

## **Results of Topic Selection Process & Next Steps**

The nominator, the American College of Physicians (ACP), is interested in a new evidence review on the management of acute diverticulitis to develop new clinical practice guidelines.

This topic will go forward for refinement as a new systematic review. The scope of this topic, including populations, interventions, comparators, and outcomes, will be further developed in the refinement phase. When key questions have been drafted, they will be posted on the AHRQ Web site and open for public comment. To sign up for notification when this and other Effective Health Care (EHC) Program topics are posted for public comment, please go to <a href="https://effectivehealthcare.ahrg.gov/email-updates">https://effectivehealthcare.ahrg.gov/email-updates</a>.

# **Topic Brief**

Topic Name: 0796 Management of Acute Diverticulitis

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**Conflict of Interest:** None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

# Background

Colonic diverticulosis is a common condition in Western countries with prevalence rates that exponentially increases with age.<sup>1</sup> Under the age of 30, only 1-2% of patients have diverticulosis but by 80 years of age the prevalence increases to 50-66%.<sup>2,3</sup> About 10-25% of patients with diverticulosis will develop inflammation leading to a condition termed acute diverticulitis.<sup>4</sup> Acute diverticulitis can be subdivided into uncomplicated and complicated categories. In their lifetime, approximately 15–20% of individuals with diverticulosis will develop acute complicated diverticulitis (ACD).<sup>5</sup> As opposed to uncomplicated diverticulitis, ACD is characterized by the presence of phlegmon, abscess, or perforation.<sup>6</sup> Recurrent episodes of ACD can lead to late complications such as stenosis or fistula.<sup>7</sup>

Recently, there has been a substantial increase in incidence rates of both complicated and uncomplicated diverticulitis as well as a considerable rise in number of hospital admissions. This has led to a significant cost burden of up to \$2.4 billion annually in the United States attributable to diverticulitis complications alone.<sup>8,9</sup>

In recent years, several controversies have emerged with regards to the optimal management of acute diverticulitis.<sup>10</sup> Whether antibiotics are truly necessary for treatment of acute uncomplicated diverticulitis has been recently questioned.<sup>11</sup> Due to unfavorable mortality and complication rates for emergent surgery for ACD, physicians have opted to delay definitive surgical management by employing antibiotics and interventional radiology procedures such as percutaneous drainage of abscess in appropriate patients. Surgical approaches have also evolved from Hartmann's procedure to primary anastomosis with protective stoma or even laparoscopic lavage and drainage for diverticulitis complicated by perforations with purulent or feculent peritonitis.<sup>12</sup> Other areas of controversy include selection of the optimal imaging modality to diagnose diverticulitis as well as appropriateness of performing distal colonoscopy following a resolved episode of diverticulitis to detect occult colonic malignancy.<sup>13,14</sup> In addition, pharmacologic and non-pharmacologic measures such as 5-aminosalicylates and dietary modification, respectively, to prevent recurrent diverticulitis have been of recent interest for physicians.<sup>15, 16</sup>

**Nominator and Stakeholder Engagement:** The nominator, the American College of Physicians (ACP), is in need of a comprehensive systematic review to inform development of a new clinical practice guideline that will focus on management of acute diverticulitis (See Appendix C). Based on a search of clinical practice guidelines on the ACP website revealed that they do not have an existing guideline on acute diverticulitis management.

## **Key Questions and PICOTS**

The key questions for this nomination are:

Key Question 1: What are the effectiveness/harms and comparative effectiveness/harms of oral or parenteral antibiotics for the treatment of acute diverticulitis?

- a. Do the effectiveness/harms vary by route of administration of antibiotic, type of antibiotic, duration of course of antibiotic?
- b. Do the effectiveness/harms vary by patient characteristics or presentation of illness?

Key Question 2: What are the benefits and harms of CT imaging for the initial diagnosis of acute diverticulitis?

a. Do the benefits and harms vary by patient characteristics or presentation of illness?

Key Question 3: What are the benefits and harms of distant colonoscopy following an episode of acute diverticulitis?

a. Do the benefits and harms vary by patient characteristics or presentation/course of illness?

Key Question 4: What are the benefits and harms of interventional versus surgical management of recurrent diverticulitis?

a. Do the benefits and harms vary by patient characteristics or presentation/course of illness?

Key Question 5: What are the effectiveness and harms of pharmacological (e.g., mesalamine) and non-pharmacologic (e.g., dietary advice) interventions to prevent recurrent diverticulitis?

a. Do the effectiveness and harms vary by patient characteristics or presentation/ course of illness?

To define the inclusion criteria for the key questions we specify the population, interventions, comparators, outcomes, timing, and setting (PICOTS) of interest (Table 1).

Table 1. Key Questions and PICOTS

|               | KQ1: Antibiotics   | KQ2: Diagnostic<br>imaging   | KQ3: Follow-up<br>colonoscopy   | KQ4: Surgical and interventional treatments   | KQ5: Prevention<br>of recurrence  |
|---------------|--|--|---|---|---|
| Population    | Adults with diverticulitis   | Adults with diverticulitis   | Adults with resolved episode of ACD   | Adults with recurrent diverticulitis (complicated or uncomplicated)   | Adults with history of diverticulitis   |
|               | Subgroups: age,<br>ethnicity, gender,<br>comorbidities,<br>disease<br>presentation | Subgroups: age,<br>ethnicity, gender,<br>comorbidities,<br>disease<br>presentation | Subgroups: age,<br>ethnicity, gender,<br>comorbidities, disease<br>presentation | Subgroups: age, ethnicity, gender, comorbidities, disease presentation  | Subgroups: age,<br>ethnicity, gender,<br>comorbidities,<br>disease<br>presentation        |
| Interventions | Antibiotics (oral or parenteral)   | CT scan, MRI,<br>ultrasound  | Colonoscopy   | <ul> <li>Laparoscopic lavage and<br/>drainage</li> <li>Percutaneous drainage<br/>(interventional radiology)</li> <li>Surgical resection with primary<br/>anastomosis</li> <li>Hartmann's procedure</li> </ul> | Drug (ex. 5-amino<br>salicylates, etc.)<br>and non-drug (ex.<br>dietary)<br>interventions |

|             | KQ1: Antibiotics   | KQ2: Diagnostic                           | KQ3: Follow-up  | KQ4: Surgical and interventional   | KQ5: Prevention  |
|-------------|--|---|---|--|--|
|             |  | imaging                                   | colonoscopy   | treatments   | of recurrence  |
| Comparators | No antibiotics,<br>clear liquid diet<br>only, antibiotics by<br>other route of<br>administration,  | Other included<br>intervention            | No colonoscopy  | No intervention, other active intervention<br>Comparisons of interest:   | No intervention,<br>other drug, other<br>non-drug, drug vs.<br>non-drug,<br>combinations |
|             | type of antibiotic,<br>duration of course  |   |   | All ACD stages:<br>Intervention (surgery/laparoscopic<br>lavage and drainage) vs. no<br>intervention/antibiotics only  |  |
|             |  |   |   | For peri-colic and pelvic abscesses<br>(Hinchey stages I, II):<br>Percutaneous or laparoscopic<br>drainage vs. surgery |  |
|             |  |   |   | For purulent and feculent peritonitis<br>(Hinchey stages III, IV):<br>Laparoscopic lavage and drainage<br>vs. surgery  |  |
|             |  |   |   | For surgical approaches:<br>Primary anastomosis (with or<br>without<br>protective stoma) vs. Hartmann's<br>procedure   |  |
| Outcomes    | Resolution of<br>diverticulitis,<br>recurrent<br>diverticulitis,<br>avoidance of<br>surgery,<br>morbidity,<br>mortality, adverse<br>events | Diagnostic<br>accuracy, adverse<br>events | Occult colorectal<br>cancer, recurrent<br>diverticulitis, adverse<br>events | Resolution of diverticulitis,<br>morbidity, mortality, adverse events  | Recurrent<br>diverticulitis,<br>adverse events   |
| Timing      | All  | All                                       | Acute vs. convalescent  | All  | All  |

|         | KQ1: Antibiotics | KQ2: Diagnostic | KQ3: Follow-up | KQ4: Surgical and interventional | KQ5: Prevention |
|---------|------------------|-----------------|----------------|----------------------------------|-----------------|
|         |                  | imaging         | colonoscopy    | treatments                       | of recurrence   |
| Setting | Inpatient,       | Inpatient,      | Outpatient     | Inpatient, outpatient            | Outpatient      |
|         | outpatient       | outpatient      |                |                                  |                 |

Abbreviations: KQ=Key Questions; ACD=Acute Complicated Diverticulitis; MRI=Magnetic Resonance Imaging; CT=Computed Tomography

# Methods

We assessed nomination 0796 Management of Acute Diverticulitis, for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix A for detailed description of the criteria.

- 1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
- 2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
- 3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
- 4. Assess the potential impact a new systematic review or other AHRQ product.
- 5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
- 6. Determine the *potential value* of a new systematic review or other AHRQ product.

#### **Appropriateness and Importance**

We assessed the nomination for appropriateness and importance.

#### **Desirability of a New Review**

We searched for high-quality, completed or in-process evidence reviews published in the last three years on the key questions of the nomination. See Appendix B for sources searched.

#### Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

## Feasibility of New Evidence Review

We conducted a literature search in PubMed from August 2013 and August 2018. Due to diversity in the nature and the anticipated literature base for each KQ and to increase our specificity, we conducted separate searches for each KQ. The number of citations resulting from each KQ-specific search was less than 300 (74 for KQ1, 139 for KQ2, 84 for KQ3, 245 for KQ4, and 211 for KQ5). Thus, all abstracts for these citations were reviewed for potential inclusion in a systematic review. Recognizing that the evidence base for a clinical topic of interest likely grows exponentially over time, the size of a new systematic review was estimated by doubling the number of abstracts found to be relevant to KQs. See Table 2, Feasibility Column, Size/Scope of Review Section for the citations of included studies. See Appendix C for the PubMed search strategy and links to the ClinicalTrials.gov search.

## Value

We assessed the nomination for value. We considered whether or not the clinical, consumer, or policymaking context had the potential to respond with evidence-based change; and if a partner organization would use this evidence review to influence practice.

# Results

See Appendix A for detailed assessments of all EPC selection criteria.

#### **Appropriateness and Importance**

This is an appropriate and important topic. Diverticulitis represents a significant health burden with a prevalence rate that exponentially increases with age and its management exerts a significant cost burden in the United States and worldwide.

## **Desirability of a New Review/Duplication**

A new evidence review would not be duplicative of an existing evidence review. We found two systematic reviews from Cochrane that addressed two of the key questions. One was relevant to KQ4 that focused on laparoscopic versus open resection.<sup>17</sup> Though of high-quality, other treatments were not covered by the review. We also found one Cochrane review on mesalamine as a pharmacologic agent to prevent recurrent diverticulitis that is relevant to KQ5.<sup>18</sup> However, the review did not cover other drug classes or non-pharmacologic interventions. No reviews were found relevant to KQs 1-3.

We did not consider these systematic reviews duplicative because they only cover specific comparisons of the broader KQs and would not sufficiently address the needs of the nominator. See Table 2, Duplication column.

#### Impact of a New Evidence Review

A new systematic review may have high impact as the standard of care is unclear due to various available management interventions. Furthermore, as new data on minimally-invasive treatments emerge, recommendations continue to evolve.

#### Feasibility of a New Evidence Review

We found eight studies for KQ1 (antibiotic treatment); one for KQ2 (CT scan for diagnosis); 15 for KQ3 (follow-up colonoscopy); 23 for KQ4 (surgical and interventional radiology treatment); and one for KQ5 (prevention of recurrence). Many studies included individuals with diverticulitis and it was unclear whether subgroup analysis was performed for those with recurrent diverticulitis where inclusion for KQ4 was evaluated. Despite the absence of this information, we were inclusive and included those studies.

For KQ1, we identified three randomized controlled trials (RCTs) that compared treatment with antibiotics versus observation among patients with acute diverticulitis.<sup>19-21</sup> We also identified five observational studies which were primarily retrospective cohort studies that compared patients who received antibiotics versus those who did not receive antibiotics.<sup>11, 22-25</sup>

For KQ 2, we identified one observational study comparing CT to ultrasound for the diagnosis of diverticulitis.<sup>26</sup> This study included adults with right lower quadrant pain, and was not restricted to those with suspected acute complicated diverticulitis.

For KQ 3, we identified 15 studies on follow-up colonoscopy all of which were observational,<sup>27-41</sup> which included secondary analysis of RCT data.

KQ 4, we identified 23 studies including seven RCTs of surgical and other treatments for acute diverticulitis across a variety of interventions and comparators:

## <u>RCTs</u>

- Laparoscopic lavage vs. operative resection<sup>42-46</sup>
- Observation vs. elective surgery<sup>47</sup>
- Hartmann's procedure vs. primary resection and anastomosis<sup>48</sup>

#### Observational studies

- Non-operative management (no comparator)<sup>49-51</sup>
- Non-operative management (antibiotics, bowel rest, percutaneous drainage) vs. surgery<sup>52, 53</sup>
- Laparoscopic sigmoid colectomy (no comparator)<sup>54</sup>
- Laparoscopic vs. open sigmoid colectomy<sup>55-57</sup>
- Non-operative management vs. surgery vs. laparoscopic lavage<sup>58</sup>
- Hartmann's procedure vs. primary resection and anastomosis<sup>59</sup>
- Laparoscopic lavage and drainage (no comparator)<sup>60, 61</sup>
- Laparoscopic lavage and drainage vs. Hartmann's procedure<sup>62</sup>
- Laparoscopic lavage and drainage vs. Hartmann's procedure vs. primary resection and anastomosis<sup>63, 64</sup>

However, the patient population was broader and included all individuals with history of acute diverticulitis. Separate analysis of those with history of recurrent diverticulitis was variably reported in the abstracts. In the absence of clarity regarding this information, we included those studies.

For KQ 5, we identified five studies which examined chemopreventive approaches mostly using mesalazine (aka mesalamine), a 5-aminosalicylate used to treat ulcerative colitis, to prevent recurrent diverticulitis. Three were RCTs and two were observational covering a variety of comparisons:

<u>RCTs</u>

- Mesalazine with probiotics vs. mesalazine alone vs. probiotics alone<sup>65</sup>
- Mesalazine (varying dosages) vs. placebo<sup>66, 67</sup>

## Observational studies

- Intermittent vs. daily mesalazine<sup>68</sup>
- Mesalazine vs. rifaximin<sup>69</sup>

We also found 15 RCTs on ClinicalTrials.gov relevant to four of the five KQs. See Table 2 for breakdown by KQ and Appendix C for hyperlinks.

| Key Question     | Duplication (08/2015-04/2018)                    | Feasibility (08/2013-08/2018)  |
|------------------|--|--|
| KQ1: Antibiotics | Total number of identified systematic reviews: 0 | Size/scope of review<br>Relevant Studies Identified: 8<br>• RCT – 3 <sup>19-21</sup><br>• Observational studies – 5 <sup>11, 22-25</sup> |
|                  |  | Clinicaltrials.gov<br>• Completed: 2   |

#### Table 2. Key Questions and Results for Duplication and Feasibility

| Key Question    | Duplication (08/2015-04/2018)         | Feasibility (08/2013-08/2018)                                  |
|-----------------|---------------------------------------|--|
| KQ2: Diagnostic | Total number of identified systematic | Size/scope of review   |
| imaging         | reviews: 0                            | Relevant Studies Identified: 1                                 |
|                 |                                       | <ul> <li>Observational studies – 1<sup>26</sup></li> </ul>     |
|                 |                                       |  |
|                 |                                       | Clinicaltrials.gov   |
|                 |                                       | Recruiting: 1  |
| KQ3: Follow-up  | Total number of identified systematic | Size/scope of review   |
| colonoscopy     | reviews: 0                            | Relevant Studies Identified: 15                                |
|                 |                                       | <ul> <li>Observational studies – 15<sup>26-41</sup></li> </ul> |
|                 |                                       |  |
|                 |                                       | <u>Clinicaltrials.gov</u>                                      |
|                 |                                       | None   |
| KQ4: Surgical   | Total number of identified systematic | Size/scope of review   |
| and             | reviews: 1                            | Relevant Studies Identified: 23                                |
| interventional  | Cochrane: 1 <sup>17</sup>             | • RCT – 7 <sup>42-48</sup>                                     |
| management      |                                       | <ul> <li>Observational – 16<sup>49-64</sup></li> </ul>         |
|                 |                                       |  |
|                 |                                       | <u>Clinicaltrials.gov</u>                                      |
|                 |                                       | Completed: 4   |
|                 |                                       | Recruiting: 3  |
|                 |                                       | Unknown: 2   |
| KQ5: Prevention | Total number of identified systematic | Size/scope of review   |
| of recurrence   | reviews: 1                            | Relevant Studies Identified: 5                                 |
|                 | Cochrane: 1 <sup>18</sup>             | • RCT – 3 <sup>65-67</sup>                                     |
|                 |                                       | <ul> <li>Observational - 2<sup>68,69</sup></li> </ul>          |
|                 |                                       |  |
|                 |                                       | <u>Clinicaltrials.gov</u>                                      |
|                 |                                       | Completed: 2   |
|                 |                                       | Not yet recruiting: 1  |

Abbreviations: KQ=Key Question; RCT=Randomized Controlled Trial

# Value

The potential for value is high. A high-quality systematic review will inform clinical decisionmaking on managing patients with acute diverticulitis. In addition to the nominator, other medical specialty societies will find the new review useful for development of their practice guidelines.

# **Summary of Findings**

- <u>Appropriateness and importance</u>: The topic is both appropriate and important.
- <u>Duplication</u>: A new review would not be duplicative of an existing product. We found Cochrane reviews that are relevant but do not fully address the pertinent KQs.
- <u>Impact</u>: A new systematic review would have high impact because it would help resolve current controversies and lead to a clinical practice guideline that will promote better patient outcomes and reduce unnecessary healthcare expenditure.
- <u>Feasibility</u>: A new review is feasible. The evidence base is likely medium-sized.
- <u>Value</u>: The potential for value is high.

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# Appendix A. Selection Criteria Summary

| Selection Criteria  | Assessment  |
|---|---|
| 1. Appropriateness  |   |
| 1a. Does the nomination represent a health care<br>drug, intervention, device, technology, or health care<br>system/setting available (or soon to be available) in<br>the U.S.?     | Yes, this topic represents health care drugs and interventions available in the U.S.  |
| 1b. Is the nomination a request for a systematic review?  | Yes, this topic is a request for a systematic review.   |
| 1c. Is the focus on effectiveness or comparative effectiveness?   | The focus of this review is on both effectiveness and comparative effectiveness.  |
| 1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?                                   | Yes, it is biologically plausible. Yes, it is consistent with what is known about the topic.  |
| 2. Importance   |   |
| 2a. Represents a significant disease burden; large proportion of the population   | Yes, this topic represents a significant burden<br>with a prevalence rate that exponentially<br>increases with age.   |
| 2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population                  | Yes, this topic affects heath care decisions with significant cost differences based on choice of treatment intervention. Clinical outcomes may vary as well.   |
| 2c. Represents important uncertainty for decision makers  | Yes, this topic represents important uncertainty for decision makers.   |
| 2d. Incorporates issues around both clinical benefits and potential clinical harms  | Yes, this nomination addresses both benefits and potential harms.   |
| 2e. Represents high costs due to common use, high<br>unit costs, or high associated costs to consumers, to<br>patients, to health care systems, or to payers                        | Yes, the total national cost attributable to<br>treatment of diverticulitis complications in the<br>United States is approximately \$2.4 billion<br>annually. This does not even include the cost of<br>managing uncomplicated diverticulitis.  |
| 3. Desirability of a New Evidence<br>Review/Duplication   |   |
| 3. Would not be redundant (i.e., the proposed topic<br>is not already covered by available or soon-to-be<br>available high-quality systematic review by AHRQ or<br>others)          | Yes. Existing systematic reviews do not address the full scope of the topic nomination.   |
| 4. Impact of a New Evidence Review  |   |
| 4a. Is the standard of care unclear (guidelines not<br>available or guidelines inconsistent, indicating an<br>information gap that may be addressed by a new<br>evidence review)?   | Yes, the standard of care is unclear due to<br>various available management interventions.<br>Recommendations among clinical experts vary<br>and guidelines are inconsistent particularly with<br>regards to optimal treatment for specific<br>subtypes of ACD. Furthermore, as new data on<br>minimally-invasive treatments emerge,<br>recommendations continue to evolve. |
| 4b. Is there practice variation (guideline inconsistent<br>with current practice, indicating a potential<br>implementation gap and not best addressed by a<br>new evidence review)? | Yes, there is wide practice variation due to conflicting data/opinion.  |

| 5. Primary Research   |   |
|---|---|
| <ul> <li>5. Effectively utilizes existing research and<br/>knowledge by considering:</li> <li>Adequacy (type and volume) of research for<br/>conducting a systematic review</li> <li>Newly available evidence (particularly for updates<br/>or new technologies)</li> </ul> | <i>Size/scope of review:</i> We estimate that the total size of the relevant literature may be approximately 108 studies across the five key questions (low confidence). The scope of the review is likely medium-sized.  |
|   | <i>ClinicalTrials.gov</i> : We found two RCTs relevant to KQ1, one relevant to KQ2, nine relevant to KQ4, and one relevant to KQ5.  |
| 6. Value  |   |
| 6a. The proposed topic exists within a clinical,<br>consumer, or policy-making context that is amenable<br>to evidence-based change   | Yes, this topic will inform clinical decision-<br>making on managing patients with acute<br>diverticulitis.   |
| 6b. Identified partner who will use the systematic<br>review to influence practice (such as a guideline or<br>recommendation)   | Yes, ACP will use a systematic review to<br>formulate a new guideline. It may potentially be<br>utilized by AAFP as well as. In addition, AHRQ<br>will reach out to gastroenterology (ex. AGA)<br>and colorectal surgery societies (ex. ASCRS) to<br>determine their interest in participating as<br>formal non-sponsoring partners for the review. |

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; KQ=Key Question; ACP=America College of Physicians; AAFP=American Academy of Family Physicians; RCT=Randomized Controlled Trial; AGA=American Gastroenterological Association; ASCRS=American Society of Colon and Rectal Surgeons; ACD=Acute Complicated Diverticulitis

# Appendix B. Search for Evidence Reviews (Duplication)

Listed are the sources searched.

AHRQ: Evidence reports and technology assessments, USPSTF recommendations

VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program

Cochrane Systematic Reviews and Protocols <u>http://www.cochranelibrary.com/</u> PubMed

PROSPERO Database (international prospective register of systematic reviews and protocols) <a href="http://www.crd.york.ac.uk/prospero/">http://www.crd.york.ac.uk/prospero/</a>

# Appendix C. Search Strategy & Results (Feasibility)

| Topic: Management of Acute  |   |
|---|---|
| Diverticulitis  |   |
| Date: August 13, 2018   |   |
| Database Searched: Ovid   |   |
| MEDLINE(R) Epub Ahead of  |   |
| Print In-Process & Other  |   |
| Non-Indexed Citations Ovid  |   |
| MEDINE(D) Deily and Ovid  |   |
|   |   |
| MEDLINE(R) 1946 to Present  |   |
| CONCEPT   | SEARCHES  |
| *Overell Secret*  |   |
| Divertionalitie   | Disentiaulitie. Optenia/ en disentiaulitie toulet   |
| Diverticulitis  | Diverticulitis, Colonic/ or diverticulitis.tw,kt.   |
| AND   |   |
| Acute   | acute disease/ or acute.tw,kt.  |
| Limit to last 5 years, English  | Filter activated: published in the last 5 years, English  |
| N=606   |   |
|   |   |
| *Search by Key Question*  |   |
|   |   |
| Key Question 1  |   |
|   | Overall Search Results  |
| AND   |   |
| Antibiotics   | exp Anti-Bacterial Agents/ or ((oral* or parenteral*) adj3 (antibiotic* or  |
|   | antibacterial* or anti-bacterial*)).tw,kf.  |
| N=74  |   |
|   |   |
|   |   |
| Key Question 2  |   |
| Key Question 2  | Overall Search Results  |
| Key Question 2  | Overall Search Results  |
| Key Question 2<br>AND   | Overall Search Results  |
| Key Question 2<br>AND<br>Imaging  | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)) tw kf ) and (exp Diagnosis/ or diagnos* tw kf, or   |
| Key Question 2<br>AND<br>Imaging  | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di fs.)  |
| Key Question 2<br>AND<br>Imaging  | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)  |
| Key Question 2<br>AND<br>Imaging<br>N=139   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)  |
| Key Question 2<br>AND<br>Imaging<br>N=139<br>Key Question 3   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)  |
| Key Question 2         AND         Imaging         N=139         Key Question 3   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)  |
| Key Question 2 AND Imaging N=139 Key Question 3 AND   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)<br>Overall Search Results  |
| Key Question 2         AND         Imaging         N=139         Key Question 3         AND   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)<br>Overall Search Results  |
| Key Question 2         AND         Imaging         N=139         Key Question 3         AND         Colonoscopy (KQ3)   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)<br>Overall Search Results<br>colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*) tw kf   |
| Key Question 2         AND         Imaging         N=139         Key Question 3         AND         Colonoscopy (KQ3)   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)<br>Overall Search Results<br>colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*).tw,kf.  |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84  | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)<br>Overall Search Results<br>colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*).tw,kf.  |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84  | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)<br>Overall Search Results<br>colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*).tw,kf.  |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)<br>Overall Search Results<br>colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*).tw,kf.  |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4   | Overall Search Results<br>(Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.)<br>Overall Search Results<br>colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*).tw,kf.  |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4         AND   | Overall Search Results (Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.) Overall Search Results colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*).tw,kf. Overall Search Results Overall Search Results   |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4         AND         Treatments (KQ4)                                      | Overall Search Results (Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.) Overall Search Results colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*).tw,kf. Overall Search Results Coverall Search Results Device a constraint of the second secon |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4         AND         Treatments (KQ4)                                      | Overall Search Results         (Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2 (scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or di.fs.)         Overall Search Results         colonoscopy/ or sigmoidoscopy/ or (colonoscop* or sigmoidoscop*).tw,kf.         Overall Search Results         Overall Search Results         Laparoscopy/ or Therapeutic Irrigation/ or Radiology, Interventional/ or Drainage/ or (drainage or Hartmann or irrigat* or laparoscop* or lavage   |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4         AND         Treatments (KQ4)                                      | Overall Search Results         (Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2 (scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or di.fs.)         Overall Search Results         colonoscopy/ or sigmoidoscopy/ or (colonoscop* or sigmoidoscop*).tw,kf.         Overall Search Results         Overall Search Results         Colonoscopy/ or sigmoidoscopy/ or (colonoscop* or sigmoidoscop*).tw,kf.         Doverall Search Results         Doverall Search Results         Overall Search Results   |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4         AND         Treatments (KQ4)         N=245                        | Overall Search Results         (Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2 (scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or di.fs.)         Overall Search Results         colonoscopy/ or sigmoidoscopy/ or (colonoscop* or sigmoidoscop*).tw,kf.         Overall Search Results         Overall Search Results         Laparoscopy/ or Therapeutic Irrigation/ or Radiology, Interventional/ or Drainage/ or (drainage or Hartmann or irrigat* or laparoscop* or lavage or "primary anastomosis" or radiolog* or resect*).tw,kf.  |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4         AND         Treatments (KQ4)         N=245                        | Overall Search Results         (Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2 (scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or di.fs.)         Overall Search Results         colonoscopy/ or sigmoidoscopy/ or (colonoscop* or sigmoidoscop*).tw,kf.         Overall Search Results         Overall Search Results         Doverall Search Results         Colonoscopy/ or sigmoidoscopy/ or (colonoscop* or sigmoidoscop*).tw,kf.         Doverall Search Results         Doverall Search Results         Overall Search Results         Dirainage/ or (drainage or Hartmann or irrigat* or laparoscop* or lavage or "primary anastomosis" or radiolog* or resect*).tw,kf.   |
| Key Question 2         AND         Imaging         N=139         Key Question 3         Colonoscopy (KQ3)         N=84         Key Question 4         AND         Treatments (KQ4)         N=245         Key Question 5 | Overall Search Results (Tomography, X-Ray Computed/ or ((ct or comput*-tomograph*) adj2<br>(scan* or imag*)).tw,kf.) and (exp Diagnosis/ or diagnos*.tw,kf. or<br>di.fs.) Overall Search Results colonoscopy/ or sigmoidoscopy/ or (colonoscop* or<br>sigmoidoscop*).tw,kf. Overall Search Results Uaparoscopy/ or Therapeutic Irrigation/ or Radiology, Interventional/ or<br>Drainage/ or (drainage or Hartmann or irrigat* or laparoscop* or lavage<br>or "primary anastomosis" or radiolog* or resect*).tw,kf.  |

| AND                         |  |
|-----------------------------|--|
| Recurrence prevention (KQ5) | Recurrence/ or Secondary Prevention/ or Tertiary Prevention/ or  |
|                             | (prevent* or recurr*).tw,kf.   |
| OR                          |  |
| Prevention strategies       | Mesalamine/ or exp Diet/ or Dietary Fiber/ or Probiotics/ or (5-<br>aminosalicylate* or "5-amino salicylate*" or diet* or drug* or fiber or<br>fibre or mesalamine or non-drug or nondrug or non-pharmacol* or<br>nonpharmacol* or pharmacol* or probiotic*).tw,kf. or dh,dt,tu,pc.fs. |
| N=211                       |  |

## ClinicalTrials.gov

99 studies found for: diverticulitis (relevant trials broken down by KQ below) https://clinicaltrials.gov/ct2/results?cond=diverticulitis&term=&cntry=&state=&city=&dist=

KQ 1 (Antibiotics)

- Antibiotics vs. resection (completed) <u>https://clinicaltrials.gov/ct2/show/NCT01986686?cond=diverticulitis&draw=2&rank=15;</u>
- Antibiotic vs. resection (completed)
   <u>https://clinicaltrials.gov/ct2/show/NCT01276886?cond=diverticulitis&draw=4&rank=37</u>
- KQ 2 (Diagnostic Imaging)
  - Low-dose CT vs routine CT (recruiting)
     <u>https://clinicaltrials.gov/ct2/show/NCT03443011?cond=diverticulitis&rank=2</u>

## KQ 3 (Follow-up Colonoscopy)

- None
- KQ 4 (Treatments)
  - Hartmann vs. sigmoid resection and anastomosis (completed)
     <u>https://clinicaltrials.gov/ct2/show/NCT01239927?cond=diverticulitis&draw=4&rank=32</u>
  - Laparoscopic vs. open sigmoid colectomy (completed) <u>https://clinicaltrials.gov/ct2/show/NCT00453830?cond=diverticulitis&draw=4&rank=40</u>
  - Primary vs secondary anastomosis (completed) <u>https://clinicaltrials.gov/ct2/show/NCT00692393?cond=diverticulitis&draw=5&rank=49</u>
  - Hartmann's vs. primary anastomosis (completed) https://clinicaltrials.gov/ct2/show/NCT01233713?cond=diverticulitis&draw=7&rank=64
  - Lap peritoneal lavage vs. lap sig (recruiting)
     <u>https://clinicaltrials.gov/ct2/show/NCT03008707?cond=diverticulitis&rank=7</u>
  - Laparoscopic lavage (recruiting)
     <u>https://clinicaltrials.gov/ct2/show/NCT02662088?cond=diverticulitis&draw=5&rank=41</u>
  - Elective laparoscopic sigmoid resection vs. dietary supplement (recruiting) https://clinicaltrials.gov/ct2/show/NCT02174926?cond=diverticulitis&draw=6&rank=51
  - Hartmann's or resection with anastomosis vs. lap lavage (unknown) <u>https://clinicaltrials.gov/ct2/show/NCT01019239?cond=diverticulitis&rank=8</u>
  - Lap peritoneal lavage vs resection (unknown)
     <u>https://clinicaltrials.gov/ct2/show/NCT01317485?cond=diverticulitis&draw=3&rank=28</u>
- KQ 5 (Recurrence prevention)
  - SPD476/Mesalazine (completed) https://clinicaltrials.gov/ct2/show/NCT00545740?cond=diverticulitis&draw=3&rank=29; https://clinicaltrials.gov/ct2/show/NCT00545103?cond=diverticulitis&draw=3&rank=30
  - Rifaximin (not yet recruiting)
     <u>https://clinicaltrials.gov/ct2/show/NCT03469050?cond=diverticulitis&rank=3</u>