severity of the populations is taken into consideration	Given the poor state of the evidence in terms of whether studied women with urgency or stress (or mixed) UI, we have maintained as our preliminary analyses all studies and all interventions. However, we have added better sections of subgroup analyses regarding urge vs. stress, which in part separates out interventions commonly used only for urgency or only for stress UI. The Evidence Summary and the specific sections for KQ 1 to KQ 4 now focus more on four groups of analyses: Stress UI 1st and 2nd line vs 1st and 2nd line comparisons, Stress UI 3rd line vs. 3rd line comparisons; Urgency UI 1st and 2nd line vs 1st and 2nd line comparisons, Urgency UI 3rd line vs. 3rd line comparisons
General comments	Public Reviewer #2 Emily Lukacz	It is also not clear why you would consider interstim as “non-surgical.” This IS a surgical procedure (although minimally invasive, it would be comparable to midurethral sling with that respect). I don’t think the population that get’s interstim OR botox is comparable to other non surgical therapies, thus outcomes can’t be fairly compared (except for ABC trial). Urethral bulking is also for much more severe population and would never be used as first line therapy.	We acknowledge that there is diagreement about which interventions are pharmacological, nonpharmacological, and surgical or nonsurgical. We have added a statement to the Methods about this. We categorized InterStim as nonsurgical for the same reason a pacemaker would be considered nonsurgical (compared with surgical ablation). BTX is clearly a nonsurgical intervention, even though it is injected. We do not claim that periurethral bulking would be used as first line therapy.
General comments	Public Reviewer #3 Alex Gomelsky, Society of	On behalf of the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU), we applaud the	Thank you

Research Review Section	Reviewer	Comment	Response
	Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	Agency for Healthcare Research and Quality for their outstanding systematic review of nonsurgical treatments for female urinary incontinence. This is a worthwhile effort and dovetails beautifully with the goals and mission statements of our society. As female urinary incontinence is a prevalent, bothersome, and costly problem, any systematic evaluation of the existing literature is not only welcome, but necessary.	
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	We would like to contribute some comments regarding the study design, and the grouping and inclusion of some of the treatment options. 1) In the alpha-agonist category, midodrine is not FDA-approved for urinary incontinence.	As typical for most systematic review approach, we did not consider FDA approval, per se. The drug has been studied in and is used for this population.
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	2) Duloxetine is a selective neurotransmitter reuptake inhibitor for serotonin, norepinephrine, and dopamine, and is not technically an alpha-agonist.	It is correct that duloxetine is an SNRI and acts in this way for depression. However, it is the alpha agonist mechanism of action that affects the bladder. We have not changed the categorization.

Research Review Section	Reviewer	Comment	Response
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	3) Duloxetine did not gain FDA approval in the U.S. for UI, and several European practice guidelines and systematic reviews have cited SUI improvement with duloxetine, but have cautioned against its use as a first-line treatment. Furthermore, adverse events (nausea and emesis) may exceed 80% and, hence, discontinuation rates are high	We have not added in a specific discussion of duloxetine in the Discussion. While it is true that clinical practice guidelines do not recommend against it for first line therapy, there are not general recommendations to avoid its use. We present the evidence regarding its relative effectiveness and adverse events.
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	4) Pregabalin is, likewise, not FDA approved for UI	As typical for most systematic review approach, we did not consider FDA approval, per se. The drug has been studied in and is used for this population.
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	5) TENS units are not typically used for UI.	TENS has been evaluated by numerous studies. We have clarified that it includes transvaginal, surface, and related electric stimulation.
General comments	Public Reviewer #3 Alex Gomelsky, Society of	6) The grouping of onabotulinumtoxinA (BTX) in the medication category is surprising, since this is actually more like a non-	We acknowledge that there is diagreement about which interventions are pharmacological, nonpharmacological, and surgical or nonsurgical. We have added a statement to the

Research Review Section	Reviewer	Comment	Response
	Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	pharmacological intervention. With the exception of periurethral bulking (another non-pharmacological intervention, in our opinion), the other pharmacological treatments are all administered orally or transdermally.	Methods about this. Although it is reasonable to consider these separately then oral medications, they are not behavioral interventions or devices, and we chose not to create a third in-between category.
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	7) In the same vein, sacral neuromodulation (SNM) is a surgical procedure, and, theoretically, doesn't fit into the definition of "non-surgical" treatments evaluated in this review.	We acknowledge that there is diagreement about which interventions are pharmacological, nonpharmacological, and surgical or nonsurgical. We have added a statement to the Methods about this. We categorized sacral neuromodulation as nonsurgical for the same reason a pacemaker would be considered nonsurgical (compared with surgical ablation).
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	Key Question 1: Addition of behavioral therapy to neuromodulation resulted in better rates of improvement than neuromodulation alone (moderate SoE). This conclusion highlights the findings of AUA OAB Guidelines (Updated 2014), which state that behavioral intervention such as bladder training, bladder control strategies, pelvic floor muscle training (PFMT), and fluid management should be offered as first-line therapy to all patients with OAB [Standard (SoE Grade B)] and that behavioral therapies may be combined with pharmacologic	We are pleased that the guidelines are in agreement with the evidence.

Research Review Section	Reviewer	Comment	Response
		management [Recommendation (SoE Grade C)]. Likewise, the AUA/SUFU SUI Guidelines (2017) state that women with SUI or stress-predominant MUI wishing to undergo treatment should be counseled regarding the availability of observation, PFMT (± biofeedback), and other nonsurgical options (e.g. incontinence pessaries), in addition to surgery (Clinical Principle). We believe that tailoring treatment to a patient's lifestyle and goals, while minimizing adverse effects of intervention, is a fundamental principle of treating all forms of UI and is beyond dispute.	
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	Key Question 2: BTX resulted in better UI outcomes than other pharmacological interventions (moderate SoE compared with anticholinergics; low SoE compared with alpha agonists, hormones, and periurethral bulking agents). There is a significant amount of inherent bias in this conclusion. Since BTX is typically used for UUI refractory to other, less-invasive treatments, these women have already typically failed oral pharmacological interventions. Thus, better outcomes may be expected for BTX. Furthermore, the comparison with periurethral bulking is an unusual one, since BTX is used for UUI and	Given the poor state of the evidence in terms of whether studied women with urgency or stress (or mixed) UI, we have maintained as our preliminary analyses all studies and all interventions. However, we have added better sections of subgroup analyses regarding urge vs. stress, which in part separates out interventions commonly used only for urgency or only for stress UI. The Evidence Summary and the specific sections for KQ 1 to KQ 4 now focus more on four groups of analyses: Stress UI 1st and 2nd line vs 1st and 2nd line comparisons, Stress UI 3rd line vs. 3rd line comparisons; Urgency UI 1st and 2nd line vs 1st and 2nd line comparisons, Urgency UI 3rd line vs. 3rd line comparisons

Research Review Section	Reviewer	Comment	Response
		bulking for SUI. Likewise, the comparison between BTX (for UUI) and alpha agonists (presumably for SUI) is unusual.	
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	Key Question 3: Behavioral therapy alone, neuromodulation alone, and the combination of the two resulted in better UI outcomes than various pharmacological interventions (alpha agonists, anticholinergics, and hormones) (moderate SoE for behavioral therapy or neuromodulation vs. anticholinergics and for combination neuromodulation and behavioral therapy vs. alpha agonists; low SoE for other comparisons). As in the previous statement, a certain amount of bias exists in these conclusions. SNM is a third-line therapy for OAB that is refractory to behavioral and pharmacologic management, and these patients would have typically failed more conservative management strategies already. Thus, better outcomes may be expected for SNM. Also the comparison between SNM (for UUI) and alpha agonists (presumably for SUI) is an unusual one.	Given the poor state of the evidence in terms of whether studied women with urgency or stress (or mixed) UI, we have maintained as our preliminary analyses all studies and all interventions. However, we have added better sections of subgroup analyses regarding urge vs. stress, which in part separates out interventions commonly used only for urgency or only for stress UI. The Evidence Summary and the specific sections for KQ 1 to KQ 4 now focus more on four groups of analyses: Stress UI 1st and 2nd line vs 1st and 2nd line comparisons, Stress UI 3rd line vs. 3rd line comparisons; Urgency UI 1st and 2nd line vs 1st and 2nd line comparisons, Urgency UI 3rd line vs. 3rd line comparisons
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics,	Key Question 4: Addition of behavioral therapy to anticholinergics resulted in better satisfaction (but not cure or improvement) than anticholinergics alone (moderate	We have redone the tables in the Evidence Summary. We believe they are clearer and more coherent. We captured the Amundsen paper in our updated literature search. Thank you.

Research Review Section	Reviewer	Comment	Response
	Female Pelvic Medicine & Urogenital Reconstruction	SoE). We agree completely. Table E ranks the intervention categories by the mean percent of women who achieve favorable UI outcomes for each intervention category. BTX resulted in the highest percentages of women with cure, improvement, and satisfaction. While this may be true, significant bias exists as stated before. Other pharmacological interventions alone (not in combination with nonpharmacological interventions) ranked among the interventions with the lowest rates of favorable UI outcomes. However, the reader should refer back to Tables C and D to evaluate specific comparisons among the interventions. It is important to note that a lot of the relationships in Table D are indirect, indicating that no study directly compared the intervention to sham or placebo. As stated before, some of the comparisons are unusual (i.e. comparisons between alpha-agonists vs. SNM (± behavioral therapy) or BTX or SNM vs. bulking). Also, the ROSETTA trial detailing a comparison between BTX and SNM is glaringly absent (Amundsen CL et al. OnabotulinumtoxinA vs sacral neuromodulation of refractory urgency urinary	

Research Review Section	Reviewer	Comment	Response
		incontinence in women: a randomized clinical trial. JAMA 2016; 316(13): 1366-1374.)	
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	As such, some of the conclusions are directly impacted by the grouping of treatments. 1) BTX was also significantly more effective than other treatments, in particular other pharmacological interventions. There is selection bias favoring BTX here and BTX may not actually be a pharmacologic intervention	We have added in subgroups (and better emphasis) on separating first and second line therapies from third line therapies.
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	2) The other pharmacological interventions, when used without nonpharmacological interventions, had lower effectiveness to achieve favorable UI outcomes. It is important to note that several of the pharmacological interventions are off-label for UI.	We do not comment on FDA approval. Many interventions in common use for many conditions are off-label. If policymakers or guideline developer (or others) feel this is an important issue, they should include it in their guidelines (or other reports).
General comments	Public Reviewer #3 Alex Gomelsky, Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction	3) Serious adverse events were generally rare, with the notable exception of periurethral bulking agents which resulted in erosion or need for surgical removal of the agents in about 5 percent of women. It is important to note that several of these periurethral bulking agents may have already been removed from the market.	This is an important point. Thank you. We have added a sub-analysis of adverse event rates only among those periurethral bulking agents that are still on the market.

Research Review Section	Reviewer	Comment	Response
General comments	Public Reviewer #4 Colleen Skau, American Uro-gynecologic Society	Thank you for providing the opportunity to comment on the AHRQ/PCORI Systematic Review Update regarding nonsurgical treatments for urinary incontinence in women. As a group of providers who take care of a large proportion of women with urinary incontinence, the American Urogynecologic Society is very supportive of this effort, and we have several comments and suggestions.	Thank you
General comments	Public Reviewer #4 Colleen Skau, American Uro-gynecologic Society	1. Categorization: Consider providing background and clarification on how treatments were categorized; such as why sacral neuromodulation and periurethral bulking were considered non-surgical. Additional clarification on the "Nonpharmacological" category would be useful. The current classification under Nonpharmacological treatments is very broad including behavioral therapy, neuromodulation, and intravesical pressure release devices. The categorization of certain devices (such as pessaries, which have been studied with Level 1 evidence) as behavioral management may be not be entirely accurate. Consider adding a "Device" category in which intravesical pressure release devices,	We have added text about our categorization of interventions. We maintained the overall classification of interventions based on the protocol and have not added new categories.

Research Review Section	Reviewer	Comment	Response
		pessaries, and other intravaginal devices can be placed	
General comments	Public Reviewer #4 Colleen Skau, American Uro-gynecologic Society	2. Pessary: Strongly suggest adding a statement about pessaries. There is level 1 evidence for incontinence pessaries (i.e. Richter 2010) which was included in "Table 5: All studies with urinary incontinence outcomes", but not included in the "overview of the evidence base addressing all key questions". Given wide-spread use of incontinence pessaries, a statement regarding pessaries should be included perhaps with the caveat that there are no new data.	We have clarified that pessaries are included as a form of bladder support.
General comments	Public Reviewer #4 Colleen Skau, American Uro-gynecologic Society	3. Policy issues: We recommend highlighting that caution needs to be applied when information and recommendations are based on indirect network analyses and comparisons, particularly when those indirect analyses result in high odds ratios with broad confidence intervals (example Tables C and D).	We have added in the Discussion the following caution: "In our analyses we used indirect data to inform comparisons between interventions. However, indirect comparisons rely on an assumption that there are no influential systematic differences in the distribution of effect modifiers in the synthesized studies. We have examined the validity of this assumption qualitatively, by comparing the results of analyses by intervention categies versus specific interventions; in sugbroup analyses by UI type (stress versus urge) or by participant mean age; and in sensitivity analyses (split-node analyses to compare the direct and indirect estimates of studies). In all we do not have major indications that the assumptions necessary for the indirect

Research Review Section	Reviewer	Comment	Response
			comparisons are violated." We agree that conclusions should be measured, and believe that we have not overinterpreted the results. We also believe that the same considerations apply to qualitative indirect comparisons, which are much more common in EPC reports.
General comments	Public Reviewer #4 Colleen Skau, American Uro-gynecologic Society	Furthermore, please consider providing commentary addressing how systematic reviews do not fully consider efficacy versus adverse events. An important example is with regards to medication. There are no randomized trials involving mirabegron and thus this drug could not be studied for efficacy. However, mirabegron was studied for adverse events and appears to have a more favorable profile compared to other drugs (e.g. anticholinergics). Thus the current systematic review does not provide enough evidence to guide policy decisions regarding whether to choose a drug like mirabegron compared to an anticholinergic. This is especially important when clinicians are faced with situations where efficacy needs to be balanced against potential adverse cognitive effects. This may be highlighted for policy makers as many insurance providers (esp. Medicare/Medicaid) require anti-cholinergic medications as first line treatment, which can	We have added to the limitations section a paragraph about issues related to comparing benefits and harms, and also specifically about mirabegron.

Research Review Section	Reviewer	Comment	Response
		disproportionately affect the elderly and many at risk for cognitive decline. We are concerned that the systematic review may reinforce these practices in in instances where another drug may be beneficial due to the adverse event profile (as you have stated in your review).	
General comments	Public Reviewer #4 Colleen Skau, American Uro-gynecologic Society	4. Future Research Opportunities: We suggest adding that additional level one evidence studies on Mirabegron and other therapies are needed along with studies focusing on cognitive effects of anti-cholinergic medications. Finally, consider a statement that there are several up and coming treatments for urinary incontinence, some of which are already being marketed directly to patients, (i.e. radiofrequency laser) that are lacking high level evidence.	We have added a paragraph about future trials of various interventions.
General comments	Public Reviewer #5 Gavin Corcoran/Kent McKinney, Allergen	Recomendation: Since the approved dose of onabotulinumtoxinA (BOTOX) for the treatment of OAB is lOOU, Allergan recommends that AHRQ either only include studies and data for outcomes based on the approved dose of onabotulinumtoxinA (ie, BOTOX tOOU), or acknowledge in the report that studies of onabotulinumtoxinA (BOTOX)	We have added to the eligibility criteria (PICOTS) table that all doses and variations of interventions are included regardless of regulatory body approval.

Research Review Section	Reviewer	Comment	Response
		included unapproved doses (ie, higher doses) which should be taken into consideration when using this information for decision making.	
General comments	Public Reviewer #5 Gavin Corcoran/Kent McKinney, Allergen	Recomendation: Since urinary incontinence treatment outcomes vary greatly by underlying etiology and are not comparable across etiologies, Allergan strongly recommends that AHRQ revise its Key Questions and analytical methodology in the draft report to properly reflect the benefits and risks of treatment options by underlying etiology, i.e. separate analyses for UUI and SUI.	Given the poor state of the evidence in terms of whether studied women with urgency or stress (or mixed) UI, we have maintained as our preliminary analyses all studies and all interventions. However, we have added better sections of subgroup analyses regarding urge vs. stress, which in part separates out interventions commonly used only for urgency or only for stress UI. The Evidence Summary and the specific sections for KQ 1 to KQ 4 now focus more on four groups of analyses: Stress UI 1st and 2nd line vs 1st and 2nd line comparisons, Stress UI 3rd line vs. 3rd line comparisons; Urgency UI 1st and 2nd line vs 1st and 2nd line comparisons, Urgency UI 3rd line vs. 3rd line comparisons
General comments	Public Reviewer #6 Tanaz R. Ferzandi	Thank you for opening the comment period allowing medical stakeholders to lend their thoughts on this important review of nonsurgical treatments for urinary incontinence in adult women. As stated in the review, there is evidence to support the use of nonpharmacological as well as pharmacological intervention or a combination of both; which is a great asset to us helping these women who often “suffer in silence.”	Thank you

Research Review Section	Reviewer	Comment	Response
General comments	Public Reviewer #6 Tanaz R. Ferzandi	I wanted to bring up some thoughts, as it is tailored in the review. My concern is the "lumping" of the various modalities of treatment for "incontinence," especially for those non-surgical therapies. This is important because some therapies (for example intravaginal electrical stimulation) have been studied extensively over the decades, while other therapies such as TENS have limited data supporting its use. The review seems to categorize pelvic floor electrical stimulation as TENS which is an inaccurate categorization. Combining these categories limits the ability of the medical professional to understand which non-surgical modalities are the most effective with the most favorable side effect profile. This can also be said for the behavioral modification category where the review combines a multitude of options without subdividing out the various interventions or modalities used to draw upon this systematic review for accurate guidance.	It is true that given the very large number of specific interventions, we have lumped many together into fewer (but still a large number) categories. Readers interested in comparisons of specific interventions can find them in the appendixes.
General comments	Public Reviewer #6 Tanaz R. Ferzandi	There are significant differences between the mechanism of action for each treatment option reviewed and then grouped together. It appears that neuromodulation is grouped into	We determined the intervention categories based on clinical judgment. We acknowledge that not all would agree with the categorization. Readers interested in specific comparisons

Research Review Section	Reviewer	Comment	Response
		one category and behavioral modification into another, and all nonsurgical/ nonpharmacological treatments fall under these 2 categories. It would be helpful if the review could provide greater specificity and differentiation within the categories listed, as there are the various modalities incorporated in the review, much as the mechanism of action defines the multiple pharmaceutical categories. We deal with various discrete algorithms for stress urinary incontinence versus overactive bladder.	(which have even less robust evidence) can review the appendix comparisons of all specific interventions.
General comments	Public Reviewer #6 Tanaz R. Ferzandi	My hope is that there is a deeper dive into this review and adjust the findings to provide a greater understating of the various treatment options available. In order words, it is important to separate the 'apples from the oranges' in this challenging topic.	We hope that our revision has met your needs.
General comments	Public Reviewer #7 Dustienne Miller, Flourish Physical Therapy	In your review, as is often the case, "biofeedback" is a term assigned uniformly to all forms of biofeedback and I believe it is helpful to define this term and to better understand the various subcategories of biofeedback used in the treatment of UI in women if conclusions are to be made regarding its role in treatment. Biofeedback has been defined by the Cochrane	We have not separated biofeedback into multiple subcategories. The existing evidence is already extremely heterogeneous with sparse evidence for specific comparisons based on our categorizations. We acknowledge that not all readers will agree with our categorization system. We have, however, separated out vaginal weights and cones from biofeedback. We agree that this is a sufficiently distinct category of interventions.

Research Review Section	Reviewer	Comment	Response
		Collaboration as “augmented, concurrent, or terminal feedback of biological signals that enables a person to identify and modify a bodily function of which they are usually unaware.”5 The primary biological signals measured are electrical activity, squeeze pressure, and movement, although technologies to reliably use movement as a form of biofeedback have only recently emerged and are not yet in widespread practice. In all biofeedback, devices record the biologic signal during a voluntary pelvic floor muscle contraction and provide visual and/or auditory information to the user about their performance and are described as follows: • Surface Electromyography (sEMG): Metal plates on the surface of vaginal or anal sensors or cutaneous sensors affixed to the perineum record the electrical activity of the pelvic floor muscles with a voluntary contraction. They are sensitive to any increased electrical activity in the area, and so can be influenced by contraction of muscles in the pelvic floor, as well as those adjacent and accessory to the pelvic floor. The strength of the signal thus is subject to	

Research Review Section	Reviewer	Comment	Response
		electrical artifact and noise. Ten trials included in the most recent Cochrane Library Review on the subject investigated sEMG. • Pressure Perineometry: Vaginal or anal probes with pressure sensors, or air or water-filled balloon devices quantify the squeeze pressure exerted through the vaginal or anal walls and through to the probe during a voluntary pelvic floor contraction. Nine trials included in the most recent Cochrane Library Review on the subject investigated pressure perineometry. • Movement of the Pelvic Floor: Movement of the pelvic floor in space is another biofeedback option. Measuring movement allows for biofeedback to be provided with lifting of the pelvic floor, but also to measure the response with bearing down. Real-time ultrasound imaging (RUSI), measuring the amount the bladder neck is lifted during a pelvic floor contraction, is the only clinically-available tool for movement-based pelvic floor biofeedback. RUSI affords a clear view of movement during voluntary PFM contraction; however, it is clinician dependent to perform (e.g. no options for home or independent use exist; multiple	

Research Review Section	Reviewer	Comment	Response
		home sEMG and pressure systems are available) and is limited to observation in supine, prone, or side-lying positions (e.g. ultrasound cannot be used for biofeedback independently by the user or in standing). It is the most costly and cumbersome of the biofeedback options described in this document. One trial included in the most recent Cochrane Library Review on the subject investigated RUSI.	
General comments	Public Reviewer #7 Dustienne Miller, Flourish Physical Therapy	I bring all of this to your attention because I think that emerging technologies or future innovation may afford us new options for biofeedback and these various options (sEMG, pressure, movement, or anything that emerges) cannot be assumed to be equivalent. I would encourage you to differentiate the various biofeedback options available now and to closely monitor	Given the plethora of specific treatments, we have lumped all specific biofeedback interventions. Our primary analyses are intead based on categories of interventions.
General comments	Public Reviewer #7 Dustienne Miller, Flourish Physical Therapy	Additionally, I have seen recent digital advances in accessing professional education (https://www.medbridgeeducation.com/ for example) and platforms that dually address community and health care professional education, namely the “Pelvic Guru” website, in person and virtual education, and social media. For example, Pelvic Guru curates	Thank you. Studies on these types of interventions would have been included. We have included one study of yoga.

Research Review Section	Reviewer	Comment	Response
		educational content in maternal and pelvic health and act to promote access to high quality pelvic health care through training health care providers and connecting individuals around the world who are seeking information and health care to the individuals and organizations that can help. I have experience and success leveraging technology to promote access to care through my "Your Pace Yoga" platform (https://yourpaceyoga.com/), which makes digital yoga programs that are condition specific available to individuals with pelvic health conditions, including urinary incontinence. This is relevant to your document, 'Evidence Summary on Nonsurgical Treatments for Urinary Incontinence in Women: A Systematic Review Update', as I see no mention of the state of and potential for digital health to impact women with urinary incontinence. You are aware of the prevalence and impact of UI, but I believe that digital health has enormous potential for helping providers like me to amplify our reach. Most women with UI are under-served by the current system and treatment options, thus a critical look at how	

Research Review Section	Reviewer	Comment	Response
		leveraging technology can have a positive impact on UI treatment is very important for consideration. I would encourage you to seek out the current literature in this area and to keep open the possibility that this could bring meaningful improvements in treatment and simultaneously promote access to these treatments.	
General comments	Public Reviewer #7 Dustienne Miller, Flourish Physical Therapy	Lastly, I would encourage reclassification of "TENS". Transcutaneous electrical nerve stimulation is defined by the American Physical Therapy Association, as the application of electrical stimulation to the skin for pain control. It is administered by a small batterypowered device that applies an electric current via two or more non-invasive skin electrodes to stimulate underlying nerves and thus reduce pain perception. This is distinct from the form and properties of all intravaginal electrical stimulation devices used in current treatment, thus continued use of TENS can be confusing to all readers of the document.	The term is used in the UI literature. We have clarified which devices are included in the category.
General comments	Public Reviewer #7 Dustienne Miller, Flourish Physical Therapy	I have attached for your reference the most recent Cochrane Library publication to discuss various pelvic floor biofeedback approaches. Again, I am very happy to see that PCORI and AHRQ are dedicating effort	Thank you. We have reviewed the 2012 Cochrane review and we have included some studies that were omitted from the 2012 AHRQ report.

Research Review Section	Reviewer	Comment	Response
		to non-surgical management of female UI and grateful for this opportunity to submit comments.	