Comparative Effectiveness Review Disposition of Comments Report

Research Review Title: Treatments for Fecal Incontinence

Draft review available for public comment from June 1, 2015 to June 29, 2015.

Research Review Citation: Forte ML, Andrade KE, Butler M, Lowry AC, Bliss DZ, Slavin JL, Kane RL. Treatments for Fecal Incontinence. Comparative Effectiveness Review No. 165. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-2012-00016-I.) AHRQ Publication No. 15(16)-EHC037-EF. Rockville, MD: Agency for Healthcare Research and Quality; March 2016. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. 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 Agency for Healthcare Research and Quality.

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Commentator & Affiliation	Section	Comment	Response
TEP 1	General comments	This report is meaningful, as it addresses a condition that is lacking in strong research. Key questions are explicitly stated and are relevant clinically.	Thank you
TEP 2	General comments	The report is clinically meaningful, the target population is defined, and the key questions are appropriate.	Thank you
TEP 2	General comments	In general the state of the science is poor, and more research with clearly defined outcome measures is needed. This come across clearly in the manuscript and I believe is a reflection of the state of the science.	We agree – thank you for your feedback
TEP 2	General comments	I have the following other general comments for consideration by the authors: 1. There is a great deal of emphasis on FI etiology - while it might be helpful for authors to include the eitiology of the FI that is being treated in FI studies, often the etiology is not known, and, in addition, FI etiologies are really not well understood. As an investigator, I would have a tough time providing the FI etiology, other than to carefully describe my patient population. I would suggest making some statement to the fact that etiology may be difficult, but at least some attempt at discussion of stool consistency and detailed patient characteristics and comorbid conditions are needed.	Thank you for your suggestion. We added: *Multiple causes of FI in individual adults are common and a dominant etiology may not be *sought or* determinable. (pg. 1) * *Multiple etiologies may contribute to FI, and etiologies were variably reported in the literature. One-third of RCTs provided no etiologic information, while other authors provided great detail of nonmutually exclusive contributing factors. No study provided information about the frequency of multiple FI etiologies per enrolled adult in baseline patient information tables, such as summary counts per patient or common etiologic combinations. Baseline testing was commonly conducted to ascertain the presence and degree of anal sphincter tearing, but further etiologic identification was less commonly reported. In addition to FI severity at baseline, etiologic multiplicity information could advance understanding of which etiologic factors respond best to given treatments or treatment combinations….Careful descriptions of patients in clinical studies, including baseline characteristics, comorbid conditions and etiologies, would improve understanding of the applicability of results from individual studies and in future literature syntheses.*(pg. 32)

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TEP 2	General comments	2. All of the outcome measures currently used to measure FI have had limited patient input, including the FISI, FIQL, etc. These scales may not reflect was is important to patients. QOL and symptom scales that have patient input are needed so that researchers can design trails that are meaningful to patients.	We agree that understanding what is most important to patients is a top priority. However, we disagree about patient input to date; a number of measures solicited patient input (Rockwood x 2, others). We added a statement to the Discussion under Research Gaps: *Validated outcome measures that capture the FI impact features most meaningful to patients are critical, in addition to the standardized labeling of such measures across studies (see Applicability and Limitations of the Evidence Base); only some of the current outcome measures solicited patient input during instrument construction. (pg.38)*
TEP 2	General comments	3. While this document focuses on FI and not AI - some mention should be made of flatal incontinence. In Rockwood's work, women with flatal incontinence were significantly bothered by their incontinence, and the impact of flatal incontinence on QOL should at least be mentioned. In addition, nearly all of the scales used for FI include flatal incontinence.	Thank you for your feedback but we disagree. The report is on FI, not AI. We added a statement in Table 1 PICOTS about this exclusion.
TEP 2	General comments	4. FI usually does not exist in isolation, particularly in women who often have both UI and POP as well. In addition, improvement in FI without improvement in UI, may not result in improved patient satisfaction. Since these other disroders are so intertwined some mention should be made that they should be included as possible areas of bias in clinical studies...	We added a statement in the Discussion where we described the need for more comprehensive patient information at baseline, including comorbid conditions, including urinary incontinence. (page 36, Applicability and Limitations of the Evidence Base). Comorbidities are generally under-reported in this literature set.
TEP 3	General comments	This is the most comprehensive report regarding fecal incontinence that I have read. It provides a concise overview of each study in the literature regarding fecal incontinence and the strengths and weaknesses of the each study. The assessments are uniform in their critique of each study.	Thank you for your positive and specific feedback.

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TEP 2	General comments	When clinicians treat patients with fecal incontinece they separate patients as a rule into those with severe incontinece and those with minor incontinence and treatment options are based on that. The only time that fecal incontinence is typically thought of as neurologic is really for those with spinal cord injury because retraining treatment is the most used option. The authors have divided the causes of FI into neurological and nonneurological etiologies, but for most practiciing care givers this type of breakdown is not necessarily the case in treating these patients.	Thank you for your feedback. We disagree with your suggestion to classify patients by severity only. Studies often included patients by etiology (e.g. obstetric anal sphincter tear) then often (but not always), selected samples by some minimum severity measure. The range and type of minimum FI severity score or episode criteria required for study inclusion varied greatly, and no specific severity range for any measure was apparent that would enable clinicians to label patients as having mild, moderate or severe FI. We also disagree that clinicians and study investigators only classified adults with SCI as having neurogenic FI. Rather, we found that *neurogenic FI* was used in a number of studies for anyone without a major anal sphincter tear. We have included information in the Discussion on page 35 regarding this etiologic labeling problem that would be helpful for the field to resolve.
TEP 5	General comments	This review is meaningful in that we now have a much clearer view of the gaps in the treatments for patients with Fecal Incontinence. It has long been thought by many that more standardization is needed as well as better quality in the study designs and measurements, which has been demonstrated in this review. It paints the picture that Primary Care providers really have very little to offer patients with FI.	Thank you for your feedback. Importantly, It shows that improvements in the literature (study reporting and in the conduct of clinical trials) could improve the evidence base. Doing so may provide higher quality evidence on which to base clinical decisions.
TEP 5	General comments	The target population and audience are explicitly defined. The key questions are appropriately stated.	Thank you
Peer Reviewer 1	General comments	Yes, the report is clinically relevant. The target population is very clearly defined, as are the key questions, and the key questions have significant implications for clinical practice and for future research. The authors have done an excellent job of synthesizing and summarizing the data from very disparate studies and identifying implications for future study.	Thank you for your positive feedback.
Peer Reviewer 1	General comments	Minor editorial comments: Page 14-121: Results of Literature Searches, last paragraph, last sentence. Should this read: "Evidence of publication bias was identified ..."	Thank you for catching our error. The statement has been corrected.
Peer Reviewer 1	General comments	Minor editorial comments: Page 32-121: Key Points: last bullet point needs to be edited for clarity.	We edited the last bullet under Key Points for Surgical treatments KQ 1 page 25 for clarity.

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TEP 6	General comments	Yes clinically meaningful, mostly demonstrating that more rigorous research needs to be done that offers consistency of interventions and outcomes measured, identifying specific groups that would benefit from specific treatments, etc. My comments throughout are few and minor - very well done and thorough	Thank you for your comment
Peer Reviewer 2	General comments	The report is exhaustive and methodologically sound however there is lack of realistic clinicaly applicability. The majority of the pharmacologic methods evaluated, meaning the topical medications are almost never used and add little to the usefulness of the study, as well as external anal electrostimulation	Thank you for your feedback. We added a paragraph in the Discussion under Limitations of the Evidence Base: *We did not find RCT or OBS evidence for all available FI treatments. The studies included in this review may not reflect the frequency of which specific treatments are used in clinical practice. For example, the easiest treatments to study (drugs) are not necessarily those that are used most often. According to our TEP, topical medications, narcotics, and one or two surgical procedures are no longer commonly used, but are still FDA-approved for use in the US.*
TEP 7	General comments	As a researcher who is an active participant in ongoing clinical trials to improve outcomes for patients with fecal incontinence, I found this review somewhat difficult to read mainly due to terminology inconsistencies. The written section reporting outcomes for pelvic floor muscle therapy with or without biofeedback (PFMT-BF) could be better explained to match the data from the corresponding tables for this section.	Thank you for your feedback. We edited the PFMT section (pg. 11-12) for clarity; the text now matches the table sequence.
TEP 7	General comments	KQ#1 attempts to evaluate treatments by FI etiology (Appendix Table F3). The etiologies for FI are not presented clearly in this review which makes this question difficult to answer. FI is multifactorial in nature, as are the treatments. The etiologies presented in this review (Table 1) are not substantiated by current reviews or other literature on this topic. “Geriatric” is listed as an etiologic subgroup in Table 1. The other subgroups are not well defined, “mixed,” “structural,” and “GI.” Separation of neurological causes, such as spinal cord injury or multiple sclerosis, is more consistent with the literature. See more comments in the introduction section below.	Thank you for your comments. Geriatric was identified as a special population; not all treatments are feasible in this group of adults where FI due to mixed etiologies is more common and physical or mental health conditions could limit feasible treatment options. -We did not change the etiologic categories – We made our etiologic classifications based on input from the literature, KIs and TEP. - We identified etiologies when possible. Although FI etiologies may be poorly identified or defined in some adults, KI and TEP input suggested that some assessment based on etiology would be helpful to the field, so these categories, although not perfect, were identified and reported when possible.

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TEP 7	General comments	The second major concern involves the section on what is named, PFMT-BF. The authors do not do balance the existing evidence representing the studies that involve PFMT -BF and the comparative effectiveness of PFMT with or without biofeedback (PFMT±BF). This section appears to have significant bias, specifically with this statement, "Nonetheless, most of the literature focused on ways to improve or prolong the purported benefits of PFMT for FI, rather than to establish the benefits of it (no references)." This consideration (and bias) has important payer implications given the lack of insurance coverage for PFMT and biofeedback for the treatment of FI. This is a major concern for my review and represents a missed opportunity for this project. Please see the methods and results section below for more comments.	We edited the PFMT section (page 10) for clarity. The text now matches the table sequence. We expected to find more (early) PFMT studies that used an inactive comparator (such as wait list) as a control. Instead, we found numerous studies of PFMT versus another form of PFMT, hence our statement, *most of the literature focused on ways to improve or prolong the purported benefits of PFMT for FI, rather than to establish the benefits of it*. One would expect to find studies that better establish whether PFMT works for FI prior to finding PFMT vs. PFMT studies, but that was not the case. We explained, *refinements in treatment delivery,* by adding, *studies that compared one form of PFMT to another*. We added references to: *improve or prolong the purported benefits of PFMT for FI.* The PFMT tables (6-12) are presented by the type of PFMT and comparator. We are unclear what the Reviewer means about balance, and are not aware of bias in our presentation of these studies.
Peer Reviewer 3	General comments	The report is clinically meaningful. The target population appears to be broad. The target population appears to include all individuals with fecal incontinence within the large subcategory is of females over 40 and nursing home residents with a breakdown of the latter into those with and without cognitive impairment. The key questions look at prevelence, etiologies, and therapies; the latter divided into nonsurgical and surgical options. The key questions appear to be appropriate and explicitly stated.	Agree-thank you
Peer Reviewer 4	General comments	The report is clinically meaningful. The key questions are appropriate and explicitly stated.	Thank you

Commentator & Affiliation	Section	Comment	Response
Public Reviewer 3: Fred Kurtz, Medtronic	General comments	The Efficacy of Sacral Neuromodulation: Key Question 1: What is the comparative effectiveness of treatments to improve quality of life and continence and lessen the severity of fecal incontinence in affected adults? While we appreciate that your review was limited to articles with a control or comparator group, we believe evidence from non-comparator studies may be meaningful for providers, patients and payer alike. Please consider the efficacy and results of the following studies: *Tjandra JJ, Chan MK, Yeh CH, et al. Sacral nerve stimulation is more effective than optimal medical therapy for severe fecal incontinence: a randomized, controlled study. Dis Colon Rectum 2008 May; 51(5):494-502* 2 Given the efficacy improvements demonstrated by sacral nerve stimulation but not by optimal medical therapy in this study, we believe the data is sufficient to demonstrate an outcome advantage of SNS. *Mellgren A, Wexner SD, Coller JA, et al. Long-term efficacy and safety of sacral nerve stimulation for fecal incontinence. Dis Colon Rectum 2011 Sep; 54(9):1065-75. PMID: 21825885.* The Mellgren et al study provides a three year follow up under an FDA approved investigational protocol.	Thank you for your input. Both studies were already included in the report. Mellgren 2011 (SNS case series, earlier report of Hull 2013) and Tjandra 2008 RCT are/were included in the report. Tjandra 2008 is in the report text on SNS on page 28, and in Appendix table F4 (KQ 1) and F8 (KQ 2). Mellgren 2011 is in Appendix F9 (KQ 2 case series). We required higher-level evidence than case series to demonstrate treatment benefits (KQ 1).
Public Reviewer 3: Fred Kurtz, Medtronic	General comments	Please consider the following study relative to SNS durability: *Long-term Durability of Sacral Nerve Stimulation Therapy for Chronic Fecal Incontinence, Tracy Hull, Chad Giese, Steven D. Wexner, Anders Mellgren, Ghislain Devroede, M.Sc.Robert D. Madoff, Katherine Stromberg, John A. Coller.* The Hull et al, study included data from 14 centers in the US from 2002 to 2012 with a focus on long term durability of the therapy. Five year data were analyzed. Highlights of this study include: 1. FIQOL: improvement in all 4 scales (lifestyle, coping/behavior, depression/self-perception, and embarrassment) from baseline to 5 years post implantation were statistically significant, 2. Number of incontinent episodes: reduced from 9.1 to 1.7 at 5 years, 89% of patients had at least a 50% improvement from baseline in weekly incontinent episodes, 36% of patient at 5 years post implantation had achieved complete continence 3. Adjusted Worse Case sensitivity analysis resulted in 69% (83/120) of patients achieving at least a 50% improvement from baseline in weekly incontinent episodes ($p < 0.0001$).	Case series were not used for KQ1 (treatment benefits) because higher-level evidence was required for KQ 1. Hull et al. 2013 is a SNS case series of 76 adults with 5-years of follow-up data. It is the 4th publication on a case series of SNS that updates 3 other articles (1 duplicate) over different time frames; We added Hull et al. 2013 to Appendix table F9 with adverse event reporting: 35.5% of patients required a device revision, replacement or explant.

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Public Reviewer 3: Fred Kurtz, Medtronic	General comments	In addition to the Mellgren and Hull observational studies, we ask that you consider the following guidelines from professional physician societies: *American Society of Colon Rectal Surgery* (ASCRS) Clinical Practice Guideline for the Treatment of FI, Dis. Colon Rectum, 2015, volume 58. (See attachment # 2, p 5-8) These practice guidelines represent the agreed upon approach based on the expertise of the physicians currently treating the dominant percentage of the affected population. These reviews include all available literature through 2014 assessing all treatments for FI, by clinicians. Sacral Nerve Stimulation received a 1B, or a Strong Recommendation, Moderate-quality evidence. ("These guidelines are intended for the use of all practitioners, health care workers, and patients who desire information about the management of the conditions addressed by the topics covered in these guidelines.") *The American Society of Gastroenterology* (ACG) Clinical Guideline: Management of Benign Anorectal Disorders, American Journal of Gastroenterology, 2014 (see attachment # 3 p. 11). The ACG recommends Sacral Neuromodulation (SNS) be considered in patients with FI who do not respond to conservative therapy (Strong Recommendation, moderate quality of evidence)	Guidelines were not part of the evidence selection. However, we have added a section in the Discussion, *Findings in Relationship to What is Already Known*, and in Appendix F13, which discusses both guidelines relative to the results of this our review. (pg. 35)
Public Reviewer 3: Fred Kurtz, Medtronic	General comments	Adverse Events Associated with Sacral Neuromodulation: Key Question 2: What adverse effects are associated with specific treatments for adults with fecal incontinence? While your review is comprehensive, most sacral nerve stimulation reported adverse events are resolved without surgical intervention, therefore your range of 2-85 % is accurate, however it represents a large range. Published adverse events and Medtronic's FDA labeling for the InterStim device may further inform the discussion. Specifically, the majority of adverse event are resolved spontaneously, with re-programming of the device (no intervention required) or with medications. Out of 120 patients implanted with the InterStim system, 38 (31.7 %) had at least one device revision, replacement (including replacements due to normal battery depletion), or explant within the first 60 months of follow up. (See attachment # 4, p. 30-32)	Thank you for your feedback. The actual range of patients who experienced any complication from SNS was 2%-93% (see Appendix F9), which we have corrected in the report text. As is noted in Appendix F9, a wide range of patients required reoperation with SNS (for any reason); often 22-41% required reoperation after SNS.

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TEP 2	Abstract	"Surgical interventions have substantial complications." This statement in the abstract seems overstated, as a number of surgical interventions do not have very morbid AEs such as neuromodulation.	We edited the abstract to read: *More invasive surgical procedures have substantial complications.* More detail is provided in the report under adverse effects noted on pg. 30-31 under KQ 2, Surgical treatments.
TEP 2	Abstract	Abstract: "Numerous outcome measures and lack of compliance with study reporting standards are modifiable impediments in the field." I think that this should state the positive direction – "Standardization of outcome measures and adherence to study reporting standards are modifiable actions that are able to be implemented in the field"	Thank you for your suggestion. The statement was meant to highlight two pervasive problems in the FI literature that limit the utility of study information for clinicians and patients. We did not change the text.
TEP 1	Introduction	Appropriate Introduction, sets stage for paper. Would consider briefly discussing importance of patient-reported outcomes for this particular condition.	We added a statement to the Discussion under Research Gaps: *Validated outcome measures that capture the FI impact features most meaningful to patients are critical, in addition to the standardized labeling of such measures across studies (see Applicability and Limitations of the Evidence Base); only some of the current outcome measures solicited patient input during instrument construction. (pg.35)*
TEP 2	Introduction	"Risk factors for FI include increasing age, female sex, chronic diarrhea, nerve damage (from injury, multiple sclerosis, or chronic diabetes), postsurgical or post radiation complications, cognitive impairment, or other factors such as severe constipation.4,5" This list should include obstetrical anal sphincter laceration and other trauma that directly impacts the sphincter complex. At least OASIS should be included since it is one of the most common forms of trauma to the sphincter. While it often includes nerve damage, it can also include sphincter trauma without measurable nerve damage.	Thank you for your feedback. -Earlier in the 3rd (same) paragraph we stated: *Nonneurological causes of FI may be structural (e.g., muscle damage from episiotomy or surgery*)… -The 2nd paragraph also states: *Women over age 40 are disproportionately affected due to pelvic floor dysfunction after childbirth and obstetrical trauma*. -We added the term *obstetrical trauma* to the statement you identified in the Introduction.
TEP 2	Introduction	"Treatment goals are to decrease the frequency and severity of FI episodes. Treatments for FI are imperfect and combinations are common." This statement is confusing to me. I think the purpose is to state that treatment combinations are common, but it is not clear. In addition, I would argue that the treatment goals have not been entirely vetted with an FI population, so we really do not know what the goals or how patients would evaluate satisfactory treatment.	Thank you for your comment. The statement is written as intended: that FI treatments are imperfect (most do not fully cure FI and most are not permanent fixes,) and that treatment combinations are common. We edited the statement to read: *Treatments for FI are imperfect and treatment combinations are common."*

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TEP 2	Introduction	"As a result, the nature of patients offered different types of FI treatment can vary widely." The introduction and discussion spend a considerable amount of the discussion focused on FI etiology. In fact, FI etiology is likely multi-factorial in many patients and the types of FI are not clearly phenotyped	We clarified that multiple FI etiologies are common. We stated that the precise etiology may be indeterminable. The Introduction and Discussion have been edited regarding FI etiologies. See our response to you under General Comments, pg. 2 above.
TEP 3	Introduction	Under background, the third paragraph, I wondered where colonic hypermotility figures in? A patient can have the strongest anal sphincter muscles in the world, but if the colonic motility is strong it will overcome them. The patient may not have diarrhea for this to occur.	Thank you for your input. It would fall under other factors pg. 1): *FI etiologies fall into two broad categories: nonneurological or neurological. Nonneurological causes of FI may be structural (e.g., muscle damage from episiotomy or surgery), functional (e.g., post-radiation or muscle atrophy), due to an underlying gastrointestinal (GI) disorder (e.g., inflammatory bowel disease), from stool consistency problems, or from other factors.*
TEP 3	Introduction	In the 5th paragraph, when speaking about treatments for fecal incontinence in the US, it is important to note that muscle transposition IS NOT OFFERED BY CENTERS ANYMORE AS THE STIMULATOR FOR THE GRACILIS MUSCLE IS NOT AVAILABLE IN THE U.S. NOW. This is important because doctors who are not aware will send patients for this procedure. Writing this line in the paragraph as has been done, continues this confusion.	Thank you for your feedback. We excluded studies of dynamic graciloplasty since the procedure is effectively not done in the US anymore. We deleted the text in the Introduction on muscle transposition procedures.

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TEP 4	Introduction: page 1, paragraph 2-3	Attribution to FI for non-diagnosed populations is difficult. In individuals known to have FI the terminology 'accidental bowel leakage' (ABL) instead of incontinence has been adopted to remove some of the stigma/embarrassment which can introduce error into measurement (desirability bias). This wording has carried over into these general surveys, but introduces a significant problem - ABL is not FI. People have ABL for all kinds of reasons - not just FI. The more appropriate interpretations of this is - that x% have ABL, of which some portion have FI, but unless the survey also asks 'has a doctor ever told you that you have FI' or a similar DX question - one cannot make the attribution that the response to an ABL question identifies the rate of FI in the population. As an example in this case - it is not possible that 25% of the 'community dwelling population' has FI - it might be that 25% had an ABL event, but they don't have FI. A second issue related to these items is the definition of FI - FI is used as both a symptom and as a condition. The ABL question in a general populations treats FI as a symptom not as a condition. The studies that estimate prevalence based on the using ABL wording does not estimate FI, it estimates ABL and there is a big difference between these two things.	We edited the 2nd paragraph of the Introduction in 2 places: 1. Among community-dwelling adults, the prevalence of FI is *reported as* 8.3 percent,[2]…. 2. We added: *More recent terminology aimed at minimizing social stigma (accidental bowel leakage, ABL), may further compound the discrepancies around FI prevalence estimates, because adults can have ABL (a symptom) for many reasons, not just FI (a chronic condition).* Also, we added text to the Discussion (top of pg. 33): *Definitions of FI episodes were particularly difficult to compare across studies (soiling versus solid stool versus solid plus liquid stool versus liquid only). FI severity was defined in numerous ways (episode frequency, CCFIS or other scale at screening, etc.), and was often used as a sample selection criteria in clinical studies. Mild to severe grading is problematic because FI severity grading is not standardized.*
TEP 4	Introduction: line 38	I would agree that the goal of treatment is to do this, but wouldn't the goal of an artificial sphincter (if a truly effective one is ever developed) be to fix the cause of the problem (for individuals with sphincter damage) which results in fewer episodes? Given that this is about treatment efficacy it would seem that there are two or distinct classes of treatment - symptom reduction and 'cure.' With diet drugs being 'symptom' and replacing sphincter being 'cure' - the issue would be what does PFMT-BF do? Based on study design and measurement these studies could be construed as 'symptom reduction' or as 'cure.'	Treatment goals are to decrease the frequency and severity of FI episodes. Treatments for FI are imperfect and treatment combinations are common. *Most treatments are aimed at symptom reduction; few treatments, if any, afford long term cures for FI.* We did not further divide the treatments into symptom reduction or cure.
TEP 5	Introduction	The introduction is clear and concise. It speaks to the burden of Fecal Incontinence and the frustration that is felt by many with FI that there is not a single treatment option or combination of treatments to manage or cure FI over the long term.	Thank you for your feedback
Peer Reviewer 1	Introduction	Concise but comprehensive overview of the problem being addressed and the need for the review.	Thank you
TEP 6	Introduction	Introduction is clear and provides good overview of definitions, purpose of the paper, and results of the review.	Thank you
Peer Reviewer 2	Introduction	ok	No response needed

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TEP 7	Introduction	The introduction is clearly presented with the exception of the paragraph regarding the etiologies of and subgroups of FI. The separation of non-neurologic and neurologic causes is important. However, better defining what is meant by these two separations would help the reader. For example, if a diabetic patient with a peripheral neuropathy involving the pudendal nerve seeks FI treatment, is this considered neurologic or non-neurologic? Also, the non-neurologic subgroups do not seem consistent with the current literature. The term 'structural' is vague. Is this term also representative of anatomic injuries from obstetrical anal sphincter injuries (OASI) and hemorrhoid surgeries? The potential overlap with muscle atrophy as an etiology for the functional subgroup also can be an etiology for the structural subgroup or neurologic causes. Better defining what is meant by the subgroups, especially for GI disorders and mixed etiologies, would also help the reader. From my perspective, risk factors and etiologies are not clearly presented in this paragraph.	Thank you for your comment. We discussed the non-neurologic and neurologic distinction with our experts prior to this review (KIs and TEP). Our goal was not to make an exhaustive list of conditions that comprise the etiologic subsets. Our experts felt that broad categories with a few examples provided sufficient information without excessive detail. We better defined the term *subgroups* in the abstract and in the Introduction (pg. 2): *reported overall treatment effects and those within subgroups of adults defined by their FI etiologies (when available), or...*
TEP 7	Introduction	In the 6th paragraph of the introduction, the same concerns exist as in the 3rd paragraph on etiologies. The differences between structural weakness, structural injuries, structural problems, and structural damage are not clearly defined throughout the introduction. These terms are used interchangeably throughout the review.	Thank you for your feedback. We did not change the text in those examples. See the point above. We removed the language that the Reviewer found to be confusing.
TEP 7	Introduction	Please define what is meant for "subgroup treatment" effects. Does this mean efficacy by etiology or subgroup? Later, the terms "etiologic subgroup-specific outcomes" and "FI etiologic subgroups" are also used. If so, better defining the etiologies or subgroups in the 3rd paragraph would help the reader. Also, the term "treatment-subgroup combinations" is not clear to the reader.	We clarified the text on pg. 2 of the Introduction: *…reported overall treatment effects and those within subgroups of adults defined by their FI etiologies (when available),…*
TEP 7	Introduction	My major concern is the structure of this review by FI "subgroup" or "etiology" that is not clearly defined or supported by the literature. These two terms are used interchangeably throughout the review.	Thank you for your feedback. The report is consistent with the suggestions made by our KIs and TEP. We found inconsistent and weak etiology information in the literature, which is important for the field. More attention to what factors contribute to FI may help providers to better match treatments to patients. We clarified the text on pg. 2 of the Introduction: *…reported overall treatment effects and those within subgroups of adults defined by their FI etiologies (when available)*

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TEP 7	Introduction	The introduction of treatment options that range from nonsurgical treatments, a newly FDA-approved device, and non-invasive and more invasive surgical treatments is appreciated. However, the classification of "permanent nonsurgical" treatments seems to be a premature category given the relatively new evidence for the injectable bulking agents (which often require a second injection for efficacy – per your Appendices reference #39, Graf et al). "More invasive nonsurgical treatments" may be more appropriate.	Thank you for your suggestion. We deleted the text about permanent nonsurgical treatment. Tissue bulking injections are now listed under Nonsurgical treatments. We removed all other references to *permanent* in our discussion of nonsurgical treatments throughout the report
TEP 7	Introduction	These same subgroup/etiology issues are not presented clearly in Table 1 under the population element. The inclusion and exclusion criteria are not consistent with the terminology in the introduction. Specifically, structural problems (e.g. rectal prolapse) are excluded. This exclusion overlaps with the previously used terminology. Temporary vs permanent terminology is used in Table 1 under the intervention element.	The subgroups are listed as planned using input from the KIs and TEP. Authors defined etiologies differently. Report tables show as much consistency with the Table 1 categories as we were able to do, given the limitations of the literature. We added the term "obstetric" to the Population information in Table 1 where it also notes that we used patient- or investigator-reported FI information. We removed references to *permanent* in our discussion of nonsurgical treatments throughout the report.
Peer Reviewer 3	Introduction	The purpose of the report appears to be to compare efficacy and side effects of different therapies across different etiologies for fecal incontinence as well as across different therapies to help decision-making for patients and their doctors. It also provides a baseline foundation of research on which to perform further research.	We agree – thank you
Peer Reviewer 4	Introduction	Pg 8 line 23 – specify that you have switched back to community-dwelling adults (last sentence was nursing home) – "Monthly FI occurs in 6-25% of community-dwelling adults,"	We edited the second paragraph of the Introduction for clarity and consistency.
Peer Reviewer 4	Introduction	Pg 8 line 39 and multiple other places – the term "permanent non-surgical treatment" is odd and meaningless to me. This is further clarified on line 42 as applying to injectable bulking agents which are notoriously temporary in effectiveness. Strongly recommend against this terminology. See later discussion in Results section of this review.	We removed the temporary/permanent subheadings under Nonsurgical Treatments.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 4	Introduction	Key Questions, Table 1 – Population – How is geriatric an etiologic subgroup? FI is never the result of aging alone, although advanced age is a risk factor. Older adults have mixed etiologies for their FI that do not differ from many younger individuals. Delete "geriatric".	Thank you for your feedback. Geriatric was identified as a special population, rather than an etiologic subgroup. Not all treatments are feasible in this group of adults where FI due to mixed etiologies are more common. We retained Geriatric as a patient group of interest. We changed the text in Table 1 PICOT to: *Adults age 18 and older with patient- or investigator-reported FI. Included adults per study were classified by FI etiologic subgroups or special population: mixed, obstetric, geriatric (special population),…*
Peer Reviewer 4	Introduction	Key Questions, Table 1 - Interventions – the Temporary vs. permanent non-surgical treatment terminology comes up again here.	We removed the temporary/permanent subheadings under Nonsurgical Treatments.
Peer Reviewer 4	Introduction	Key Questions, Table 1 - Outcomes – KQ-2 – Listing colostomy as a complication of surgery is misleading. It is actually another treatment for failed surgical treatment. If you are really trying to discuss ostomy as a surgical adverse event, add ileostomy to colostomy, since both are done to divert stool – ileostomy often if unplanned, colostomy is more of a permanent diversion, but the choice may depend on the surgeon.	Thank you for your feedback. We clarified the text under KQ 2 Table 1: *surgical complications (such as infection, the need for revision surgery or other surgery (e.g. colostomy);* negative emotional/psychological effects; other adverse effect(s) related to treatment…
Public Reviewer 1 Christine Norton	Introduction	Treatment goals may include improving quality of life or successful containment and activities as well as reduction of frequency and severity of FI episodes. Later you state improvement in quality of life is a primary outcome measure	Thank you for your feedback.
Public Reviewer 2 Heidi Brown, University of Wisconsin Madison	Introduction	It is stated in the second paragraph that the prevalence of fecal incontinence FI is higher in women than men but the reference from which that citation is taken actually states that the prevalence is equal FI was found to be equally common in women 8.9 CI 7.2 10.5 and men 7.7 CI 6.0 9.4 p0.31. It is a common misperception that FI is more prevalent in women than men and this report should not perpetuate that misperception. Similarly in the third paragraph female sex should not be listed as a risk factor for FI since good populationbased data from NHANES indicate that men and women are affected equally.	FI estimates are difficult because each author used a different definition of FI. Whitehead et al. 2009 cited "FI" frequency among adults who had bowel leakage at least monthly. Not all of those individuals had diagnosed FI. We edited the 2nd paragraph of the Introduction to better discuss issues with FI prevalence estimates. Females comprised the overwhelming majority of enrolled subjects in the literature we reviewed (see page 9 of the Results under KQ 1).
TEP 1	Methods	Methods are sound and appropriate. Study inclusion and exclusion criteria, search strategies and definitions are clear and transparent. Statistical methods are appropriate.	Thank you
TEP 2	Methods	Yes to all the questions above.	No response needed

Commentator & Affiliation	Section	Comment	Response
TEP 2	Methods	Minor Statement: “For each Key Question, we will summarize the results.” This statement is in the present tense, where the rest of the section is in the past tense.	Thank you – we corrected the text
TEP 3	Methods	The methods section seems very comprehensive and the explanations for why things were carried out is reasonable. I am a clinician and do not have the expertise in statistical studies, so I cannot comment on the statistical studies used for analysis of the data.	Thank you
TEP 5	Methods	The methods section appears to be appropriate. Quality (Risk of Bias) Assessment of Individual Studies is an important factor given that there were so few studies that had a Low Risk of Bias.	Thank you
Peer Reviewer 1	Methods	Inclusion and exclusion criteria clear and, in my opinion, very appropriate. Clear explanation as to why case series reports were used for identification of adverse effects related to surgical interventions. Search strategies clearly outlined and appropriate. Authors clearly identified reasons why data could not be pooled (e.g., significant differences in outcomes measures) and why results could not be stratified based on etiology of FI.	Thank you
TEP 6	Methods	Criteria is justifiable, search strategies well explained and logical.	Thank you
TEP 6	Methods	Page 14 / 121 (numbered at top of page) - around line 4, would encourage altering wording to better reflect People First Language, such as: "Adults in clinical trials of FI treatments may have higher function, be younger, or have fewer impairments . . ."	We edited that statement on pg. 7
Peer Reviewer 2	Methods	The authors did not seem to include (unless I missed it) the 5 year f/u report by Hull et al on the durable effectiveness of SNS. This is a critical deficincy.	Thank you for your suggestion. Hull 2013 has been added to Appendix table F9 (KQ 2) of adverse effects. Hull 2013 is a longer term publication of a SNS case series with prior publications; three other articles (1 duplicate) on the same case series reported on outcomes at earlier time frames; the non-duplicates are and were included in the KQ 2 case series Appendix table F9. We required higher-level evidence than case series for KQ 1 (treatment benefits) so Hull 2013 was included for KQ 2 only.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 2	Methods	There is also a lack of data regarding tibial nerve stimulation as well as graciloplasty	The stimulator for dynamic graciloplasty is no longer available in the US so the procedure is effectively not done. PTNS was initially excluded as experimental and not FDA approved for FI after discussions with our Technical Experts and Key Informants. Since PTNS can be used off label (although typically not reimbursed by insurance for FI) and percutaneous PTNS is under study for its utility for FI (especially prior to SNS), we added PTNS to the final review after consulting with our experts. One RCT is included under Nonsurgical Treatments (page 11 and Table 16); two other PTNS RCTs are listed in Appendix C, Excluded Studies.
TEP 7	Methods	See comments above for Table 1. Inclusion and exclusion criteria are appropriate for this review, as presented in Table 2. In the methods section (Page 13 and Page 14, line 57 and 4), new terminology is introduced for a new etiology, “early” vs “chronic” FI. This terminology is not used previously. While this may be relevant, these two terms are not previously defined.	We changed the statement under Applicability to: All treatments are not feasible for all FI etiologies at all time points (*newly diagnosed or with longstanding FI*) (pg. 7)
TEP 7	Methods	Please consider these additional trials with evidence on clinicaltrials.gov and pubmed: NCT00565136, NCT00727649 (study In Press – will be happy to send page proofs to you), NCT01475474 Cichowski SB, Dunivan GC, Rogers RG, Murrietta AM, Komesu YM. Standard compared with mnemonic counseling for fecal incontinence: a randomized controlled trial. Obstet Gynecol. 2015 May;125(5):1063-70 Sjödahl J1, Walter SA, Johansson E, Ingemansson A, Ryn AK, Hallböök O. Combination therapy with biofeedback, loperamide, and stool-bulking agents is effective for the treatment offecal incontinence in women - a randomized controlled trial. Scand J Gastroenterol. 2015 Aug;50(8):965-74.	We reviewed the four studies and none meet the study selection criteria for this review.

Commentator & Affiliation	Section	Comment	Response
TEP 7	Methods	***Consideration should be given for studies and the level of evidence for randomized trials that use PFMT vs PFMT with biofeedback. This evidence from the literature is not well-represented in this written review, but does exist in the tables for the results section. For example, the 2013 Cochrane review by Norton and Cody clearly presents this topic. Only data presented on PFMT-BF with or without electrostimulation is presented. This is a major concern for my review and represents a missed opportunity for this project (repeated twice for emphasis).	Thank you for your comment. Norton & Cody 2012 Cochrane review on biofeedback and sphincter exercises included 21 studies; 3 of their studies were not eligible for this review (an abstract, a conference abstract and an Australian government report). All other studies are listed in Tables 6-12, or are included in Appendix C of Excluded Studies. All studies of various PFMT iterations that met study selection criteria are presented in Tables 6-12. Table 7 contains PFMT-BF vs. PFMT alone. Authors sometimes used digital rectal feedback but called it *only PFMT*, which we considered to provide some feedback to patients over exercise training alone without digital (and verbal) feedback from the provider who provided the digital maneuver. So tables 8 and 9 may also cover some of the literature the Reviewer was interested in. We edited the PFMT report text for clarity (pages 11-12), and to match the sequential presentation of the various iterations PFMT in Tables 6-12.
Peer Reviewer 3	Methods	The conclusion and and exclusion criteria appear to be justifiable. A search strategies are explicitly stated and appeared to be logical however there is no definition given for "gray literature". The definitions and diagnostic criteria appear to be appropriate. I cannot comment on the statistical methods	We edited the statement on page 3. Grey literature has not been formally/commercially published (government or industry information, etc.)
Peer Reviewer 4	Methods	The methodology is very clear.	Thank you
Peer Reviewer 4	Methods	Appendix C – I take issue with some of these exclusions, but at least they are listed. #12 – the Glazener study is one of the few that has examined long-term effectiveness of a behavioral therapy (nurse-led PFME training). New publication this year examined 12-year outcomes. I recommend including that study series.	The Glazener articles are on UI and FI, and are listed in the Excluded Studies (Appendix C) with rationale. The authors failed to separately identify the initial group of FI patients in outcomes reporting (2001) and for baseline and outcomes reporting in subsequent study reports (2005, 2014). Since the incidence of FI increased over time in the entire sample (as did the number of drop outs), it is impossible to estimate the long term effects of treatment on the sample who initially had FI. All Glazener et al. studies were therefore excluded.

Commentator & Affiliation	Section	Comment	Response
TEP 1	Results	Evidence profiles are comprehensive and provide enough information.	Thank you
TEP 2	Results	A lot of discussion in this document focuses on the FI etiology and I think that there should be some discussion of the fact that patient often have multiple etiologies for their FI. In addition, FI phenotyping is incomplete. So, if we are to tailor treatments then more information must be known about the phenotyping.	We edited our etiologic statements on pg. 1 of the Introduction and extensively in the Discussion.
TEP 2	Results	Minor Comment: "Durasphere®76,77 (FDA-approved for vaginal bulking for urinary incontinence)." This should be changed to urethral bulking agent.	We changed the statement as suggested to urethral bulking agent (pg. 13 Results)
TEP 2	Results	"Low-strength, evidence at 6 months post-treatment suggests that dextranomer tissue-bulking injections are more effective than sham injections on FI quality of life, the number of FI-free days, and in reducing FI episodes 50 percent or more from baseline over 6 months; but no more effective than sham injection on FI severity and FI episode frequency." This is not clear to me – how can it reduce frequency by 50% but not change FI episode frequency?	We noted the same apparent discrepancy, but the authors (Graf et al. 2011) did not explain it in their article. Table 1 of the article shows the median FI frequency over 2 wks. at baseline was (15 injection group vs. 12.5 sham). The accompanying information shows wide *interquartile ranges* as (IQR 9.6 to 27.5 episodes injection vs 8 to 28 episodes sham). We corrected this statement to read, "…but no more effective than sham injection on FI severity and *median decrease in number of FI episodes from baseline*, which is directly stated in Graf et al. 2011 on page 1000 of their article. Graf et al. reported that their primary outcome (50% reduction in FI over 2 wks.) was based on the number of FI episodes (p 999 article). Changes in the median number of FI episodes from baseline between groups did not differ significantly at 3 months of 6 months but the actual change in number of FI episodes from baseline to 6 month follow-up per group was never reported. The finding could suggests that those who improved in both groups may have been on the lower end of FI frequency (e.g. ≥50% reduction in FI over 2 wks.) since it does not seem plausible that those with high FI frequency (28+ episodes per 2 wks.) in the sham group would have improved that much without treatment.

Commentator & Affiliation	Section	Comment	Response
TEP 2	Results	For the anal sphincter repair section, I think that it would be important to state that none of the RCT's examined one type of repair over the other, since this is a common point of discussion among surgeons.	Thank you for your suggestion. We did not include a statement regarding the lack of RCT information on overlapping vs. other types of repair; we reported on the comparisons we found to treat FI, but did not enumerate what we did not find. Technique comparisons that were not identified as being performed specifically to treat FI were excluded.
TEP 2	Results	Some comment should be made about the research that has been done for OASIS injuries, which is often extrapolated to non-OASIS lacerations. There are a number of RCTs that compare sphincter injuries in this population.	The results are limited to studies that were included in this report. We did not change the text
TEP 3	Results	As I stated above, this is the most comprehensive review of fecal incontinence literature.	Thank you
TEP 4	Results: page 8	Nonsurgical Key Points-first bullet: Is there an ability to differentiate this by type? Reducing 'gas' loss by 2.5 is very different than reducing 'solid' loss by 2.5. Most self-reported measures of frequency*type (Vaizey, FISI) etc. can be used for this, but are not likely to be reported that way due to the preference for reporting a single score. Perhaps part of the message to the research community and journal editors is - that full presentation of data as opposed to summary presentation would significantly improve our understanding	Thank you for your suggestions. Bliss et al. 2014 reported reductions in FI episodes. We called for more complete patient information at baseline in the Discussion pg. 35 under Limitations of the Evidence Base.
TEP 4	Results: page 8	Nonsurgical Key Points-2nd bullet: As a researcher I know what the Vaizey score is - but doubt that the general public will or even a person with FI will. What about providing a definition or at least reference so that people can look up what is being measured. (See Page 78: http://gut.bmj.com/content/44/1/77.full.pdf+html)	We added text to that Key Point (See Appendix E for FI outcome measures)
TEP 4	Results: page 25	Surgical Key Points, bullet 5 on MID: what definition(s) is/are have been used? 1/2 standard deviation, anchor (guyatt), delphi, expert?	We have added the method by which minimal clinically important differences were determined –see Appendix E: Common FI Outcome Measures.
TEP 5	Results	Adverse Events are addressed in the text but perhaps an additional column could be added in the tables of the treatments to include AE's. The amount of detail in the results section is appropriate.	Thank you for your suggestion. We retained the separate presentation of KQ1 (benefits of treatment) and KQ2 (adverse effects) that address each Key Question.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 1	Results	Results appropriately summarized, with tables used to provide details of the various studies: N, n, outcomes measures, treatment versus control interventions, findings, and potential for bias. I found the tables and appendices to be comprehensive and found the summary of results to be supported by the detailed data provided in the tables. I am not aware of studies that should have been included nor did I identify studies that should have been excluded.	Thank you for your compliment
TEP 6	Results	Yes, felt detail was very thorough - good job both providing summative info but also offering many details to allow reader to dig deeper	Thank you for your positive feedback
Peer Reviewer 2	Results	It is unclear to me, by which methodology the results of the SNS studies were construed as ineffective.	The evidence is insufficient because the few existing studies are of poor quality (moderate to high risk of bias) and each study differed in treatment and/or outcome used, making it impossible to aggregate data from several studies to better assess each SNS-outcome combination. Few, seriously flawed studies render the evidence insufficient at this time.
TEP 7	Results	The statement in the overview (Page 14, line 17-18), “planned to organize this section by etiologic subgroup was not possible” may need to be mentioned in the introduction given the problems with consistent terminology throughout the review.	Thank you for your suggestion. The statement refers to what was done so we left it in the Results.

Commentator & Affiliation	Section	Comment	Response
TEP 7	Results	Comments on the 'Nonsurgical Treatments' Section: Key Points do not include any evidence regarding PFMT ± Biofeedback (has RCT evidence according to the Cochrane review). Data on PFMT-BF with or without electrostimulation is presented despite the limited RCT evidence. Again, the phrase "all other PFMT studies assessed refinements in treatment delivery" is used under the key points section. This phrase needs more data presented to substantiate the statement. Please clarify what is meant by "refinements in treatment delivery." I am not convinced that the reviews understand that biofeedback is only a teaching tool for pelvic floor muscle exercises and sensation and not a stand-alone intervention. Pelvic floor muscle exercises can be taught with and without the use of instrumented biofeedback. The current evidence shows that biofeedback may be more beneficial than pelvic floor muscle exercise alone (study reference 56) after a run-in period to manage stool consistency. However when directly compared to advice alone, pelvic floor muscle exercises, home biofeedback or office-based instrumented biofeedback, no differences were seen between the groups (reference 55).	We edited the PFMT Results text for clarity pg. 11). We clarified the "refinements" terminology in this section We understand that biofeedback is used as a teaching tool for PFMT. However, the PFMT literature for FI poorly defined treatments, such that abstracts and article titles (and one professional guideline) often referred to the entire therapy as "biofeedback". We call for standardized terminology for PFMT in the Discussion, pg. 36*: Inconsistencies in the labeling of PFMT were particularly confusing….*
TEP 7	Results	The term "standard care" is NOT defined in the introduction but used in the results section when discussing stool consistency management/medication management and PFMT-BF. Stool modifying drugs are listed as BOTH pharmacological treatments and standard care treatments. Please clarify.	There is no standard care for FI. Each author defined their own "standard care". We clarified this point in the text: *standard care (such as …),* and in the report tables (see columns 2 vs 4 in the PFMT tables)
TEP 7	Results	Reference 52 appears to be misplaced under PFMT and adjunctive modalities. This is a drug treatment observational study.	The reviewer is correct. We have edited the reference with the correct citation on page 12 under PFMT.
TEP 7	Results	Again, the terminology for "Non-surgical Treatments with Permanent Effects" may not be the correct terminology.	We removed the subheadings in the Nonsurgical section.
TEP 7	Results	Table 3-6 are very clear and provide accurate information along with the appropriate level of risk assessment	Thank you

Commentator & Affiliation	Section	Comment	Response
TEP 7	Results	Table 7-10 could be combined. The issue of "standard care" makes these more difficult to discern as separate types of studies. For the Heymen study, please clarify that the "run-in" period maximized stool consistency treatment first. While I agree that these studies have differences in the delivery of PFMT, these differences are clearly presented in the Tables but not the text. Some clarification of the differences is needed in the text and not with the statement, "all other PFMT studies assessed refinements in treatment delivery." I struggle with term, "standard care treatment," for FI when so little evidence exists to inform the "standard" of care.	Thank you for your suggestion. We did not combine the tables. Each table reports a different treatment-comparator combination. We reported the terms (standard care) used by the authors in column2 of the PFMT tables, and then better defined the treatment in the same row of each table, in column 4 under Study Groups.
TEP 7	Results	Table 13/14 could be combined.	Thank you for your suggestion. We did not change the tables. Each table reports a different treatment-comparator combination.
TEP 7	Results	Table 15, 16, and 17 are clear and concise.	Thank you
TEP 7	Results	Surgical Treatments: Key points adequately summarize surgical trial findings. Clarification of the term "supportive care" is needed for this section. How does this differ from standard care treatments?	Same as above for nonsurgical tables
TEP 7	Results	The adverse events section was clearly presented.	Thank you
Peer Reviewer 3	Results	The results appear to be clearly presented and subcategorized by the different types of therapy. The studies appeared to be clearly presented and categorized in and easily understood fashion.	Thank you
Peer Reviewer 4	Results	Pg. 11, line 16 – Although it is stated that the cut off was October 2014, there is at least 1 reference from 2015 (Ref 11). I guess this came from the Grey literature searches.	We edited the statement on page 3. Grey literature has not been formally/commercially published (government or industry information, etc.)
Peer Reviewer 4	Results	– I disagree with the conclusion that PFMT-BF does not offer any advantage over standard care. Stepped therapy is the norm as expressed in the Intro. Heyman's study (ref 56) used stepped care and took patients who did not respond to standard care – dietary fiber supplements, stool-modifying drugs (treatments easily implemented in primary care) and randomized them to BF or PFME (both not usually well done in primary care) and BF was more effective.	We edited the statements regarding PFMT-BF to report that the evidence is insufficient to determine if there is a difference in the effects of the treatment vs. the comparator. See the footnote under Table 18**.** Heymen 2009 et al. only reported outcomes for randomized patients at 3 months; only successes (from either group) were selectively followed beyond 3 months up to 1 year (which is not the same as following all randomized patients to 1 year).

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 4	Results	Pg 18 – again we have the Nonsurgical Treatments with Permanent Effects and clearly the effects are not permanent. This terminology is misguided. Perhaps: Nonsurgical Treatments requiring More Invasive Procedures (although some would consider BF with an anal probe invasive) or just call this section "Perianal Injection Therapy". Or move BF with anal probes to this section. Then you would have basic non-surgical treatments, non-surgical treatments requiring move invasive procedures, and surgical procedures.	We removed the subtitles in the Results section. Tissue bulking injections are listed last under Nonsurgical Treatments.
Peer Reviewer 4	Results	"Nonsurgical Treatments requiring More Invasive Procedures" as a heading allows a place for percutaneous posterior tibial nerve stimulation (PTNS) which increasingly is being used for FI. A paragraph or even a sentence on PTNS and the lack of adequate studies is warranted about PTNS. The AHRQ Comparative Effectiveness Review is incomplete without it. Better yet, consider including the RCT of PTNS vs. SNS (Thin NN, et al, Br J Surg, 2015). You included the vaginal pessary for FI study by Richter, et al. which also came out in March of 2015).	We added one pilot RCT of PTNS (off label for FI) vs. SNS; two other PTNS RCTs are listed in Appendix C, Excluded Studies. Several case series exist but that design was not included for nonsurgical benefits evidence (KQ 1). The vaginal pessary case series for FI by Richter, et al. 2015 was mentioned in the Introduction, but did not come up in our evidence search until this update. The study was excluded because case series evidence was excluded for KQ 1 benefits- higher level evidence was required.
Peer Reviewer 4	Results	Pg 24 – Table 8, Heymen, 2009 study. There is so little longer term data available on treatment durability, recommend adding the data for the 12-month follow-up at the end of the last sentence.	Table 8 reports RCT outcomes. Beyond 3 months, the study selectively followed successes (not an RCT). We clarified in the Table 8 information that Heyman et al. only followed adults with adequate relief (either group) beyond 3 months, and denominators were not specified.
Peer Reviewer 4	Results	Pg 33 – Key Points first bullet. Rephrase second sentence: When reported, temporary nonsurgical treatments had no to few adverse effects that were minor. Reasoning …no adverse effects that were minor" makes no sense or at worst could be misinterpreted.	Thank you. We edited the first bullet under KQ 2 key points: *Few nonsurgical RCTs reported adverse effects (AEs). When reported, temporary nonsurgical treatments had few adverse effects and most were minor*
Public Reviewer 1 Christine Norton	Results	6 months does not seem very long for long term results Results need to last for life and this is a major problem with most studies. The few studies that have followed people for longer particularly surgical studies have shown major deterioration of short term results at 510 years. The results and particularly mentioned by name in the abstract seem to give undue support for Durasphere not FDA approved for this indication so should fall within your excluded interventions and with results deteriorating after a short follow up.	Thank you for your feedback. We called for longer term studies in the Discussion. Durasphere studies were assessed in the same manner as all other included studies.

Commentator & Affiliation	Section	Comment	Response
Public Reviewer 2 Heidi Brown, University of Wisconsin Madison	Results	Page 11 Nonsurgical Treatments with Permanent Effects Anal Sphincter Tissuebulking InjectionsDurasphere is described as being FDAapproved for vaginal bulking for urinary incontinence and should actually be described as being FDAapproved for urethral bulking to treat urinary incontinence.	Thank you for your feedback. We corrected the text to read urethral bulking for UI (pg. 13)
Public Reviewer 2 Heidi Brown, University of Wisconsin Madison	Results	Page 25 Surgicallyimplanted Sacral NeurostimulationI take issue with the conclusion There is insufficient evidence that sacral neurostimulation offers any outcomes advantage over supportive care for FI up to 1 year. The Mellgren and Wexner papers demonstrate impressive symptom improvement and it is unclear to me why their findings are not highlighted.	The evidence is insufficient due to serious methodological limitations. Please see the footnote under Table 18 and Strength of Evidence in the Methods section.
TEP 1	Discussion/ Conclusion	Would consider adding brief discussion about importance of patient-reported outcomes for this condition. Since recommendations are being made for future research, would consider adding that it is critical to include patient perspective in future trials.	Added text on the importance of patient-reported outcomes for FI in the Discussion under Research gaps
TEP 2	Discussion/ Conclusion	Research gaps should include patient validated measures of FI severity and QOL impact, as none of the current measures have significant patient input. This is pivotal, because without standardized outcome measures that are meaningful to patients, the literature is unlikely to improve.	See the point above
TEP 2	Discussion/ Conclusion	In the limitations sections, one of the limitations listed was that patients were included in studies with mixed etiologies of FI - while it is a limitation, I am not sure how this would be overcome - including only patients with a single etiology would likely provide evidence for only a very small portion of the population with FI.	We added the need for specific information on etiologic factors, and why knowing those items might be clinically important on page 32 of the Discussion under Applicability and Limitations of the Evidence Base.
TEP 2	Discussion/ Conclusion	One research gap is self-management strategies, which are commonly employed by patients with FI - and not very well studied.	We assume that the Reviewer is referring to diet, over the counter drugs, PFMT, education, toileting programs or irrigation, which are all included in this report to the extent that studies met inclusion criteria. We did not divide the interventions by who delivered them, although some studies used home vs. facility-based treatments which we identified. We did not change the text in response to this comment. The studies did not specifically address self-management per se, although it was inevitably a part of many interventions.

Commentator & Affiliation	Section	Comment	Response
TEP 3	Discussion/ Conclusion	While I know this overview of the FI literature strictly follows the statistical findings uncovered looking at each paper in the literature, FI is not as cut and dried as the authors imply. For instance --if this paper is really for the clinician to guide care, many clinicians categorize FI into mild and severe and recommend treatments based on this strategy. The authors may not have recognized this based on the discussion. (I do inderstand this is not reported as an obvious criteria in most research studies for FI but it is a true consideration when actually treating patients)	FI severity, defined in numerous ways ("episode" frequency, CCFIS or other scale at screening, etc.), was often used as a sample selection criteria in FI clinical studies. The problem with using mild to severe grading is that FI severity grading is not standardized in the provider community, or among patients. Moreover, both groups may disagree on FI severity rating for a given patient situation. So the field suffers from consistency problems in defining an FI episode, and grading the severity of those episodes, which we have now added to the Discussion under Applicability and Limitations of the Evidence Base.
TEP 3	Discussion/ Conclusion	While the literature is substandard as they state for FI, I am not sure why they are so surprised. Again FI is not as black and white as they imply. There are numerous factors that impact control of stool and they are dynamic and change frequently. Trying to categorize this is nearly an impossible task and has been attempted by numerous excellent clinicians. Standardization of definitions and the scoring system to be used for studies would be a worthy task and has been attempted without success over the past 15 years. Trying to understand why this standardization has not occurred would perhaps provide more insight into the substandard literature than merely being surprised by it (again I realize it is not the pure focus of this paper, but it would put into perspective why the FI literature is substandard).	We were surprised at the extent of noncompliance with longstanding CONSORT recommendations. We have provided more examples in the Discussion to better explain research gaps and areas for improvement in the FI evidence base. Exploring reasons why standardization has not occurred was not the goal of this review, but our additional examples in the Discussion may provide more context that can help clinicians and researchers advance the field, and with greater patient input.
TEP 3	Discussion/ Conclusion	While the critique of the authors for future research is true and again straightforward when just considering the pure results of the published studies, clincians have unsuccessfully tried to be more scientific in studying these problems. It is also important to remember that clinicians treating FI patients are desparately looking for answers to the two key questions asked by the authors. I am not sure if citing the longstanding reporting recommendations of CONSORT will move the mountains needed to have meaninful research. Researchers in FI are well aware of these recommendations and have failed for nearly two decades to find a way to conduct the precise research that the authors and FI patients seek.	We added two paragraphs early in the Research Gaps section of the Discussion that provide ideas for two broad research improvements that can advance the field.

Commentator & Affiliation	Section	Comment	Response
TEP 3	Discussion/ Conclusion	Again this is the most comprehensive review of FI literature. From a pure statistical perspective looking at numbers, I can follow their recommendations and understand why they make the statements they make. From an FI researcher standpoint, the discussion is frustrating. The substandard literature is obvious and well known to FI researchers. The discussion does not provide insight into HOW to realistically overcome the problems that FI researchers already know exist conducting these studies.	We added two paragraphs early in the Research Gaps section of the Discussion that provide ideas for two broad research improvements that can advance the field. We also provided more examples of specific issues in study conduct and reporting, and how they negatively impact study quality.
TEP 4	Discussion/ Conclusion: page 28, first statement	Wording implies that only US based studies were evaluated.	Only treatments available in the US were reviewed. Studies could be based anywhere (see also Table 1). We clarified that statement: *We found low-quality evidence to inform clinical decisionmaking for the range of treatments available for FI in adults in the United States*
TEP 4	Discussion/ Conclusion: pg 28 2nd paragraph	*Low strength evidence suggests*….: To differentiate quality of life from the FIQL instrument - would use FIQoL when referring to quality of life.	We edited that statement In the Discussion to read: …. *is no more effective than PFMT-BF on FI severity and changes in the FIQL instrument scores over 2 to 3 months.* We made edits throughput the report to clarify that FIQL refers to the FIQL instrument.
TEP 5	Discussion/ Conclusion	The Discussion/Conclusion section is direct and appropriate. It is clear that the situation is fairly dismal when it comes to evidence to inform clinical decisionmaking for the range of treatments for FI in adults in the United States. The research section is clear but whether it will be translated into new and improved research only time will tell. This may require some kind of inducement such as NIH grants with some control over methodology. Investigators will need to seriously consider these findings and work to improve how they move forward with the design of research studies, conducting trials and what is the desired outcome that patients want and need.	Thank you for this suggestion. We added two paragraphs to the Discussion/Research Gaps section that better delineates simultaneous steps that could advance FI research. While we agree that in some cases, study methodology/conduct needs to improve, journal editors could help improve study reporting by holding authors to existing CONSOR reporting guidelines prior to accepting manuscripts for publication.
Peer Reviewer 1	Discussion/ Conclusion	The implications of the major findings, and, more importantly, the major gaps in the evidence base are clearly addressed, and reinforce/explain the confusion I see in clinical practice. I think the authors did an excellent job in pointing out the ways in which study methodology should be improved (e.g., closer adherence to existing recommendations for research methodology), with the goal of conducting research that can be used to guide clinical practice.	Thank you

Commentator & Affiliation	Section	Comment	Response
TEP 6	Discussion/ Conclusion	Yes, clear	Thank you
Peer Reviewer 2	Discussion/ Conclusion	SNS therapy has changed the paradigm in the way FI is managed surgically. It has excellent short and long-term results. It is not clear methodologically how the authors concluded that this has little benefit over conservative management, furthermore, reliable lon-term evidence exists (see above) and I do not believe this has been included	The quality of the literature evidence for SNS to date is weak due to methodological limitations that were discussed in the report (KQ 1 surgical, SNS page 28; KQ 2 adverse effects Appendix tables (see pg. 30). Longer term evidence is from case series, and those studies were used for adverse effects reporting only. Higher quality studies could change the conclusions of this report.
TEP 7	Discussion/ Conclusion	The phrase “the situation is more dismal” introduces bias when discussing the evidence for surgical treatments. Please consider revising the phrase.	We revised the statements in the first paragraph of the Discussion to clarify that some nonsurgical treatments have low quality evidence, but that evidence is insufficient for all surgical treatments
TEP 7	Discussion/ Conclusion	Again the phrase “treatment delivery refinements” needs to be better explained in the results and the discussion sections. This phrase suggests bias from the review. I agree that several trials of PFMT for FI do not include a no treatment group or control groups for comparison, but this concept needs to be explicated stated and not just implied with the reference used (152).	We rearranged the order of the text on pg. 32 in the 3rd paragraph of the Discussion; no additional changes were made. We now believe that the information is clear in the context of the surrounding statement, and is stated elsewhere several times, with examples, in this report.
TEP 7	Discussion/ Conclusion	I still struggle with term, “standard care treatment,” for FI when so little evidence exists to inform the “standard” of care.	See above
TEP 7	Discussion/ Conclusion	The discussion point about the standardization of BF protocols is appreciated.	Thank you – it is an important point
TEP 7	Discussion/ Conclusion	The discussion regarding the number of outcomes measures and lack of ability to compare results across studies is appreciated. One the most common outcome measure, the bowel diary, is not well-discussed as a tool to measure FI episodes and urgency.	A bowel diary is a tool to collect information on FI episodes, urgency, pad use, consistency of fecal material and other outcomes. It is not an outcome in itself. The evidence tables list specific outcomes that were collected, regardless of the collection mechanism used. We did not change the text in this regard.
TEP 7	Discussion/ Conclusion	The paragraph of multiple FI etiologies and the term neurogenic FI is appreciated	Thank you

Commentator & Affiliation	Section	Comment	Response
TEP 7	Discussion/ Conclusion	Limitations are clearly presented. Please consider the addition of the definition of "standard care" treatments.	Standard care is author and etiology-specific; it differed depending on etiology and on duration and severity of FI, since treatments are often additive. The evidence tables list the specifics of each control group intervention when "standard care" was used. We edited the Discussion text on pg. 32, 5th paragraph of the Discussion) to clarify that standard care is not really standard.
TEP 7	Discussion/ Conclusion	Comments above from ongoing studies from clinicaltrials.gov are included in the discussion.	Agree
TEP 7	Discussion/ Conclusion	Conclusion is appropriately stated.	Thank you
Peer Reviewer 3	Discussion/ Conclusion	The major findings are clearly stated in the limitations of the review are well outlined. The difficulty in this area appears to be that the group of patients with fecal incontinence is an extremely heterogeneous one and many of the patient's have been subjected to or rather undergone perhaps multiple types of therapies before undergoing the study therapy on which the research is based. In addition the entire cohort of patients with FI is composed of individuals with many different individual and sometimes multiple causes for their fecal incontinence. Adding cognitive dysfunction to this group of individuals makes for a very difficult group to follow and evaluate over time.	Thank you
Peer Reviewer 4	Discussion/ Conclusion	Appendix F1 emphasizes the plethora of outcomes very well.	Thank you
Peer Reviewer 4	Discussion/ Conclusion	Paragraph 2 – You probably meant to say psyllium decreases FI episode frequency by 1 per month. However on page 16 you said psyllium decreases FI episodes by 2.5 per week. Of course without the baseline either of these statements are difficult to interpret.	Thank you – we corrected the statement to read: *Low-strength evidence suggests that dietary fiber supplementation with psyllium decreases FI episode frequency by 2.5 per week after 1 month of use;*
Peer Reviewer 4	Discussion/ Conclusion	Paragraph 4 – again you say "insufficient evidence that PFMT-BF offers any advantage over standard care with (dietary fiber and stool modifying drugs) for FI." Problems with this are noted in my earlier comment about the Heymen trial of stepped therapy. To be most accurate, would say "dietary fiber supplementation" since one could argue that fiber supplements differ from dietary fiber. Your criticism of lack of detail for the behavioral therapy protocols is well justified!	We edited the text in the Discussion, pg. 32 to: *We found insufficient evidence that PFMT-BF offers any advantage over standard care (such as dietary fiber supplementation, stool-modifying drugs, and education) for FI.*

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 4	Discussion/ Conclusion	Table 18 – Should really add the Heymen study (Ref 56). It significantly adds to the literature.	Table 18 membership required 1 high quality (low risk of bias) RCT for that treatment-outcome comparison (see Table 18 footnote). Heymen 2009 has moderate risk of bias and Whitehead 1985 of the same comparison has high risk of bias, so that comparison has insufficient literature evidence and therefore is not in Table 18. (See table footnote).
Peer Reviewer 4	Discussion/ Conclusion	Pg 38, lines 36-37 – Urgency is quite bothersome, but FI is exponentially worse. It is certainly awful and can be quite disabling to frequently have to rush to a bathroom and bathroom "map" or even restrict activities due to fear of FI. It is quite another to stand in a grocery store line and feel liquid stool run down your legs into your shoes. FI requires finding not only a bathroom, but often returning home to fully clean up. The currently phrasing demonstrates a clear underestimation of the burden of FI.	We edited the text in this area in the spirit of your suggestion but without the amount of detail that you have offered.
Peer Reviewer 4	Discussion/ Conclusion	Research Gaps section was well done in general. Conclusions section was well done.	Thank you
Public Reviewer 2 Heidi Brown, University of Wisconsin Madison	Discussion/ Conclusion	I agree with the conclusion that more research needs to be done before we declare certain therapies to be evidencebased but I think the evidence is stronger for SNS than your review concludes. I also think it is important to note that in the absence of clearly superior or more effective treatments engaging patients in a conversation about risks and benefits of each therapeutic option is important. Despite there being limited evidence to support PFMTBF for example there is also very little risk of harm from PFMTBF and we should be careful not to abandon therapies that are relatively safe in the absence of effective alternatives.	Thank you for your feedback. We are not suggesting that PFMT be abandoned; Rather, the quality of PFMT studies needs improvement. SNS evidence to date is largely from a few moderate to high risk of bias RCTs and a larger number of case series. Stronger designs, methodology and reporting are necessary to improve the SNS evidence quality
TEP 1	Clarity and Usability	The report is clear, and usable. Conclusions may not have immediate impact as data quality is overall limited.	Thank you
TEP 2	Clarity and Usability	With the comments above, this report does summarize and underline the deficiencies in the literature.	Thank you
TEP 3	Clarity and Usability	See above which is includes this domain	No response needed – see Peer Reviewer 3 TEP comments above

Commentator & Affiliation	Section	Comment	Response
TEP 5	Clarity and Usability	The report is well structured and main points are clearly stated. There are recommendations provided throughout the text and in the conclusion but it may be helpful to have some bullet point recommendations summarized at the end to help inform policy and or practice decisions.	Thank you for your suggestion. We used the Discussion to state of restate overarching themes and issues in the evidence base for FI treatments to date. We added ideas for advancing the research agenda for FI in the US. However, did not use a bullet point format for those recommendations.
Peer Reviewer 1	Clarity and Usability	I am a clinician rather than a researcher, and I found the report to be easy to follow, with summary statements clearly linked to the Tables and Appendices that provide supporting data. I believe the authors appropriately limited their conclusions to those supported by the data, which clearly identifies the huge gap in evidence related to this topic, and will hopefully result in increased funding and interest in FI-related research.	Thank you for your positive feedback.
TEP 6	Clarity and Usability	Yes - very clear, structured, like the tables that offer the basic information from the studies - easy to read and follow.	Thank you
Peer Reviewer 2	Clarity and Usability	the report spend too much time evaluating and discussing methods that are rarely, if ever, currently used, and I believe (but simply would like to be proven one way or the other) under asseses the clinical utility of the more commonly used, and more effective modalities of SNS	We reported on the available FI treatment evidence for FDA approved treatments. We did not select treatments on the frequency of use. We agree that some treatments (such as topical medications) are rarely used because evidence shows that they do not work for FI. We added this information to page 36 under Limitations of the Evidence Base
TEP 7	Clarity and Usability	While this review is extensive and comprehensive, some the existing evidence on BF and PFMT could be more clearly presented. Clarification of terminology is needed, especially in the introduction section. The discussion section is clearly stated with the exception of the two phrases/terms mentioned above. The tables and evidence summaries are valid. The Appendixes are also appreciated, especially the comments regarding the outcome measures.	We edited the PFMT-BF section for clarity and consistency with the order the tables were presented.
Peer Reviewer 3	Clarity and Usability	The report as well structured and organized and the main points are clearly presented. As a practitioner I found the conclusions somewhat helpful to my clinical practice. I find it difficult to see how this will be relevant for policy decisions.	Thank you – we agree on policy decisions based on current evidence.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer 3	Clarity and Usability	The multiple causes of fecal incontinence as well as the difficulties in performing research including the patient population with dementia as well as the difficulty of performing sham surgeries as comparisons for the surgical options continued to conspire to make challenging the possibilities for Future research as well as treatment of patients in clinical practice.	Agree
Peer Reviewer 4	Clarity and Usability	The report is well structured and organized. The main points are clearly presented, but need some editing as suggested above. The conclusions are relevant to policy and practice decisions. The report should contribute to understanding of FI treatments and the state of the science.	Thank you
TEP 4	Appendix	Title: “Analytic framework for treatments for fecal incontinence” Are you referring to the questionnaire or to FIQL in general? Confusing.	We clarified quality of life in Appendix A
Peer Reviewer 4	Appendix: Analytic framework	The figure is helpful for showing the key questions.	Thank you

Key: KIs=Key Informants; OBS = observational study with comparison group; pg. =page; RCT= randomized controlled trial; TEP=Technical Expert Panel