Comparative Effectiveness Review Disposition of Comments Report

Research Review Title: *Management of Colonic Diverticulitis*

Draft report available for public comment from June 2, 2020 to June 29, 2020.

Research Review Citation: Balk EM, Adam GP, Cao W, Danko K, Bhuma MR, Mehta S, Saldanha IJ, Beland MD, Shah N. Management of Colonic Diverticulitis. Comparative Effectiveness Review No. 233. (Prepared by the Brown Evidence-based Practice Center under Contract No. 290-2015- 00002-I.) AHRQ Publication No. 20(21)-EHC025. Rockville, MD: Agency for Healthcare Research and Quality; October 2020. DOI: 10.23970/AHRQEPCCER233. Posted final reports are located on the Effective Health Care Program search page.

Comments to Draft Report

The Effective Health Care (EHC) Program encourages the public to participate in the development of its research projects. Each draft report is posted to the EHC Program Web site or AHRQ Web site for public comment for a 3-4-week period. Comments can be submitted via the Web site, mail or E-mail. At the conclusion of the public comment period, authors use the commentators' comments to revise the draft report.

Comments on draft reports and the authors' responses to the comments are posted for public viewing on the Web site approximately 3 months after the final report is published. Comments are not edited for spelling, grammar, or other content errors. Each comment is listed with the name and affiliation of the commentator, if this information is provided. Commentators are not required to provide their names or affiliations in order to submit suggestions or comments.

This document includes the responses by the authors of the report to comments that were submitted for this draft report. 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.

Summary of Peer Reviewer Comments and Author Response

This research review underwent peer review before the draft report was posted for public comment on the EHC website.

- Technical Expert Panel (TEP) reviewer 1 noted a missing article about 5-ASA that had been omitted due to confusing language in the abstract. Study was added.
- TEP reviewer 2—
    - Highlighted a number of sentences and phrases in the Evidence Summary main points and the Results section's Key Points that needed clarification or further expounding. Edits were made. Most of the issues related to specifying more explicitly what comparisons were being made and in whom.
    - The reviewer also suggested evaluating colorectal cancer (CRC) rates found on colonoscopy by country. We added information about country to the Results, but were unable to discern patterns.
    - The reviewer suggested adding information about colonoscopy complication rates from the general population. We added a comment on this in the Discussion.
    - The reviewer suggested adding information about numbers needed to treat (NNT) and harm (NNH) for elective surgery. We responded that we do not attempt to determine a net benefit (e.g., NNT minus NNH) and that we believe that NNT and NNH are too unstable to be generalizable outside the individual studies.
- TEP reviewer 3 suggested possibly trimming the section on colonoscopy findings and reorganizing placement of figures. We did not make changes since we think the level of detail was appropriate and figure placement was standard for this type of report.
- TEP reviewer 4 found the report to be of "excellent quality" and did not make specific suggestions.
- TEP reviewer 5 regretted the lack of data on nutritional interventions and did not comment otherwise.
- Peer reviewer 1—
    - Recommended better specification of percutaneous drainage (than interventional radiology). We agreed and made changes accordingly.
    - Made several recommendations for the Introduction regarding more up-to-date information about incidence and prevalence in the United States. We made changes accordingly, including replacing some references with those suggested by the reviewer.
    - Made suggestions about putting the computed tomography (CT) findings into better clinical context regarding cost, radiation exposure, and poor accuracy of clinical (nonimaging) diagnosis. We revised the Discussion along these lines.
    - Suggested a specific study for possible inclusion regarding CT. We did not include the study because it did not provide sufficiently clear analyses of outcomes of interest.
    - Suggested newly published studies. The studies were found in the updated literature search, and the ones that met eligibility criteria were added.
    - Made various suggestions to clarify some language or to avoid misinterpretation. Changes were made accordingly.
- Peer reviewer 2 was highly complimentary and made no specific suggestions.

Public Comments and Author Response *for reports with sequential peer review and public comment*

Commentator & Affiliation	Section	Comment	Response
Public reviewer 1 Frank Hamilton, NIH/NIDDK	General Comments	The executive summary was clear. No suggestions.	Thank you
Public reviewer 1 Frank Hamilton, NIH/NIDDK	General Comments	One of the complications of acute diverticulitis that was not listed is bleeding	Bleeding may occur with acute diverticulitis but is not an indication of inflammation or of complicated presentation. As it is not a component, per se, of acute diverticulitis, we have omitted the concept.
Public reviewer 1 Frank Hamilton, NIH/NIDDK	Introduction	Introduction was clear . I was struck by lack of data about the sex, gender, and ethnic breakdown of US studies or (did I overlook these demographics).	We have added information in from NIS about gender and race.
Public reviewer 1 Frank Hamilton, NIH/NIDDK	Methods	Methods section was clear.	Thank you

Commentator & Affiliation	Section	Comment	Response
Public reviewer 1 Frank Hamilton, NIH/NIDDK	Results	Under "Summary of Evidence Pertaining to Antibiotics" This statement need editing. "As summarized in the evidence profile (Table 8), there is insufficient evidence regarding the relative value of antibiotics to affect the most pertinent clinical outcomes of death, treatment failure, length of hospital stay, diverticulitis-related morbidities, pain and tenderness, rehospitalization, or adverse events. Largely, this was due to sparse events or only a single study with evidence, making estimates highly imprecise or inconclusive." SUGGESTION: clinical outcomes of treatment failure, length of hospital stay, diverticulitis-related morbidities, pain and tenderness, rehospitalization, or adverse events and death.	With new evidence from newly published studies, the list of clinical outcomes is now shorter. We have listed the outcomes in order of clinical importance (or at least a reasonable approximation of this).
Public reviewer 1 Frank Hamilton, NIH/NIDDK	Results	I thought it would have been helpful to better describes the PREVENT study for non GI doctor/other healthcare providers who may not be familiar with the study and what the rationale of using 5 ASA commonly prescribed for inflammatory bowel disease.	We describe the PREVENT trials equally as the other studies. We have added short descriptions of 5-ASA, rifaximin, and probiotics at the start of each relevant Results section.
Public reviewer 1 Frank Hamilton, NIH/NIDDK	Discussion/conclusions	Reference section was appropriate.	Thank you

Commentator & Affiliation	Section	Comment	Response
Public reviewer 1 Frank Hamilton, NIH/NIDDK	Discussion/conclusions	the problem addresses a commo situation encountered in EDs and outpatient setting in normal or non compromised individuals. Since many ember sof the US population have several co morbidities , i.e.. heart disease, diabetes, hypertension, it may have been worthwhile to have mentioned that the treatment should take into account these comorbidities when planning treatment strategies with the patient and their family.	We have added to a sentence in the Discussion (under Elective Surgery): However, none of the studies addressed which patients may benefit more (or less) from elective surgery, in particular based on factors such as severity or frequency of diverticulitis, comorbidities, or age
Public reviewer 1 Frank Hamilton, NIH/NIDDK	General Comments	The report was easy to read	Thank you
Public reviewer 1 Frank Hamilton, NIH/NIDDK	General Comments	There was one table 6 Quality of life would benefit from a brief interpretation of the findings Table 6	We believe the accompanying text adequately describes the findings/outcome. Since there was no difference in effect, we did not elaborate about clinical effect size.
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	General Comments	Most of this is rehashing of the summary preceding summary statements, though the implications and conclusions are a bit more in depth. Here the authors again clearly state that very few if any guidelines can be provided based on the existing data and that further study is warranted.	Based on the needs and requirements for these reports, there is a fair amount of repetition across sections.
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	General Comments	Structured Abstract: This is a very well written section. The statements are concise and reflect the body of the manuscript, stating the purpose and methods, summarizing the findings in step by step fashion, presenting a very conservative conclusion.	Thank you

Commentator & Affiliation	Section	Comment	Response
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Methods	Methods are rigorous, meticulous and standardized. Each key questions criteria are defined and the related literature evaluated for bias, synthesized, analyzed and graded. Search yielded over 14K citations which were narrowed to 673 for further review, of which 71 primary studies were evaluated along with two systematic reviews. The group was quite clear about their exclusion criteria. Each Key Question was then reviewed, starting with a summary of the key points and findings for each. This detail is appreciated, with the data from studies either summarized or including figures from the actual papers.	Thank you
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Results	The statement regarding CT for diagnosis is convoluted. As written, itâ€™s difficult for the reader to understand the manuscripts guidance on this topic. That is to say it seems strange to be use the two qualifiers: "probably highly", in particular when the strength of evidence is quite high with a sensitivity of 94% and a specificity of 99% for diagnosis. An attempt should be made for clarity, and it seems reasonable to remove both qualifiers. "CT is accurate to diagnosis..." Though it is appreciated that there was an issue with the reference standard for these studies. The remainder of the CT recommendations are based on low strength of evidence.	In the Main Points, we have removed "probably higher" to state more definitively ("is accurate").

Commentator & Affiliation	Section	Comment	Response
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Results	The statements of treatment for acute diverticulitis are clear that there is not enough evidence to make a recommendation.	Thank you
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Results	The statements of colonoscopy following acute diverticulosis are clear, suggesting colonoscopy has value following an event in those 50 or older, while there is poor evidence otherwise.	Thank you
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Results	The statement on 5-ASA is clear that it is neither beneficial or harmful.	Thank you
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Results	The statement of elective surgery following acute diverticulosis for prevention is beneficial to reducing recurrent events is clear. Rates of complications are described.	Thank you

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Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Results	It is clear that an extensive amount of effort was made to formulate a series of key questions and then analyze existing literature for answers. A review of the studies incorporated into the analyses demonstrates that they chose only systematic reviews, randomized controlled trials, and large nonrandomized studies spanning nearly the past 30 years. They are quite clear that there were areas of interest that did NOT have existing studies to allow for guidelines on several of topics. Bias was evaluated for each study using appropriate tools. While the summary statements were designed for brevity, a large Appendix (D) was provided including detailed study level results on each topic. Strength of evidence was evaluated using the standard of AHRQ.	Thank you
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Appendices	Appendix A demonstrates the analytic approach to each of the key questions and then reviews in detail the methods used for study selection. Also the methods to assess the risk of bias were described along with details of data synthesis and analysis and grading the strength of evidence.	Thank you
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Appendices	Appendix B describes the excluded studies and the categorized reasoning.	Thank you

Commentator & Affiliation	Section	Comment	Response
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Appendices	Appendix C describes the included studies for each key question and then delineates the study design details and risk of bias for each. This is very detailed and well laid out.	Thank you
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	Appendices	Appendix D details the grading for each of the questions and details the results of each of the included studies which were then analyzed.	Thank you
Public reviewer 2 Lauren Loeding, American Society for Gastrointestinal Endoscopy	General Comments	Presented is a well written 79 page manuscript as well as 4 comprehensive appendices. The authors and or investigators were omitted and therefore personal bias to the literature is not feasible to evaluate.	Thank you. The authors (etc.) were redacted for the draft per AHRQ policy. They are listed in the final report.
Public reviewer 3 Anonymous commenter from American College of Physicians	General Comments	Thank you for the opportunity to review and comment on the draft comparative effectiveness review on the management of colonic diverticulitis. On behalf of ACP's Clinical Guidelines Committee, please find a summary of comments on the draft report. Please note that we identify page numbers as those provided in the footers (rather than PDF page number).	Thank you for your careful reading and comments.
Public reviewer 3 Anonymous commenter from American College of Physicians	Evidence Summary	1. We find the key messages (p.2) to be redundant of the "main points" (p.11).	As per the new AHRQ template, the Key Messages have been deleted. ted

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Public reviewer 3 Anonymous commenter from American College of Physicians	Evidence Summary	2. We recommend defining “recent diverticulitis” (with timeframe in parentheses), and “complicated diverticulitis” briefly within the text of the executive summary.	Thank you. We have added info about timing of colonoscopies to the Key Messages, Evidence Summary, and relevant Key Points.
Public reviewer 3 Anonymous commenter from American College of Physicians	Evidence Summary	3. On p. ES-1, the following sentence is difficult to follow: "There is low SoE that antibiotics for patients with uncomplicated diverticulitis do not affect risk of recurrence or quality of life but may reduce the need for surgery over the following year.” Consider breaking this into two sentences, one for “do not affect risk of recurrence or quality of life” and a second for "may reduce the need for surgery.”	After the update, the conclusions have changed, so the sentence is now simpler.
Public reviewer 3 Anonymous commenter from American College of Physicians	Evidence Summary	4. In the main points under “Colonoscopy following an episode of acute diverticulitis” (p.ES-1), we suggest briefly defining “complicated” in the following bullet point: “Among people with recent acute diverticulitis, those 50 or older or who had complicated diverticulitis.”	We've added "(with abscess, peritonitis, etc.)".
Public reviewer 3 Anonymous commenter from American College of Physicians	Evidence Summary	• It would also be helpful to provide a timeframe for the last bullet point: “Colonoscopies after acute diverticulitis rarely have complications or incomplete tests (high SoE).”	We have added a timeframe.

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Public reviewer 3 Anonymous commenter from American College of Physicians	Introduction	In the introduction (p.2), please clarify if the increased rate only applies to patients with recurrent or complicated diverticulitis in the following sentence: “Nevertheless, the rate of elective hemicolectomies in the U.S. following an episode of acute diverticulitis continues to rise (through 2016), particularly among those between 65 and 79 years old.”	We've revised the sentence so that it should be clearer now and have corrected the reference.
Public reviewer 3 Anonymous commenter from American College of Physicians	Methods	5. Data Synthesis and Analysis (p.8): Please check the following sentence: “When feasible and appropriate, we conducted random effects model pairwise meta-analyses. Details are in Appendix B.” Appendix B appears to summarize studies.	Apologies. Corrected. Now Appendix A.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Key Points	6. When summarizing areas of insufficient evidence under the main points and key points under each key question, it would be helpful to briefly note the reasons the evidence was insufficient (e.g. due to sparse data, small number of events, evidence too weak or inconsistent, etc.).	We have added reasons for insufficient evidence for all key/main points.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 9	7. Key Question 1 (p.9): The 4th bullet point (“Based on 3 studies, misdiagnoses on CT (i.e., false positive or negative CT scans) did not clearly result in poor clinical outcomes (low SoE)”seems inconsistent with the conclusions reported in the Summary of Findings table (“CT may have resulted in some cases of inappropriate management due to misdiagnosis”). This bullet point is more consistent with the key messages (p. ii “may not increase the risk”) but the inconsistent language describing the conclusion may cause confusion.	Thank you for finding the error in the SoE table. We have revised and confirmed the consistency of language throughout.

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Public reviewer 3 Anonymous commenter from American College of Physicians	Methods/Key Questions	8. Key Question 2: Dietary management is considered a mainstay of inpatient diverticulitis management (often in addition to antibiotics) - what is the role of dietary changes in reducing inflammation (clear liquid diet/NPO) during the acute episode? It is quite likely that there are insufficient data to answer this question, but it seems like a question related to diet may be worth considering under this key question.	Unfortunately, this was not included in the protocol as a Key Question of interest. KI and TEP discussions did not raise this as a Key Question to add. A scan through our list of rejected studies (accepted at the abstract level, but rejected in full text) did not find any studies of dietary management of acute diverticulitis.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 19	9. Key Question 2a (p.19) : The 3rd bullet point states that there is no evidence of a difference – we suggest rephrasing to clarify that there is "low-certainty evidence of no difference" or to make the phrasing consistent with the Main Points (p.ES-1, "there is low-certainty evidence that…rates…are similar).	Thank you. We have revised the Key Point to similar language as the Main Points.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 24	10. Key Question 2b (p.24): As with Key Question 2a, we suggest checking for consistency in how findings are reported in the summary of findings tables, the main points, the key messages, and various key points sections. Here, the key points state "studies found no differences" while the summary of findings table uses "no evidence of a difference."	We have rewritten the Key Messages (etc.) in a more conservative manner to describe as no evidence of a difference (rather than evidence of no difference). For the sake of conciseness, we did not revise the Abstract.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 24	• Also on p.24 – please check the first bullet point, should it read "…the evidence does not support that there are differences in most clinically important outcomes between either use of antibiotics or not or in choice of antibiotic regimens"?	Thank you. Typo corrected.

Commentator & Affiliation	Section	Comment	Response
Public reviewer 3 Anonymous commenter from American College of Physicians	Throughout	• Throughout, we recommend using the term “antibiotic treatment” when you are referring to antibiotics. E.g., instead of “There is low SoE that antibiotics for patients…” replace with “There is low SoE that antibiotic treatment for patients…”	We agree and have made changes throughout.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 32	11. Key Question 2c (p. 11; p.32): Please clarify what types of conclusions you are referring to in the line: “Interventional radiology (percutaneous drainage): The evidence is insufficient to make conclusions.”	We have clarified in the Key Messages and Main Points.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 37	12. Key Question 3 (p.37): The key points (5th bullet point) highlights a finding that older people are at higher risk for CRC than younger patients but we question why this particular finding is worth calling out. We suggest that the authors review this statement and clarify its intent.	Age is a typical factor to evaluate for subgroup differences. It's not clear to us that this subgroup difference requires explanation in the Key Points. We presume the reason for the age 50 cutpoint (used by 5 studies) is to match general population guidance for CRC screening. We discuss the possible implications of the findings in the Discussion (on page 78).
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 37	• Also on p. 37 – the following statement is reported in the main points (p.11) but not in the key points here: “There is low SoE that patients with recent diverticulitis may have an increased likelihood of having undiagnosed CRC or advanced colonic neoplasia (CRC or advanced adenomas).” Does this refer to diverticulitis vs. general population? If so, should probably report under key points on p. 37. For this same statement, please also confirm that certainty of evidence for premalignancy – should it be insufficient instead of low?	Yes, we have added clarifying text that this is compared with healthy controls. We have also corrected to remove premalignancy.

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Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 52	13. Key Question 4a/b (p. 52): Please check the certainty of evidence that is reported under key points for risk of recurrence and risk of adverse events – reported as high certainty in Table 15 but moderate in the key points.	Thank you. We corrected the Key Points.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 62	14. KQ 4c: The results only report on surgical management for recurrent or complicated diverticulitis - there is no statement regarding surgery following an initial episode of uncomplicated diverticulitis, though you do not explicitly exclude this from the key questions or discussion of related methods. Please clarify in your key questions and methods if you only addressed surgery for recurrent or complicated diverticulitis and if this is not the case, we recommend including a statement about what evidence, if any, there is for surgery after an initial episode of uncomplicated or non-recurrent diverticulitis.	We have edited to clarify that the conclusion refers to patients with history of complicated diverticulitis or smoldering/frequently recurrent after uncomplicated diverticulitis. We have added that "No eligible studies evaluated the relative effect of elective surgery for patients with nonrecurrent uncomplicated diverticulitis." We have also made this more explicit in the Evidence Profile.
Public reviewer 3 Anonymous commenter from American College of Physicians	Results/Page 62	• Also for this key question (p. 62), the implications section states that patients who undergo elective surgery “are at greatly reduced risk of recurrent diverticulitis” but the results do not present any sense of the absolute benefit, the though the absolute harm (death from surgery) is summarized. It would be helpful to the absolute reduction in recurrent diverticulitis and to provide information on the follow-up/timeframe.	We have more fully described the absolute rates, including NNT in the text of the Results. We have also added an implied summary NNT.