

American Gastroenterological Association Institute Technical Review on the Management of Acute Diverticulitis



Lisa L. Strate,^{1,*} Anne F. Peery,^{2,*} and Ignacio Neumann^{3,4}

¹Division of Gastroenterology, Department of Medicine, University of Washington School of Medicine, Seattle, Washington; ²Division of Gastroenterology, Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina; ³Department of Internal Medicine, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile; and ⁴Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada

See commentary on page 1650; Guideline on page 1944; and commentary by Robert M. Centor in *Annals of Internal Medicine*. <http://annals.org/article.aspx?doi=10.7326/M15-2499>

Diverticulosis is a condition in which sac-like protrusions develop in the wall of the colon. The prevalence of diverticulosis increases with age; less than 20% of people younger than 40 years of age are noted to have diverticulosis on colonoscopy, compared with more than 60% of people older than 70 years of age.¹ Acute diverticulitis is macroscopic inflammation of a diverticulum or diverticula. An abscess, perforation, fistula, or colonic obstruction resulting from diverticulitis is designated as complicated diverticulitis. An estimated 4% of patients with diverticulosis will develop acute diverticulitis;² of those, 15% will have complicated disease.³ After recovery from a first episode of diverticulitis, 15% to 30% of patients will experience recurrence.^{4–6} Patients with diverticulosis can also develop other disease manifestations, including symptomatic uncomplicated diverticular disease (SUDD), diverticular bleeding, and segmental colitis associated with diverticulosis, which will not be the focus of this review. In addition, this review does not examine the prevention of incident diverticulitis in patients with diverticulosis or the management of complicated diverticulitis.

The classic patient with diverticulitis presents with pain in the left lower quadrant of the abdomen, fever, and leukocytosis,⁷ although many patients present without this triad. Other presenting signs and symptoms include a change in bowel habits, nausea, vomiting, urinary symptoms, and elevated inflammatory markers. Diverticulitis is considered a disease of older people but is increasingly being diagnosed in patients younger than 40 years of age.⁸ Of those older than 65 years of age, diverticulitis appears to be more common in women; however, there is a male predominance in younger age groups.⁹

Diverticulitis is often diagnosed clinically in patients with consistent signs and symptoms on history and physical examination, particularly those who have had a previous episode.¹⁰ However, computed tomography (CT) scanning is used to assess severity of disease and rule out other disorders that can mimic diverticulitis, such as malignancy, ischemic colitis, inflammatory bowel disease, appendicitis, and gynecological disorders.^{11,12}

In the United States, acute diverticulitis is one of the most common first-listed gastrointestinal diagnoses in outpatient clinics and emergency departments.¹³ Acute diverticulitis is the third most common inpatient gastrointestinal diagnosis in the United States, at a cost of \$2.1 billion.¹³ It is also a leading indication for elective colectomy.⁴ In addition, diverticulitis appears to affect quality of life beyond the period of acute illness.^{14,15}

The literature on acute diverticulitis has recently grown considerably, with several studies challenging long-standing management recommendations such as the need for antibiotic treatment during an acute episode and the role of surgery in the setting of recurrent disease.^{16,17} Given the substantial burden of disease and recent literature, the American Gastroenterological Association identified acute diverticulitis to be a priority topic for the generation of updated practice guidelines.

This technical review addresses 11 key questions regarding the management and prevention of acute diverticulitis. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to rate the quality of the evidence. We examined whether antibiotics rather than no antibiotics in patients with acute uncomplicated diverticulitis improves resolution of symptoms and reduces the risk of diverticular complications. We assessed whether a colonoscopy should be performed after an episode of diverticulitis to rule out the possibility of a misdiagnosis. We also assessed whether dietary or lifestyle modification in patients with a history of acute uncomplicated diverticulitis reduces the risk of recurrent disease or complications. Similarly, we assessed whether pharmacotherapy or elective colonic resection reduces the risk of recurrence or complications. The results of this technical review were used to develop a set of recommendations that accompany this report.

*Authors share co-first authorship.

Abbreviations used in this paper: CI, confidence interval; CT, computed tomography; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HR, hazard ratio; NSAID, nonsteroidal anti-inflammatory drug; RR, risk ratio; SUDD, symptomatic uncomplicated diverticular disease.

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0016-5085/\$36.00

<http://dx.doi.org/10.1053/j.gastro.2015.10.001>

Methods

Defining the Clinical Questions

Through an iterative process, the authors of the technical review and the guideline panelists defined the clinical questions that the guideline would address. We focused on the medical management of patients with acute uncomplicated diverticulitis and developed 11 clinical questions that we considered relevant for clinicians. No question was excluded from the technical review. For each question, we specified the population of interest and one or more alternative management strategies (Table 1). Clinical questions provided the framework for formulating study inclusion and exclusion criteria and guided the literature search.

Selecting the Outcomes

For each question, we developed a comprehensive list of potentially relevant outcomes. Then, along with the guideline panelists, we independently rated the importance of each outcome on a scale from 1 to 9, considering the patients' perspective. Outcomes with a median rating of 1 to 3 were considered not important to patients and were not included in the evidence tables. Outcomes with a median rating of 4 to 6 were considered important to patients, and outcomes with a median rating of 7 to 9 were considered critical to patients. The important and the critical outcomes were included in the evidence tables. At the end of the process, we readjusted the ratings to ensure consistency across clinical questions.

Identifying the Evidence

Estimates of the effect. With the help of a specialized librarian, we conducted an electronic search in MEDLINE, EMBASE, and the Cochrane Library in August 2014. We first searched for recent systematic reviews (2009 and onward). We then conducted a search for primary studies, using the search date of the latest systematic review identified as a starting point. Finally, we reviewed the reference lists of included studies and the clinicaltrials.gov Web site for additional trials. The literature search is described in detail online in Appendix 1.

The methodologist screened the list of hits retrieved and obtained the full text of relevant citations. The inclusion and exclusion of studies was decided by consensus of the technical review team. Included studies were restricted to randomized trials but included observational studies when there were no data from randomized trials.

Values and preferences. We also conducted a search for studies evaluating the values and preferences of patients in relation to outcomes and treatment alternatives for diverticulitis. We conducted an electronic search in November 2014 of MEDLINE and EMBASE without a time limit.

Summarizing the Evidence

Relative effect. We were able to identify current systematic reviews reporting the effect estimates for the outcomes of interest for some of our questions. In such instances, we used the data provided by the systematic review without retrieving the primary studies. More often, however, the systematic reviews identified did not include all the primary studies available or did not provide numeric estimates for the outcomes of interest. In those cases, we

retrieved the studies identified by the systematic review (plus any others identified by the search strategy) and calculated the effect estimates. In one case (mesalamine vs placebo), we conducted our own meta-analyses using the Mantel-Haenszel method random effect model (Appendix 2). The pooled estimates were presented as risk ratios with their 95% confidence interval (CI).

In one question (elective colonic resection), we pooled studies without control arms. We first transformed the proportions reported using the Freeman-Tukey double arcsine transformation and then pooled the results using the generic of the inverse variance method.¹⁸ All of the meta-analyses were conducted using Review Manager version 5.3 software (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

In another question (high-fiber diet), we used evidence from a case-control study to estimate the relative effect. Because it is not possible to calculate risk ratios in case-control studies, we estimated the "plausible risk ratio" using the method proposed by Grant.¹⁹

Baseline risks. We estimated the baseline risk for the outcomes of interest from 2 sources. When the population included in the studies used to estimate the relative risk was similar to the population of interest, we used the median risk among control groups. When the population included in the studies used to determine the relative effect had substantial differences from the population of interest, we obtained the baseline risk from large population-based cohorts. To ensure consistency across clinical questions, we used the same baseline risks on the questions addressing alternative interventions for the same population.

Absolute effects. Trading off desirable and undesirable consequences requires estimates of absolute effect. We calculated the absolute effect of the interventions by applying the risk ratios to the baseline risks. The results are expressed in natural frequencies per 1000 patients treated with their corresponding 95% CI. The time frame of the absolute effects presented corresponds to the time frame in which the baseline risks were measured, assuming that the risk reduction was relatively constant over time.

In the case of the meta-analysis of proportions, we back-transformed our pooled estimates using the inverse of the Freeman-Tukey double arcsine transformation²⁰ and expressed the results as natural frequencies.

Use of indirect evidence. A prominent issue in our technical review was the scarcity of direct evidence from patients with a previous episode of diverticulitis. In such instances, we used indirect evidence, generally from people with SUDD (when evaluating probiotics) or from the general population in studies of incident diverticulitis (when evaluating nuts and seeds, aspirin, and physical activity) and rated down the quality of the evidence (see the following text). The underlying assumption was that beyond differences in the baseline risk, the effect of the interventions might be similar in people with or without a previous episode of diverticulitis.

Evaluating the Quality of the Evidence

We assessed the quality of evidence using the system described by the GRADE working group.²¹ In short, the quality of evidence is classified as "high," "moderate," "low," or "very low" based on the study design and judgments about methodological characteristics of the available body of evidence. The

Table 1. Clinical Questions

Question no.	Informal question	Population	Intervention(s)	Comparator	Outcomes
1	Should antibiotics rather than no antibiotics be used in patients with acute uncomplicated diverticulitis confirmed by CT scan?	Patients with acute uncomplicated diverticulitis	Antibiotics	Placebo/no antibiotics	Critical Resolution of symptoms Diverticular complications Surgery Important Colostomy Recurrence Sepsis
2	Should a colonoscopy be performed versus no colonoscopy after an episode of acute diverticulitis confirmed by CT scan?	Patients with recent acute uncomplicated diverticulitis	Colonoscopy	No colonoscopy	Critical Polyp/cancer detection Important Perforation Burden
3	Should elective colonic resection be performed versus medical management after an episode of acute uncomplicated diverticulitis?	Patients with a history of uncomplicated acute diverticulitis	Elective colonic resection	Medical management	Critical Diverticular complications Recurrence Important Resolution of symptoms Surgery Colostomy Surgical complication
4	Should a high-fiber diet, rather than a regular diet, be advised in patients with a history of acute diverticulitis?	Patients with a history of acute diverticulitis	High-fiber diet	Unrestricted diet	Critical Recurrence Important Diverticular complications Surgery Chronic abdominal pain
5	Should consumption of corn, nuts, and popcorn be avoided in patients with a history of acute diverticulitis?	Patients with a history of acute diverticulitis	Corn, nuts, and popcorn	Regular diet	Critical Recurrence Important Diverticular complications Surgery Chronic abdominal pain
6	Should aspirin be avoided in patients with a history of acute diverticulitis?	Patients with a history of acute diverticulitis	Aspirin	Placebo/no intervention	Critical Recurrence Important Diverticular complications Surgery Chronic abdominal pain
7	Should nonaspirin NSAIDs be avoided in patients with a history of acute diverticulitis?	Patients with a history of acute diverticulitis	Nonaspirin NSAIDs	Placebo/no intervention	Critical Recurrence Important Diverticular complications Surgery Chronic abdominal pain
8	Should mesalamine rather than no therapy be used in patients with a history of acute uncomplicated diverticulitis?	Patients with a history of acute uncomplicated diverticulitis	Mesalamine	Placebo/no therapy	Critical Recurrence Important Diverticular complications Surgery Chronic abdominal pain
9	Should rifaximin rather than no therapy be used in patients with a history of acute uncomplicated diverticulitis?	Patients with a history of acute uncomplicated diverticulitis	Rifaximin	Placebo/no therapy	Critical Recurrence Important Diverticular complications Surgery Chronic abdominal pain

Table 1. Continued

Question no.	Informal question	Population	Intervention(s)	Comparator	Outcomes
10	Should probiotics rather than no therapy be used in patients with a history of acute diverticulitis?	Patients with a history of acute diverticulitis	Probiotics	Placebo/no therapy	Critical Recurrence Important Diverticular complications Surgery Chronic abdominal pain
11	Should physical activity rather than regular activity be encouraged in patients with a history of acute diverticulitis?	Patients with a history of acute diverticulitis	Physical activity	Regular activity	Critical Recurrence Important Diverticular complications Surgery

quality of the evidence reflects our confidence that the estimates of the effect calculated from the body of evidence lie close to their true value.

- High-quality evidence: We are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate-quality evidence: We are moderately confident in the estimate of the effect; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low-quality evidence: Our confidence in the estimate of the effect is limited; the true effect may be substantially different from the estimate of the effect.
- Very low-quality evidence: We have very little confidence in the estimate of the effect; the true effect is likely to be substantially different from the estimate of the effect.

In the GRADE approach, randomized trials start as high-quality evidence, but the evidence can be rated down if the primary studies have a high risk of bias, the results are imprecise, there is substantial inconsistency, there is a high probability of publication bias, or the evidence found does not apply directly to the population of interest. Observational studies, in turn, start as low-quality evidence, and it is also possible to rate down the quality with the situations just mentioned. However, it is also possible to increase the quality of the evidence in special situations, such as a large observed effect or the observation of a dose-response gradient.

In each clinical question, the methodologist evaluated the quality of the evidence for each outcome. Those judgments were discussed with the rest of the technical review team, and disagreements were resolved by consensus. We considered the overall quality of the evidence as the lowest rating among the critical outcomes.

Evidence Tables

We summarized the estimates of the effect and the judgments regarding the quality of the evidence in the tables. We used the alternative format proposed by Carrasco-Labra et al, because evidence shows that this format improves understanding of risk differences and helps with the interpretation of the results.²²

Results

Question 1. Should Antibiotics Rather Than No Antibiotics Be Used in Patients With Acute Uncomplicated Diverticulitis Confirmed by CT Scan?

Key messages. In patients with acute uncomplicated diverticulitis confirmed by CT scan, treatment with broad-spectrum antibiotics for at least 7 days may not improve symptom resolution. However, antibiotics may decrease the risk of recurrence and diverticular complications in comparison with no antibiotics. The effect of antibiotics on the development of sepsis and the need for surgery or colostomy is uncertain. (*Low quality of evidence*)

Effect estimates. We identified 2 recent systematic reviews,^{23,24} and both included only one trial comparing antibiotics with no antibiotics in patients with acute uncomplicated diverticulitis (Table 2).¹⁶ Another trial was just completed, but the results are only partially available.^{25,26} The first trial was conducted in 10 centers in Sweden and Iceland and included 669 patients with acute uncomplicated left-sided diverticulitis diagnosed on CT. Participants were predominantly women (approximately two-thirds), with an average age of 57 years. Approximately 40% had a previous episode of diverticulitis. Patients allocated to the antibiotic arm received initial intravenous treatment with a second- or third-generation cephalosporin plus metronidazole or with carbapenem antibiotics or piperacillin/tazobactam. Upon improvement, patients were switched to oral ciprofloxacin or cefadroxil combined with metronidazole. The total duration of antibiotic therapy was at least 7 days. Patients allocated to the control arm received intravenous fluids only. The second trial included 528 patients with diverticulitis who had a CT- or ultrasonography-proven diagnosis of a first episode of mild, acute, left-sided, uncomplicated (modified Hinchey stage 1a or 1b) diverticulitis. Participants were randomized to amoxicillin-clavulanate (1200 mg intravenously 4 times a day and switched to oral

Table 2. Question 1: Should Antibiotics Rather Than No Antibiotics Be Used in Patients With Acute Uncomplicated Diverticulitis Confirmed by CT Scan?

Outcomes/no. of participants (no. of studies)	Risk ratio (95% CI)	Anticipated absolute effects			Quality of the evidence (GRADE)	What happens
		Without antibiotics	With antibiotics ^a	Difference (95% CI)		
Resolution of symptoms (follow-up: 30 days)/1151 patients (2 studies) ^{16,25}	—	Two randomized trials reported no significant differences in symptom resolution			⊕⊕⊕⊕ Low ^{b,c,d} due to risk of bias and imprecision	Antibiotics may not influence symptom resolution
Diverticular complications (follow-up: 30 days)/623 patients (1 study) ¹⁶	0.49 (0.12–1.95)	19 complications per 1000 patients at 30 days ^e	9 complications per 1000 patients at 30 days ^f	10 fewer complications (from 17 fewer to 18 more per 1000 patients)	⊕⊕⊕⊕ Low ^{b,c} due to risk of bias and imprecision	Antibiotics may decrease complications
Surgery/623 patients (1 study) ¹⁶	2.95 (0.31–28.2)	3 surgeries per 1000 patients at 30 days ^g	9 surgeries per 1000 patients at 30 days ^h	6 more surgeries (from 2 fewer to 81 more per 1000 patients)	⊕⊕⊕⊕ Low ^{b,c} due to risk of bias and imprecision	The effect of antibiotics on the risk of surgery is unclear
After discharge (follow-up: 12 mo)	0.33 (0.07–1.61)	19 surgeries per 1000 patients at 12 mo ⁱ	6 surgeries per 1000 patients at 12 mo ^j	13 fewer surgeries (from 18 fewer to 11 more per 1000 patients)	⊕⊕⊕⊕	
Recurrence (follow-up: 12 mo)/623 patients (1 study) ¹⁶	0.97 (0.67–1.41)	162 recurrences per 1000 patients at 12 mo	157 recurrences per 1000 patients at 12 mo	5 fewer recurrences (from 54 fewer to 66 more per 1000 patients)	⊕⊕⊕⊕ Low ^{b,c} due to risk of bias and imprecision	Antibiotics may decrease recurrence
Colostomy	—	No data	No data	No data	—	No data
Sepsis	—	No data	No data	No data	—	No data

NOTE. Population: patients with acute uncomplicated diverticulitis; setting: inpatient; intervention: broad-spectrum antibiotic therapy^a; comparison: no antibiotic therapy. ^aIn one trial, intravenous treatment included (1) a combination of a second- or third-generation cephalosporin plus metronidazole or (2) carbapenem antibiotics or piperacillin/tazobactam followed by oral antibiotics such as ciprofloxacin or cefadroxil combined with metronidazole for at least 7 days. In the other trial, intravenous treatment included amoxicillin-clavulanate (1200 mg 4 times a day for at least 2 days followed by oral administration of 625 mg 3 times a day for a total duration of 10 days). ^bImprecision due to few events and CIs including appreciable benefit or harm. ^cThe study was unblinded, the sequence of randomization was not appropriately concealed (sealed envelopes), and only 623 of the 669 patients randomized were reported. ^dOne study was only available as a conference abstract. ^eIn the group of 309 patients treated without antibiotics, 3 patients had sigmoid perforation and 3 had abscess formation. ^fIn the group of 314 patients treated with antibiotics, 3 patients had sigmoid perforation. ^gIn the group of 309 patients treated without antibiotics, one patient developed a perforation requiring emergent sigmoid resection. ^hIn the group of 314 patients treated with antibiotics, 3 patients developed a perforation requiring emergent sigmoid resection. ⁱIn the group of 309 patients treated without antibiotics, 6 patients underwent surgery during follow-up because of SUID, stricture, fistula, recurrent diverticulitis, recurrent diverticulitis with abscess formation, and colonic perforation that occurred during preparation for colonic examination (1 patient each). ^jIn the group of 314 patients treated with antibiotics, 2 patients underwent surgery for stricture during follow-up.

administration of 625 mg 3 times a day after 2 days for a total duration of 10 days) or placebo.

The results of both trials suggested that the use of broad-spectrum antibiotics in patients with acute uncomplicated diverticulitis does not reduce the duration of symptoms; however, according to the data from the trial by Chabok et al,¹⁶ it may reduce the risk of diverticular complications with 10 fewer events at 30 days per 1000 treated patients (95% CI from 17 fewer to 18 more; low quality of evidence) and the risk of recurrence with 5 fewer events at 12 months per 1000 treated patients (from 54 fewer to 66 more; low quality of evidence). We found inconsistent data regarding the effect of antibiotics on the risk of surgery, because use of antibiotics may increase the need for surgery during the index hospitalization but may decrease the need for surgery after discharge. Finally, we found no data regarding the effect of antibiotics on risk of colostomy or sepsis.

Quality of the evidence. We rated the quality of the evidence as low because one of the trials identified had a high risk of bias (the study was unblinded, the sequence of randomization was not appropriately concealed, and only 623 of the 669 patients randomized were actually reported) and the other was only available in abstract form. Also, there were only a small number of events in both trials (imprecision).

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. Broad-spectrum antibiotics have been the mainstay of treatment for patients with acute diverticulitis.^{7,27,28} However, few studies have evaluated the use of antibiotics in patients with acute uncomplicated diverticulitis, and this practice is based largely on expert opinion and medical dogma. Modern theories suggest that diverticulitis may have a primarily inflammatory, not infectious, basis.²⁹ In addition, there is increasing general concern regarding antibiotic resistance and antibiotic-related complications, namely *Clostridium difficile* colitis (these problems are not known to affect patients with diverticulitis differently).²² These issues have led to studies evaluating the need for antibiotic therapy in patients with uncomplicated diverticulitis.

We evaluated 2 systematic reviews of one randomized trial and results from a trial published in abstract form comparing patients with CT- or ultrasonography-confirmed acute uncomplicated diverticulitis.^{16,25} Based on data from both studies, we found that treatment with broad-spectrum antibiotics may not reduce the duration of symptoms. Results from the fully published study indicate that complications and recurrences were less frequent in the antibiotic arm compared with the no antibiotic arm. However, the number of complications was very low (3 perforations in patients treated with antibiotics and 3 perforations and 3 abscesses in patients treated without antibiotics), and the confidence bounds for both estimates centered around 1. Therefore, the benefit of antibiotics in reducing complications and recurrences is uncertain. Ten patients in the no antibiotic arm were started on antibiotics due to increasing pain, fever, or C-reactive protein level, and all of them

recovered without complications. The effect of antibiotics on the need for surgery during or subsequent to hospitalization differed with antibiotics, resulting in more inpatient surgeries but fewer outpatient surgeries. Although one study was available only in abstract form, the final results are unlikely to alter the strength of our recommendations because of the small number of anticipated events, particularly with respect to the important outcomes of diverticular complications and surgery.

In addition to the randomized trials used in our analysis, 2 retrospective studies have examined the treatment of CT-confirmed uncomplicated diverticulitis with or without antibiotics and found no difference in treatment failures or subsequent events.^{30,31} Patients receiving antibiotics in these studies appeared to have more severe disease on presentation (based on inflammatory markers, temperature, and/or findings on CT), and the selection of patients with mild disease for conservative treatment may have influenced the results.³¹ However, based on one trial, outcomes were similar with and without antibiotics in patients with severe uncomplicated disease defined by higher C-reactive protein level, body temperature, and/or pain scores.¹⁶

It is important to note that only patients with mild disease confirmed via radiological procedures (uncomplicated diverticulitis; modified Hinchey stage 1a or 1b) were included in the existing trials. Patients with clinical signs or symptoms of sepsis or severe disease were excluded, as were immunocompromised patients and those with significant comorbid disease. In addition, all patients in the published trial were admitted and observed in the hospital. Therefore, these findings cannot be extrapolated to more complicated disease (ie, large or distant abscess, peritonitis, perforation) or to patients who received a diagnosis on clinical grounds alone.

Question 2. Should a Colonoscopy Be Performed Versus No Colonoscopy After an Episode of Acute Diverticulitis Confirmed by CT Scan?

Key messages. In patients with a recent episode of acute diverticulitis, performing a colonoscopy after 4 to 8 weeks may identify a few cases of colorectal carcinoma. The risk of perforation after a case of diverticulitis is uncertain. Colonoscopy represents a moderate burden for patients. (*Very-low quality of evidence*)

Effect estimates. We identified 3 recent systematic reviews in our search (Table 3).^{32,34,35} We selected the review by Daniels et al³² because it had the most updated search and reported an assessment of the risk of bias of the primary studies. Eight observational studies were included in this review, 6 of them retrospective. Patients included had a mean age of approximately 60 years, and all had an imaging-proven diagnosis (CT scan or ultrasonography) of diverticulitis. A subsequent colonoscopy was performed in

Table 3. Question 2: Should a Colonoscopy Be Performed Versus No Colonoscopy After an Episode of Acute Diverticulitis Confirmed by CT Scan?

Outcomes/no. of participants (no. of studies)	Anticipated absolute effects (95% CI) in patients with acute diverticulitis	Quality of the evidence (GRADE)	What happens
Risk of colorectal carcinoma (follow-up, 1 mo to 11 y)/1796 patients (8 studies) ³²	15 colorectal cancers per 1000 patients (from 10 to 23 per 1000), typically within the first 4–8 wk	⊕⊕⊖⊖ Low	Colonoscopy may detect a few cases of cancer in patients with diverticulitis
Risk of perforation (follow-up, 1 wk after colonoscopy)/277,434 patients (1 study) ³³	0.8 perforations per 1000 patients ^a (from 0.7 to 1.0 per 1000) 1 wk after colonoscopy	⊕⊖⊖⊖ Very low ^b due to indirectness	The risk of perforation is uncertain in patients with recent diverticulitis
Burden of the intervention (0 studies)	Short-term dietary restrictions, bowel preparation, and missed activities	⊕⊕⊕⊕ High	Colonoscopy represents a moderate burden for patients

NOTE. Population: patients with recent acute diverticulitis; setting: outpatient; intervention: colonoscopy; comparison: no colonoscopy.

^aMost of the studies included in the review did not mention adverse events. The 3 studies that did so reported none. We based our estimate on the results of a large population-based study.³³

^bThe estimate comes from a population without recent diverticulitis (indirect evidence).

most patients (85% to 93% had a complete examination to the cecum) after 4 to 8 weeks.

The pooled analysis suggested that performing a colonoscopy after an episode of acute diverticulitis can detect 15 colorectal cancers per 1000 patients tested (95% CI from 10 to 23; low quality of evidence) and 38 advanced adenomas (defined as an adenoma ≥ 10 mm, $\geq 25\%$ villous features [also classified as tubulovillous or villous histology], or with high-grade dysplasia) per 1000 patients tested (95% CI from 27 to 53; moderate quality of evidence).

Most of the studies included in the review did not mention adverse events. The 3 studies that did so reported none. Therefore, to estimate the risk of perforation, we used data from a large population-based study.³³ According to these data, the risk of perforation within 7 days after a colonoscopy is 0.8 per 1000 patients tested (95% CI from 0.7 to 1; very-low quality of evidence). This estimate is consistent with what has been reported by other studies.³⁶

Quality of the evidence. We rated down the quality of the evidence of the outcome of perforation because we used indirect evidence from the general population to calculate our estimates. We judged the overall quality of the evidence to be low.

Patients' values and preferences. We found no study evaluating patients' values and preferences for undergoing a colonoscopy after an episode of acute diverticulitis. We estimated that the burden of a colonoscopy is moderate because it requires short-term dietary restrictions, bowel preparation, discomfort, and missed work and activities.

Discussion. In the past, guidelines have recommended colonoscopy after an episode of acute diverticulitis. The goal of performing colonoscopy was to rule out colon cancer or inflammatory bowel disease, either of which might have been misdiagnosed as diverticulitis.^{7,10,28} We considered whether patients who have had an episode of acute diverticulitis confirmed by CT scan should undergo a

colonoscopy to rule out the possibility of a misdiagnosis. We weighed the probability of diagnosing colorectal cancer by colonoscopy with the burden of undergoing a colonoscopy and its risks.

Using data from a systematic review that included patients with imaging-confirmed acute diverticulitis between 2000 and 2010 who underwent a colonoscopy after the episode, we found that the risk of missed colorectal cancer is substantial.³² From these data, an estimated 1 in 67 patients with confirmed acute diverticulitis would have a misdiagnosed colorectal cancer found on follow-up colonoscopy. Almost all of the misdiagnosed colorectal cancers in the systematic review were located in the area of "diverticulitis"; in other words, they were true misdiagnoses. Of those studies that detailed the location of the missed colorectal cancer, only 1 of 27 cancers was in the proximal colon. In most of the studies in the review (1189 patients), colonoscopy was performed 6 to 8 weeks after the episode of diverticulitis. However, the study by Westwood et al (205 patients) included patients who may have had a colonoscopy up to 2 years before an episode.³⁷ It is not clear what proportion of these patients had a colonoscopy before versus after an episode. In the study by Elmi et al (402 patients), only one-third of this population had a colonoscopy within 6 months of the episode. However, 8 of the 9 misdiagnosed colorectal cancers were found within 6 months of the misdiagnosis of diverticulitis.³⁸

There is a significant risk for selection bias in most of the data published to date. Patients with more questionable results on imaging or failure to improve clinically with antibiotics are more likely to have a colonoscopy after an episode of diverticulitis than those with an uncomplicated episode who improved on antibiotics. Moreover, several of the studies in the review included patients with a history of complicated diverticulitis, and complicated disease may be a risk factor for misdiagnosis.³⁹ As such, we have likely

Table 4. Question 3: Should Elective Colonic Resection Be Performed Versus Medical Management After an Episode of Acute Uncomplicated Diverticulitis?

Outcomes/no. of participants (no. of studies)	Anticipated absolute effects (95% CI) in patients with uncomplicated diverticulitis	Quality of the evidence (GRADE)	What happens
Outcomes of patients treated medically			
Risk of recurrence (follow-up, 1–9 y)/ 25,388 patients (10 studies) ^{4–6,40,47–52}	189 recurrences per 1000 patients ^a (from 185 to 193 per 1000), typically at 5 y	⊕⊕⊕⊖ Low	Approximately 1 of 5 of the patients treated medically may experience a new event; this risk is slightly higher in younger patients (younger than 45–50 y of age)
Risk of diverticular complications (follow-up, 1–5 y)/ 1095 patients (3 studies) ^{6,49,50}	42 diverticular complications per 1000 patients ^a (from 30 to 54 per 1000), typically at 5 y	⊕⊕⊕⊖ Low	The risk of diverticular complications may be small in patients with uncomplicated diverticulitis treated medically
Risk of emergency surgery (follow-up, 5 y)/21,154 patients (4 studies) ^{4,49,53,54}	43 emergency surgeries per 1000 patients ^a (from 41 to 46 per 1000) at 5 y	⊕⊕⊕⊖ Low	The risk of emergency surgery may be small in patients with uncomplicated diverticulitis treated medically
Risk of colostomy (follow-up, 5 y)/ 20,647 patients (3 studies) ^{4,49,54}	22 colostomies per 1000 patients ^a (from 21 to 25 per 1000) at 5 y	⊕⊕⊕⊖ Low	The risk of colostomy may be small in patients with uncomplicated diverticulitis treated medically
Outcomes of patients treated with elective surgery^b			
Risk of surgical complications (follow-up, 21 days)/ 360 patients (3 studies) ^{55–57}	Open surgery: 111 complications per 1000 patients ^{a,c} (from 20 to 273 per 1000) at 21 days Laparoscopic surgery: 87 complications per 1000 patients ^{a,d} (from 49 to 130 per 1000) at 21 days	⊕⊕⊕⊖ Low due to risk of bias ^e and imprecision ^f	Approximately 10% of the patients treated with elective surgery may experience a short-term complication
Risk of recurrence (follow-up, 7 y)/268 patients (2 studies) ^{58,59}	76 recurrences per 1000 patients ^a (from 48 to 111 per 1000) at 7 y	⊕⊕⊕⊖ Very low due to imprecision ^f	The risk of recurrence with surgery is uncertain

NOTE. Population: patients with recent acute uncomplicated diverticulitis; setting: outpatient and inpatient; intervention: elective colonic resection; comparison: medical management.

^aPooled estimates calculated from proportions reported in primary studies using the Freeman–Tukey double arcsine transformation and using the generic inverse variance approach for the meta-analysis. We back-transformed the pooled estimate using the inverse of the Freeman–Tukey transformation to report the number of events per 1000 patients.

^bMost patients were treated with an open or laparoscopic sigmoid resection.

^cTypically anastomotic leakage, intra-abdominal abscess, and mechanical ileus.

^dTypically anastomotic leakage, small-bowel perforation, and mechanical ileus.

^eOne trial was not blinded; in 2 trials, there were missing outcome data.

^fSmall number of patients studied.

overestimated the risk of misdiagnosed colorectal cancer in those with imaging-confirmed acute uncomplicated diverticulitis.

Other misdiagnoses are also possible but have not been directly studied. Of the 8 studies in the systematic review, 6 studies do not mention other potential misdiagnoses. In the study by Westwood et al, there was one diagnosis of inflammatory bowel disease among 205 patients.³⁷ In the study by Lau et al, there was a missed diagnosis of inflammatory bowel disease, ischemic colitis, and 2 cases of nonspecific ulcerations among 319 patients.³⁹ The risk of misdiagnosis should decrease as the diagnostic performance of abdominal imaging continues to improve.

Colonoscopy is associated with a very small risk of iatrogenic perforation in the general population.³³ The risk of

perforation may increase in the setting of active diverticulitis, and therefore a delay of colonoscopy for 6 to 8 weeks after treatment is generally recommended.¹⁰ A very small study of early versus late colonoscopy in patients with acute uncomplicated diverticulitis found no increased risk of perforation; however, the study was not powered to estimate the risk of perforation in this population.⁴⁰ There is a small risk of diverticulitis after colonoscopy,⁴¹ but whether this risk is increased in those with a history of acute diverticulitis is unknown. Colonoscopy is also associated with a moderate burden for patients because it involves preparing for the colonoscopy, discomfort, and missed work and activities.

There are studies assessing the association of diverticulosis and diverticular disease with colorectal cancer

unrelated to our question of misdiagnosis on imaging. A history of diverticulosis or diverticular disease is a risk factor for interval colorectal cancer or cancer diagnosed within 6 to 36 months of a colonoscopy that was negative for cancer.⁴² This population did not necessarily have imaging-confirmed acute diverticulitis.

A hospital admission for diverticulosis or diverticulitis has also been associated with an increased risk of left-sided colorectal cancer in 2 retrospective Swedish studies.^{43,44} One of these studies was a retrospective cohort, and the increased risk of colorectal cancer was found more than 10 years after the hospital admission.⁴⁴ In contrast, a hospital admission for diverticulosis or diverticulitis was only associated with an increased risk of colorectal cancer in the first 12 months of follow-up in 2 different population-based case-control studies.^{45,46} Diverticulosis or diverticulitis was not associated with an increased risk after the first year. The association in the first year was attributed to misclassification and screening and indirectly suggests that there is some risk of colon cancer misdiagnosed as diverticulitis.^{45,46} These populations also did not necessarily have imaging-confirmed acute diverticulitis.

Question 3. Should Elective Colonic Resection Be Performed Versus Medical Management After an Episode of Acute Uncomplicated Diverticulitis?

Key messages. Approximately one-fifth of hospitalized patients with acute uncomplicated diverticulitis treated medically may experience a new event. This risk seems to be slightly higher in younger patients (younger than 45–50 years of age). The risk of diverticular complications, emergency surgery, and colostomy may be relatively small in this group of patients.

Approximately 10% of the patients treated with elective sigmoid resection will experience a short-term complication related to surgery. The effect of surgery on recurrence of diverticulitis is uncertain. (**Very-low quality of evidence**)

Effect estimates. *Outcomes of patients treated medically.* We identified a recent systematic review including 25 observational studies that evaluated the risk of recurrence in patients with an episode of acute diverticulitis (Table 4).⁶⁰ In general, the studies included predominantly women (51%–62%) with a mean age of approximately 60 years. We reanalyzed the data presented by Regenbogen et al,⁶⁰ including only the studies reporting the outcomes of patients with uncomplicated diverticulitis.^{4–6,40,47–53,58,61–64}

We estimated that after a first episode of acute uncomplicated diverticulitis treated medically, the risk of recurrence was 189 recurrences per 1000 patients followed for 5 years (95% CI from 185 to 193; low quality of evidence). In 3 studies, the number of recurrences per patient was reported.^{5,51,53} Among those who will have a recurrence,

approximately two-thirds will have a single recurrence and one-third will have 2 or more events over the next 2 to 9 years.

Seven studies reported the risk of recurrence in relation to age.^{4,5,40,48,50,51,53} We estimated that in younger patients (younger than 45–50 years of age), the risk of recurrence was 234 events per 1000 patients followed for 5 years (95% CI from 217 to 256; low quality of evidence). In patients 50 years of age or older, this risk seems to be lower at 166 events per 1000 patients (95% CI from 163 to 174; low quality of evidence).

We found only one small study evaluating the risk of recurrence in immunosuppressed patients (renal transplant, chronic renal failure with hemodialysis, oncologic disease, chronic immunosuppressant medication therapy, or acquired immunodeficiency syndrome). The results of this study did not exclude an increased risk of recurrence with immunosuppression.⁴⁷

We estimated that the risk of complicated recurrence after an initial episode of uncomplicated diverticulitis was 42 events per 1000 patients followed for 5 years (95% CI from 30 to 54; low quality of evidence). The risk of emergency surgery and colostomy was 43 emergency surgeries (95% CI from 41 to 46; low quality of evidence) and 22 colostomies (95% CI from 21 to 25; low quality of evidence) per 1000 patients followed for 5 years.

Outcomes of elective surgery. We identified 3 randomized trials^{55–57} evaluating short-term complications of elective surgery in patients with previous episodes of diverticulitis. The first randomized trial⁵⁶ allocated 52 patients to laparoscopic resection (55% female; mean age, 62 years) and 52 patients to open surgery (59% female; mean age of 63 years). The risk of major complications was 9.6% with laparoscopic surgery (3 anastomotic leakages, 1 intra-abdominal abscess, 1 Richter hernia) and 25% with open resection (5 anastomotic leakages, 2 intra-abdominal bleeds, 2 intra-abdominal abscesses, 1 evisceration, 1 small-bowel perforation). The second randomized trial⁵⁵ allocated 77 patients to laparoscopy (48% female; mean age, 64 years) and 79 patients to open surgery (46% female; mean age, 68 years). Major complications occurred in 9% of the patients treated with the laparoscopic approach (mainly anastomotic leakages, anastomotic stenosis, and hernias) and 12% of the patients who underwent open surgery (mainly anastomotic leakages and hernias). Finally, the third randomized trial⁵⁷ allocated 66 patients to laparoscopic resection (49% female; median age, 57 years) and 66 patients to open surgery (57% female; median age, 62.5 years). The risk of major complications was 5% with laparoscopic resection (2 small-bowel perforations; 1 small-bowel obstruction) and 2% with open surgery (1 intra-abdominal abscess). Pooling the data from these 3 trials, we estimated that the risk of major surgical complications at 21 days was 111 per 1000 patients (95% CI from 20 to 273) with open surgery and 87 per 1000 patients (95% CI from 49 to 130) with laparoscopic resection (low quality of evidence).

The systematic review by Regenbogen et al⁶⁰ identified 2 observational studies that evaluated the risk of recurrence after successful surgical treatment. We reanalyzed the data

from these 2 studies and estimated a risk of recurrence of 76 per 1000 patients followed for 7 years (95% CI from 48 to 111; low quality of evidence). This risk is likely lower than that observed in patients treated medically.

Quality of the evidence. We did not find studies evaluating outcomes of medical and surgical treatment in the same cohort. Thus, we summarized the observational data from patients treated medically and from patients treated with surgical resection. For the outcome of risk of surgical complication, we rated down the quality of the evidence due to risk of bias (there was an important proportion of missing outcome data in 2 trials, and one trial did not have blinded adjudication of the outcomes) and imprecision (small number of patients studied). We also rated down the quality of the evidence in the outcome of recurrence after surgical treatment due to the small number of patients studied. We judged the overall quality of the evidence as very low.

Patients' values and preferences. We did not find studies evaluating the value that patients place on avoiding recurrence or complications. In relation to the burden of surgery, we identified a study reporting an improvement in quality of life and social functioning after an elective sigmoid resection.⁶⁵ Another study suggested that patients who underwent sigmoid resection may have a similar long-term quality of life compared with the general population.⁶⁶

Discussion. Until recently, guidelines recommended elective colonic resection after 2 episodes of acute uncomplicated diverticulitis.^{27,28} Elective surgery was recommended after a single episode in young adults and those who are immunosuppressed. Recurrent episodes were believed to be associated with a high risk of diverticular complications, emergency surgery, colostomy, or even death. An elective surgery was recommended to reduce these risks.

Recent data, however, suggest that recurrent episodes tend to be uncomplicated. We sought to further clarify the role of elective resection versus medical management in patients with a history of acute uncomplicated diverticulitis. We found no single study comparing medical with surgical intervention, and therefore we summarized studies of these interventions separately. We are aware of an ongoing multicenter randomized trial comparing surgical with conservative therapy for patients with recurrent diverticulitis that we hope will generate high-quality evidence to better address this question.⁶⁷

We identified and reviewed 11 observational studies that included a population with medically managed acute uncomplicated diverticulitis.^{4-6,40,47-51,53,54} We found that a substantial proportion (~20%) of those admitted for acute uncomplicated diverticulitis will be readmitted with a recurrence. Most of these readmissions will be uncomplicated, and very few will require emergency surgery or colostomy. Notably, these risk estimates were based almost entirely on a single study that included only patients hospitalized for diverticulitis. The study was not designed to include only incident disease.

Acute uncomplicated diverticulitis is also a common outpatient disease.¹³ Few observational studies of

recurrence or complications have accounted for outpatient diagnoses. This suggests that we have underestimated the risk of recurrence and the number of recurrences while possibly overestimating the risk of complications. One of the few studies that included outpatient disease, a population-based cohort in the United Kingdom, found that most cases of complicated diverticular disease occurred with an initial episode of acute diverticulitis.⁶⁸

After an initial episode of acute uncomplicated diverticulitis, some proportion of patients will go on to have multiple recurrences, likely in the outpatient setting. Only 3 studies assessed re-recurrent disease and were limited to episodes associated with a hospital admission.^{5,51,53} We know surprisingly little about this population, the natural history of their illness, and their burden of disease.

Early work in acute diverticulitis suggested that "young" patients (ie, patients younger than 50 years of age) had an increased risk of more aggressive forms of disease.⁶⁹⁻⁷² Specifically, it was believed that these patients were at increased risk for recurrence and perforation. Indeed, we found that young patients have an increased risk of recurrence compared with older adults.^{4,5,40,48,50,51,53} Again, this estimate was based on studies of diverticulitis diagnosed during a hospital admission. Without outpatient diagnoses, we have likely underestimated the risk of recurrence in young adults.

There are important uncertainties regarding the care of immunosuppressed patients with diverticular disease. Until recently, these patients were believed to be at increased risk for morbidity and mortality associated with recurrence based on 2 small case series.^{73,74} We reviewed a retrospective cohort that assessed the risk of recurrent diverticulitis among patients who are immunosuppressed compared with those who are not immunosuppressed.⁴⁷ The study found that patients who are immunosuppressed did not have an increased risk of recurrence, but the study was of low quality.

The risk of postoperative morbidity and mortality must be balanced with any potential benefit of elective surgery. Our analysis of 3 studies found that approximately 10% of patients with uncomplicated diverticulitis who pursue an elective resection experience a major surgical complication. Laparoscopic resection compared with open resection seems to have a somewhat reduced risk of postoperative complications, although the risk is still substantial. Advancing age substantially increases the risk of adverse events.^{8,64} For example, in one study, the odds of inpatient mortality after elective resection were 12 times greater in patients 85 years of age or older than in those between 65 and 69 years of age.⁶⁴ We did not find data on the risk of colostomy after elective surgery for uncomplicated diverticulitis, but the reported risk in heterogeneous study populations that included patients undergoing elective surgery for complicated or uncomplicated diverticulitis is as high as 13%.⁶⁴ In general, the risk of complications, colostomy, and mortality is lower in the setting of elective compared with emergent surgery for diverticulitis.^{4,8,64}

It is important to note that surgery does not eliminate the risk of recurrence due to the possibility of residual or newly formed colon diverticula. Surgical technique seems to

play a role in the risk of recurrence after surgery, although the literature on this issue is limited and beyond the scope of this review. For example, studies suggest that a greater extent of resection (eg, colorectal vs colosigmoid anastomosis) reduces the risk of recurrence.^{59,75,76} In addition to attention to the distal anastomosis, it is likely also important to resect all areas previously involved with diverticulitis (eg, distal descending and sigmoid).⁷⁷ Data on nonoperative risk factors for recurrence after elective resection are limited. Younger age and persistent postoperative symptoms were risk factors for recurrent diverticulitis in a single study.⁵⁸

We found that the recurrence rate in studies of elective resection for uncomplicated diverticulitis was lower than the recurrence rate reported in studies of medical therapy. However, only 2 studies with a total of 268 patients were available for the analysis of elective resection, and therefore our estimate is imprecise.^{58,59} In comparison to studies of recurrence in medically treated patients, most patients in surgical studies had experienced more than one prior attack of diverticulitis. Surgery is generally not indicated after an initial episode of uncomplicated diverticulitis.

Surgical resection may not alleviate chronic abdominal symptoms and can result in defecatory dysfunction. In a study of 124 patients who underwent elective surgery for diverticulitis, 25% experienced persistent postoperative symptoms, including abdominal distention, cramping, and altered defecation, regardless of a history of complicated versus uncomplicated disease.⁷⁸ In another study of 325 patients undergoing sigmoid resection for diverticulitis, postoperative fecal incontinence and urgency were reported in 25% and 20%, respectively.⁷⁹ Therefore, it is important to differentiate symptoms related to recurrent attacks and ongoing inflammation from coexisting or postdiverticulitis functional bowel disease (the studies included in this review confirmed recurrent diverticulitis via CT scan)¹⁴ and to acknowledge the possibility of postoperative changes in bowel function.

The potential impact of surgery on quality of life must be weighed when considering surgical intervention for prevention of recurrence. For example, recurrent diverticulitis may lead to time away from work and other obligations as well as concern regarding the possibility of an attack when there is no immediate access to medical care. Existing data on patient-centered outcomes are limited but suggest improved to stable quality of life after sigmoid resection.^{65,66}

Question 4. Should a High-Fiber Diet, Rather Than a Regular Diet, Be Advised in Patients With a History of Acute Diverticulitis?

Key messages. We are uncertain whether a diet rich in fiber improves the risk of recurrence of diverticulitis, diverticular complications, surgery, or abdominal pain in comparison with a regular diet in patients with a history of diverticulitis. (*Very-low quality of evidence*).

Effect estimates. We identified 2 recent systematic reviews (Table 5).^{24,85} Both included 3 small randomized trials and one additional small case-control study in patients with SUDD.⁸²⁻⁸⁴ Two of the trials^{82,84} reported a significant reduction of pain with fiber supplements, and the third trial⁸³ was unable to show benefit or harm with the intervention. It was not possible to pool the results of the trials with the data available.

The small case-control study reported the outcomes of diverticular complications and need for surgery. The study compared 31 patients who consumed at least 25 g/day of dietary fiber with 25 patients who did not receive or adhere to the dietary recommendations.⁸¹ We estimated that a high-fiber diet would reduce the risk of complications with 14 fewer events at 5 years per 1000 patients treated (95% CI from 32 fewer to 17 more; very low quality of evidence) and the risk of surgery with 87 fewer procedures at 5 years per 1000 patients treated (from 105 to 4 fewer; very low quality of evidence). However, given the scarcity of data, these estimates are likely to be inaccurate.

None of the studies identified reported the effect of fiber on the risk of recurrence. However, a cohort of 47,033 men and women without previous diverticulitis suggested that a vegetarian diet (high fiber intake) was associated with a 31% reduction of the risk of diverticular disease that requires hospitalization (risk ratio, 0.69; 95% CI, 0.55-0.86).⁸⁰ Using the baseline risk of recurrence observed in the cohort of 20,136 patients with a first episode of acute uncomplicated diverticulitis treated medically⁴ and assuming that, beyond differences in baseline risk, the effect of fiber may be similar among patients with and without previous diverticulitis, we estimated that a high-fiber diet would produce a reduction of 59 recurrences at 5 years per 1000 patients treated (95% CI from 85 to 27 fewer).

Quality of the evidence. We rated down the quality of the evidence because we used indirect evidence from a population without previous diverticulitis to calculate the relative effect estimates. For the outcomes of diverticular complications, need for surgery, and abdominal pain, we also rated down by imprecision given the scarcity of data. We judged the overall quality of the evidence as very low.

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. Patients with a history of acute diverticulitis commonly seek dietary and lifestyle recommendations to reduce their risk of recurrence and/or complications. The traditional recommendation has been to consume a high-fiber diet. We considered whether a high-fiber diet should be recommended to patients with a history of uncomplicated acute diverticulitis to reduce the risk of recurrence, complications, surgery, or abdominal pain. We found no studies that assessed whether dietary fiber intake (or even supplemental fiber) reduces the risk of recurrent acute diverticulitis. Using data from a prospective cohort study that examined the association of dietary fiber intake and risk of incident hospitalization for diverticular disease,⁸⁰ we approximated that a high-fiber

Table 5. Question 4: Should a High-Fiber Diet, Rather Than a Regular Diet, Be Advised in Patients With a History of Acute Diverticulitis?

Outcomes/no. of participants (no. of studies)	Risk ratio (95% CI)	Anticipated absolute effects		Difference (95% CI)	Quality of the evidence (GRADE)	What happens
		Without a high-fiber diet	With a high-fiber diet			
Recurrence (follow-up, 11.6 y)/47,033 patients (1 study) ⁸⁰	0.69 ^a (0.55–0.86)	190 recurrences per 1000 patients at 5 y ^b	131 recurrences per 1000 patients at 5 y	59 fewer recurrences (from 85 to 27 fewer per 1000 patients)	⊕⊕⊕⊕ Very low due to indirectness ^c	The effect of fiber is uncertain
Diverticular complications (follow-up, 4–6 y)/56 patients (1 study) ⁸¹	0.30 ^d (0.05–1.51)	34 complications per 1000 patients at 5 y ^b	10 complications per 1000 patients at 5 y	14 fewer complications (from 32 fewer to 17 more per 1000 patients)	⊕⊕⊕⊕ Very low due to serious imprecision and indirectness ^{c,e}	The effect of fiber is uncertain
Surgery (follow-up, 4–6 y)/56 patients (1 study) ⁸¹	0.20 ^d (0.04–0.96)	109 surgeries per 1000 patients at 5 y ^b	22 surgeries per 1000 patients at 5 y	87 fewer surgeries (from 105 to 4 fewer per 1000 patients) ⁸	⊕⊕⊕⊕ Very low due to serious imprecision and indirectness ^{c,e}	The effect of fiber is uncertain
Chronic abdominal pain/106 patients (3 studies) ^{82–84}	—	Two small randomized trials showed reduction of pain with fiber supplements; a third randomized trial found no significant difference			⊕⊕⊕⊕ Very low due to serious imprecision and indirectness ^{c,e,f}	The effect of fiber is uncertain

NOTE: Population: patients with a history of acute diverticulitis; setting: outpatient; intervention: high-fiber diet; comparison: regular diet.

^aRelative effect estimated from a cohort of 47,033 men and women without previous diverticulitis.⁸⁰

^bBaseline risk estimated from a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

^cWe rated down the quality of the evidence because the relative effect estimate comes from a population without previous diverticulitis.

^dPlausible risk ratio estimated from the odds ratio using the procedure proposed by Grant.¹⁹

^eVery small number of patients studied.

^fThe 3 trials used fiber supplements instead of dietary fiber.

diet may reduce the risk of recurrent diverticulitis. The association between intake of dietary fiber and risk of diverticular disease in the prospective cohort was dose dependent, with progressively reduced risk for each successive quintile of intake. Therefore, compared with those in the lowest quintile of dietary fiber intake (14 g/day), participants in the third quintile (18 g/day; relative risk, 0.76; 95% CI, 0.61–0.96), fourth quintile (21 g/day; relative risk, 0.72; 95% CI, 0.57–0.92), and fifth quintile (26 g/day; relative risk, 0.59; 95% CI, 0.46–0.78) had a reduced risk of diverticular disease. Another large prospective cohort also found a progressively reduced risk of symptomatic diverticular disease for each successive quintile of intake.⁸⁶ In this second study, the source of dietary fiber was assessed, and reduced risk was greatest with cereal and fruit fiber. However, we rated the quality of this evidence as very low based on substantial differences between our target population (those with a history of diverticulitis) and those in the cohort study (those without a history of diverticulitis).

Using data from a single case-control study that included 56 participants with SUDD, we estimated that a high-fiber diet might also reduce the number of complications and need for surgery.⁸¹ Again, we rated the quality of this evidence as very low. We found 3 randomized trials that assessed whether supplemental fiber reduces the risk of chronic abdominal pain.^{82–84} Two of the studies found a reduced risk of pain with fiber supplementation, and the third study found no benefit. The quality of this evidence was also very low given the small number of participants, the use of fiber supplements instead of dietary fiber, and the use of populations without previous diverticulitis.

We focused our review on fiber as a potential means to decrease the risk of recurrent diverticulitis. We did not address the relationship between intake of fiber and the development of colonic diverticulosis or incident diverticulitis.

Question 5. Should Consumption of Corn, Nuts, and Popcorn Be Avoided in Patients With a History of Acute Diverticulitis?

Key messages. We are uncertain whether avoiding corn, nuts, and popcorn decreases the risk of recurrence of diverticulitis, diverticular complications, surgery, or abdominal pain in comparison with a nonrestricted diet in patients with a history of diverticulitis. (*Very-low quality of evidence*)

Effect estimates. We found no study evaluating the effect of corn, nuts, or popcorn on patients with a history of acute diverticulitis. Strate et al⁸⁷ evaluated the risk of a first event of diverticulitis and diverticular complications among 47,288 men between 40 and 75 years of age (Table 6). The investigators compared patients who reported consumption

of 2 or more servings per week of corn, nuts, or popcorn with those who reported consumption of less than one serving per month. The results suggested that the consumption of nuts and popcorn might reduce the risk of acute diverticulitis (nuts: adjusted hazard ratio [HR], 0.80; 95% CI, 0.63–1.01; popcorn: adjusted HR, 0.72; 95% CI, 0.56–0.92), whereas there was no significant effect with corn (adjusted HR, 1.13; 95% CI, 0.83–1.54). Also, popcorn may decrease the risk of diverticular complications (adjusted HR, 0.55; 95% CI, 0.34–0.90), whereas no significant effect of nuts was observed (adjusted HR, 0.97; 95% CI, 0.63–1.47).

We estimated that the consumption of corn would produce 25 more recurrences at 5 years per 1000 patients (95% CI from 57 fewer to 78 more; very low quality of evidence), whereas the consumption of nuts would lead to 38 fewer recurrences (95% CI from 70 fewer to 2 more; very low quality of evidence) and 1 fewer complication per 1000 patients at 5 years (95% CI from 13 fewer to 16 more; very low quality of evidence). The consumption of popcorn would produce 53 fewer recurrences (95% CI from 84 to 15 fewer; very low quality of evidence) and 15 fewer complications at 5 years per 1000 patients (95% CI from 22 to 3 fewer; very low quality of evidence).

We found no data for the outcomes of need for surgery and chronic abdominal pain.

Quality of the evidence. For the outcomes of recurrence and diverticular complications, we rated the quality of the evidence as very low, given the use of indirect evidence to estimate the relative effect of corn, nuts, or popcorn. We judged the overall quality of the evidence as very low.

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. Physicians have historically advised patients with diverticulosis to avoid nuts, seeds, and popcorn. This practice stems from a belief that these high-residue foods may obstruct or traumatize the diverticular lumen and provoke diverticulitis. However, there is little evidence to support this practice. We found one study of approximately 50,000 men without diverticulitis at baseline who were followed for 20 years with detailed dietary and medical questionnaires.⁸⁷ Using data from this study and data on the baseline risk of recurrent diverticulitis from a separate cohort study, we estimated that consumption of nuts and popcorn may decrease the number of recurrences and complications, whereas consumption of corn may increase the number of recurrences (although the HR in the primary study was close to 1 and was not significant). However, we rated the quality of the evidence as very low because the estimates were derived from a population without previous diverticulitis. Overall, a diet high in nuts has been shown to reduce the risk of other common disorders such as cardiovascular disease and diabetes,^{88,89} and the potential broader health benefits of these foods need to be weighed against any potential risk in the setting of diverticulosis.

Table 6. Question 5: Should Consumption of Corn, Nuts, and Popcorn Be Avoided in Patients With a History of Acute Diverticulitis?

Outcomes/no. of participants (no. of studies)	Anticipated absolute effects			Difference (95% CI)	Quality of the evidence (GRADE)	What happens
	Without corn, nuts, or popcorn	With corn, nuts, or popcorn	With corn, nuts, or popcorn			
Recurrence (follow-up, 18 y)/47,288 patients (1 study) ⁸⁷	Hazard ratio (95% CI) Corn: 1.13 ^a (0.83–1.54)	190 recurrences per 1000 patients at 5 y ^b	215 recurrences per 1000 patients at 5 y	25 more recurrences (from 57 fewer to 78 more per 1000 patients)	⊕ ⊕ ⊕ ⊕ Very low due to indirectness ^c	The effect of corn, nuts, and popcorn is uncertain
	Nuts: 0.80 ^a (0.63–1.01)	190 recurrences per 1000 patients at 5 y ^b	152 recurrences per 1000 patients at 5 y	38 fewer recurrences (from 70 fewer to 2 more per 1000 patients)		
	Popcorn: 0.72 ^a (0.56–0.92)	190 recurrences per 1000 patients at 5 y ^b	137 recurrences per 1000 patients at 5 y	53 fewer recurrences (from 84 to 15 fewer per 1000 patients)		
Diverticular complications (follow-up, 18 y)/47,288 patients (1 study) ⁸⁷	Nuts: 0.97 ^a (0.63–1.47)	34 complications per 1000 patients at 5 y ^b	33 complications per 1000 patients at 5 y	1 fewer complication (from 13 fewer to 16 more per 1000 patients)	⊕ ⊕ ⊕ ⊕ Very low due to indirectness ^c	The effect of corn, nuts, and popcorn is uncertain
	Popcorn: 0.55 ^a (0.34–0.90)	34 complications per 1000 patients at 5 y ^b	19 complications per 1000 patients at 5 y	15 fewer complications (from 22 to 3 fewer per 1000 patients)		
Surgery	—	No data	No data	No data	—	No data
Chronic abdominal pain	—	No data	No data	No data	—	No data

NOTE: Population: patients with a history of acute diverticulitis; setting: outpatient; intervention: corn, nuts, and popcorn; comparison: regular diet.

^aRelative effect estimated from a cohort of 47,288 men without previous diverticulitis.⁸⁷

^bBaseline risk estimated from a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

^cWe rated down the quality of the evidence because the relative effect estimates come from a population without previous diverticulitis.

Question 6. Should Aspirin Be Avoided in Patients With a History of Acute Diverticulitis?

Key messages. We are uncertain whether the regular use of aspirin increases recurrence of diverticulitis, complications, surgery, or abdominal pain. (*Very-low quality of evidence*)

Effect estimates. We found no study evaluating the effect of aspirin on patients with a history of acute diverticulitis. We estimated the relative effect from a cohort study of 47,210 men without previous diverticulitis, which compared 13,874 regular users of aspirin (mean age, 56 years; 12% with coronary heart disease) with nonusers (Table 7). The results suggested that regular use of aspirin might increase the risk of diverticulitis (adjusted HR, 1.25; 95% CI, 1.05–1.47) and the risk of complicated diverticulitis (adjusted HR, 1.13; 95% CI, 0.61–2.10).⁹⁰ We found no information regarding the effect of aspirin on the risk of surgery or abdominal pain.

Using the baseline risks observed in a cohort of 20,136 patients with a first episode of acute uncomplicated diverticulitis treated medically,⁴ we estimated that regular use of aspirin would lead to 48 more recurrences at 5 years per 1000 patients (95% CI from 10 to 89 more; very low quality of evidence) and 7 more complications at 5 years per 1000 patients (95% CI from 21 fewer to 61 more per 1000 patients; very low quality of evidence).

Quality of the evidence. For the outcomes of recurrence and complications of diverticulitis, we rated the quality of the evidence as very low because we used evidence from an observational study conducted on a population that may have substantial differences from our target population. We judged the overall quality of the evidence as very low.

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. Nonsteroidal anti-inflammatory drugs (NSAIDs), including aspirin, are increasingly recognized as risk factors for colonic events, including diverticulitis.^{91,92} Aspirin and nonaspirin NSAIDs are believed to cause direct topical injury to the colon and also to disrupt mucosal integrity through impaired prostaglandin synthesis, both mechanisms that may induce or perpetuate the development of diverticulitis.⁹² Multiple case-control studies have noted a positive association between NSAIDs and diverticulitis, particularly perforated diverticulitis.^{93–95} In general, these studies evaluated nonaspirin NSAIDs and aspirin as a combined exposure. However, because of the role of aspirin in the prevention of chronic disease, most notably secondary cardiovascular events, it is important to evaluate the effect of aspirin on diverticulitis independent of nonaspirin NSAIDs.

We used data from a large, prospective cohort of men without prior diverticulitis to address whether aspirin specifically should be used in patients with a history of acute diverticulitis.⁹⁰ Using data on the baseline risk of recurrent diverticulitis from another cohort study, we

Table 7. Question 6: Should Aspirin Be Avoided in Patients With a History of Acute Diverticulitis?

Outcomes/no. of participants (no. of studies)	Hazard ratio (95% CI)	Anticipated absolute effects		Difference (95% CI)	Quality of evidence (GRADE)	What happens
		Without aspirin	With aspirin			
Recurrence (follow-up, 22 y)/47,210 patients (1 study) ⁹⁰	1.25 ^a (1.05–1.47)	190 recurrences per 1000 patients at 5 y	238 recurrences per 1000 patients at 5 y	48 more recurrences (from 10 to 89 more per 1000 patients)	⊕⊕⊕⊕ Very low due to indirectness ^c	The effect of aspirin is uncertain
Diverticular complications (follow-up, 22 y)/47,210 patients (1 study) ⁹⁰	1.13 ^a (0.61–2.10)	55 complications per 1000 patients at 5 y ^d	62 complications per 1000 patients at 5 y	7 more complications (from 21 fewer to 61 more per 1000 patients)	⊕⊕⊕⊕ Very low due to indirectness ^c	The effect of aspirin is uncertain
Surgery	—	No data	No data	No data	—	No data
Chronic abdominal pain	—	No data	No data	No data	—	No data

NOTE: Population: patients with a history of acute diverticulitis; setting: outpatient; intervention: aspirin; comparison: placebo.

^aRelative effect estimated from a cohort of 47,210 men without previous diverticulitis.⁹⁰

^bBaseline risk estimated from a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

^cWe rated down the quality of the evidence because the relative effect estimate comes from a population without previous diverticulitis.

^dBaseline risk estimated from the risk of emergency colectomy and/or colostomy in a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

estimated that patients who used aspirin regularly (at least twice per week) had more recurrent episodes of diverticulitis and slightly more diverticular complications than those who did not use either aspirin or nonaspirin NSAIDs. However, because this study included men with incident and not recurrent diverticulitis, we rated the quality of the evidence as very low and are uncertain regarding this finding.

This study also found that the risk of diverticulitis increased with frequency of aspirin use but not dose.⁹⁰ Men who took intermediate doses of aspirin (2–6 325-mg tablets per week) had the highest risk of diverticulitis (adjusted HR, 1.26; 95% CI, 0.97–1.62), but there was no dose-response relationship. However, men who took aspirin daily had an adjusted HR of 1.46 (95% CI, 1.13–1.88, *P* for trend = .002) when compared with nonusers of aspirin and NSAIDs.

Overall, any decision regarding aspirin therapy in a patient with a history of diverticulitis must balance the increased risk of diverticulitis as well as the risk of major gastrointestinal bleeding (estimated to be 16 more events at 10 years per 1000 patients⁹⁶) with the potential benefits of aspirin. This is particularly true in patients at moderate to high risk of cardiovascular disease in whom secondary prevention with aspirin reduces the risk of myocardial infarction and death.

Question 7. Should Nonaspirin NSAIDs Be Avoided in Patients With a History of Acute Diverticulitis?

Key messages. We are uncertain whether the regular use of nonaspirin NSAIDs increases recurrence of diverticulitis, complications, surgery, or abdominal pain. (*Very-low quality of evidence*)

Effect estimates. We found no study evaluating the effect of nonaspirin NSAIDs on patients with a history of acute diverticulitis. As before, we used indirect evidence from a cohort of 47,210 men without previous diverticulitis, in which 2577 regular users of nonaspirin NSAIDs (mean age, 55 years; 38% with concurrent use of aspirin) were compared with nonusers of aspirin and NSAIDs (Table 8). The results of this study suggested that the regular use of nonaspirin NSAIDs might significantly increase the risk of recurrence of diverticulitis (adjusted HR, 1.72; 95% CI, 1.40–2.11) and the risk of complicated diverticulitis (adjusted HR, 2.55; 95% CI, 1.32–4.95).⁹⁰

Considering the baseline risks observed in a cohort of 20,136 patients with a first episode of acute uncomplicated diverticulitis treated medically,⁴ we estimated that regular use of nonaspirin NSAIDs would produce 137 more recurrences at 5 years per 1000 patients (95% CI from 76 to 211 more; very low quality of evidence) and 85 more complications at 5 years per 1000 patients (95% CI from 18 to 217 more per 1000 patients; very low quality of evidence).

Table 8. Question 7: Should Nonaspirin NSAIDs Be Avoided in Patients With a History of Acute Diverticulitis?

Outcomes/no. of participants (no. of studies)	Hazard ratio (95% CI)	Anticipated absolute effects		Difference (95% CI)	Quality of evidence (GRADE)	What happens
		Without nonaspirin NSAIDs	With nonaspirin NSAIDs			
Recurrence (follow-up, 22 y)/47,210 patients (1 study) ⁹⁰	1.72 ^a (1.40–2.11)	190 recurrences per 1000 patients at 5 y ^b	327 recurrences per 1000 patients at 5 y	137 more recurrences (from 76 to 211 more per 1000 patients)	Very low due to indirectness ^c	The effect of NSAIDs is uncertain
Diverticular complications (follow-up, 22 y); 47,210 patients (1 study) ⁹⁰	2.55 ^a (1.32–4.95)	55 complications per 1000 patients at 5 y ^d	140 complications per 1000 patients at 5 y	85 more complications (from 18 to 217 more per 1000 patients)	Very low due to indirectness ^c	The effect of NSAIDs is uncertain
Surgery	—	No data	No data	No data	—	No data
Chronic abdominal pain	—	No data	No data	No data	—	No data

NOTE: Population: patients with a history of acute diverticulitis; setting: outpatient; intervention: nonaspirin NSAIDs; comparison: placebo.

^aRelative effect estimated from a cohort of 47,210 men without previous diverticulitis.⁹⁰
^bBaseline risk estimated from a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴
^cWe rated down the quality of the evidence because the relative effect estimate comes from a population without previous diverticulitis.
^dBaseline risk estimated from the risk of emergency colectomy and/or colostomy in a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

Quality of the evidence. We rated the quality of the evidence as very low because we used evidence from an observational study conducted on a population that may have substantial differences from our target population. We judged the overall quality of the evidence as very low.

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. The literature suggests that nonaspirin NSAIDs are more strongly associated with diverticulitis than aspirin. In the cohort study used for our analysis, the adjusted HR for diverticulitis was 1.25 (95% CI, 1.05–1.47) in regular aspirin users and 1.72 (95% CI, 1.40–2.11) in regular nonaspirin NSAID users when compared with non-users of both aspirin and NSAIDs.⁹⁰ The combined use of NSAIDs plus aspirin did not appear to be associated with a greater risk than use of each medication alone.⁹⁰

Nonaspirin NSAIDs also appear to increase the risk of complicated diverticulitis. In the cohort study described in the preceding text, the risk of complications was more than 2 times higher in users of nonaspirin NSAIDs than in those who did not use aspirin or NSAIDs. Similarly, a case-control study of perforated diverticulitis in 2 hospitals in the United Kingdom found a significant association for current NSAID use (adjusted odds ratio, 1.53; 95% CI, 1.01–2.32) but not current aspirin use for cardiovascular prophylaxis (adjusted odds ratio, 1.28; 95% CI, 0.81–2.02).⁹⁴

There are numerous broad indications for nonaspirin NSAIDs, including control of pain and inflammation. We were therefore unable to systematically evaluate the benefits of nonaspirin NSAIDs in relation to the increased risk of diverticulitis. In general, the benefits of nonaspirin NSAIDs are of a less critical nature than those derived from aspirin for cardiovascular prevention. Nonetheless, in some patients, there may be limited non-NSAID options for symptom and disease control, and this must be weighed against the potential for recurrent diverticulitis and diverticular complications.

A number of other medications have been studied in association with the risk of diverticulitis. A small case-control study and a large population-based study in the United Kingdom found that opiate analgesics and corticosteroids increased the risk of perforated diverticulitis.^{94,97} On the other hand, calcium channel blockers⁹⁸ and statins may decrease the risk.⁹⁷ A formal analysis weighing the risks and benefits of each of these medications in the setting of diverticulitis was beyond the scope of this review.

Question 8. Should Mesalamine Rather Than No Therapy Be Used in Patients With a History of Acute Uncomplicated Diverticulitis?

Key messages. In patients with a history of acute diverticulitis, the use of mesalamine in comparison to no therapy probably does not reduce the risk of recurrence or the number of patients with abdominal pain and may increase the risk of surgery. The effect of mesalamine on the risk of diverticular complications is uncertain. (*Moderate quality of evidence*)

Effect estimates. We identified 6 trials (2 unpublished^{99,100} and 4 published^{101–103}) evaluating the use of mesalamine versus placebo in patients with uncomplicated diverticulitis or with a confirmed episode of uncomplicated diverticulitis in the previous 6 to 24 months (Table 9). The populations studied included predominantly women (50%–60%) with a mean age of 55 to 60 years. Mesalamine was used in doses ranging from 0.8 g for 10 days every month to 4.8 g daily.

We found that the use of mesalamine probably does not reduce the risk of recurrence (10 more recurrences at 5 years per 1000 patients, 95% CI from 28 fewer to 57 more; moderate quality of evidence) or the number of patients with abdominal pain (23 more patients at 2 years per 1000 patients; 95% CI from 20 fewer to 87 more; moderate quality of evidence). Additionally, the use of mesalamine may increase the risk of surgery (89 more surgeries at 5 years per 1000 patients, 95% CI from 58 fewer to 657 more; low quality of evidence).

We did not find data regarding the effect of mesalamine on the risk of diverticular complications.

Quality of the evidence. For the outcomes of recurrence and abdominal pain, we rated the quality of evidence as moderate because the 95% CI around the estimates for the absolute effect did not rule out substantial benefits or harms with mesalamine (imprecision). For the outcome of surgery, the quality of the evidence was considered low because the estimates were based on a very small number of events (very serious imprecision). We judged the overall quality of the evidence as moderate.

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. The histology of the diverticular mucosa in acute diverticulitis shares similarities with chronic colitis, including architectural distortion, cryptitis, and crypt abscesses.¹⁰⁴ Mesalamine is an oral 5-aminosalicylic acid that effectively maintains remission in quiescent ulcerative colitis.¹⁰⁵ Based on the efficiency in ulcerative colitis, 6 placebo-controlled trials have assessed whether mesalamine would reduce the risk of recurrent acute diverticulitis.^{99–103} None of the 6 available trials showed a statistically significant benefit of mesalamine versus placebo in the prevention of recurrence. One study showed a potential trend toward reducing the risk of recurrence at 24 months,¹⁰¹ and a post hoc analysis of another trial found a reduction in rectosigmoid symptoms.¹⁰³ However, these studies represent only 10% of the available data on mesalamine, and the results of our meta-analysis indicate no benefit of mesalamine over placebo in the prevention of recurrence, surgery, or abdominal pain.

Mesalamine has also been studied in the context of SUDD. Most of the studies used in this review included patients with a definitive history of acute uncomplicated diverticulitis and required confirmation of a recurrence with imaging to distinguish recurrence from functional symptoms or SUDD.

The majority of participants in trials of mesalamine for uncomplicated diverticulitis experienced a single episode of acute uncomplicated diverticulitis. Therefore, the results

Table 9. Question 8: Should Mesalamine Rather Than No Therapy Be Used in Patients With a History of Acute Uncomplicated Diverticulitis?

Outcomes/no. of participants (no. of studies)	Anticipated absolute effects			Quality of the evidence (GRADE)	What happens
	Risk ratio (95% CI)	Without mesalamine	With mesalamine		
Recurrence (follow-up, 1–2 y)/1816 patients (6 studies) ^{99–103}	1.05 (0.85–1.30)	190 recurrences per 1000 patients at 5 y ^a	200 recurrences per 1000 patients at 5 y ^b	⊕⊕⊕⊖ Moderate due to imprecision ^{b,c}	Mesalamine probably does not reduce recurrence
Diverticular complications Surgery (follow-up, 1–2 y)/1051 patients (2 studies) ¹⁰²	— 1.82 (0.47–7.03)	No data 109 surgeries per 1000 patients at 5 y ^a	No data 198 surgeries per 1000 patients at 5 y	— ⊕⊕⊖⊖ Low due to very serious imprecision ^{b,d}	No data Mesalamine may increase the risk of surgery
Chronic abdominal pain (follow-up, 1–2 y)/1051 patients (2 studies) ¹⁰²	1.21 (0.82–1.80)	109 patients per 1000 at 2 y ^c	132 patients per 1000 at 2 y ^c	⊕⊕⊕⊖ Moderate due to imprecision ^b	Mesalamine probably does not reduce the risk of abdominal pain

NOTE. Population: patients with a history of acute diverticulitis; setting: outpatient; intervention: mesalamine; comparison: placebo.

^aBaseline risk estimated from a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

^bThe 95% CI around the absolute effect includes substantial benefit and harm.

^cMost trials had a significant proportion of missing outcome data. However, a sensitivity analysis assuming “recurrence” in the patients with missing information did not appreciably change the results.

^dOnly a small number of events were observed.

may not pertain to the subgroup of patients with relapsing acute uncomplicated diverticulitis who may have different pathophysiology and may be more likely to benefit from preventive measures. In general, the identification of patients at high risk for recurrence is important for effective prevention. Potential risk factors for recurrence other than the number of attacks include young age at onset, multiple versus solitary diverticula, length of involved colon segment greater than 5 cm, and a family history of diverticulitis.^{4,6,106}

Question 9. Should Rifaximin Rather Than No Therapy Be Used in Patients With a History of Acute Uncomplicated Diverticulitis?

Key messages. We are uncertain whether the use of rifaximin in comparison to no therapy improves the risk of recurrence of diverticulitis, diverticular complications, surgery, or abdominal pain in patients with a history of diverticulitis. (*Very-low quality of evidence*)

Effect estimates. We identified one study evaluating the use of rifaximin against placebo in people with a recent episode of acute uncomplicated diverticulitis (Table 10).¹⁰⁷ The trial included 167 patients with a recent episode of acute diverticulitis diagnosed by computed tomography, ultrasonography, or endoscopy. Participants were randomized to receive fiber supplementation with or without rifaximin 400 mg twice daily 1 week per month for 12 months. Among the 165 participants reported, the

investigators observed fewer recurrences with rifaximin (8 of 77 vs 17 of 88 in the control arm; relative risk, 0.54; 95% CI, 0.25–1.18). Considering the baseline risk of recurrence in a population of patients treated medically for a first episode of acute uncomplicated diverticulitis, use of rifaximin would result in 88 fewer recurrences at 5 years per 1000 patients treated (95% CI from 142 fewer to 34 more; very low quality of evidence). The investigators reported no significant differences between groups in symptom intensity. The outcomes of diverticular complications and need for surgery were not reported.

Quality of the evidence. We rated down the quality of the evidence due to risk of bias and very serious imprecision. The study was unblinded, and the outcomes were mostly subjectively evaluated. The number of events was also very small, which, in addition to the premature stop of the trial, make it difficult to rule out random or systematic error as a potential explanation for the findings. We judged the overall quality of the evidence to be very low.

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. Rifaximin is a gastrointestinal selective antibiotic with a good safety profile and minimal drug interactions. Stasis within a diverticulum and bacterial overgrowth are hypothesized to contribute to the pathogenesis of acute diverticulitis.^{104,108} Using this logic, maintenance or cyclic therapy with an antibiotic such as rifaximin might reduce the risk of recurrent acute diverticulitis.

We found a single small study that assessed whether cyclic therapy with rifaximin reduces the risk of recurrent

Table 10. Question 9: Should Rifaximin Rather Than No Therapy Be Used in Patients With a History of Acute Uncomplicated Diverticulitis?

Outcomes/no. of participants (no. of studies)	Risk ratio (95% CI)	Anticipated absolute effects			Quality of the evidence (GRADE)	What happens
		Without rifaximin	With rifaximin ^a	Difference (95% CI)		
Recurrence (follow-up, 1 y)/165 patients (1 study) ¹⁰⁷	0.54 (0.25–1.18)	190 recurrences per 1000 patients at 5 y ^a	102 recurrences per 1000 patients at 5 y	88 fewer recurrences (from 142 fewer to 34 more per 1000 patients)	⊕⊕⊕⊕ Very low due to risk of bias and very serious imprecision ^{b-d}	The effect of rifaximin is uncertain
Diverticular complications	—	No data	No data	No data	—	No data
Surgery	—	No data	No data	No data	—	No data
Chronic abdominal pain (follow-up, 1 y)/165 patients (1 study) ¹⁰⁷	—	No substantial change in pain intensity during treatment was observed			⊕⊕⊕⊕ Very low due to risk of bias and very serious imprecision ^{b,d}	The effect of rifaximin is uncertain

NOTE. Population: patients with a history of acute diverticulitis; setting: outpatient; intervention: rifaximin; comparison: placebo.

^aBaseline risk estimated from a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

^bThe trial was unblinded and prematurely discontinued.

^cGiven the procedures of the study, patients could qualify as “recurrence” without having a proven episode of diverticulitis.

^dThere was a small number of events and the effect estimates do not rule out substantial harm.

acute diverticulitis. Although the study found that rifaximin reduced the risk of recurrence, the quality of the evidence was very low. The study began as a multicenter, randomized trial with the aim of enrolling 228 patients per group. However, recruitment rates were low and heterogeneous among the sites. As such, the study was converted to a “proof of concept design,” and only 165 patients were randomized. Moreover, the study was unblinded and recurrent diverticulitis was not assessed with imaging (or any uniform measure). Therefore, from our review of the literature, the effect of rifaximin on the risk of recurrent diverticulitis or associated complications is uncertain. There are no other studies assessing whether maintenance or cyclic therapy with antibiotics reduces the risk of recurrent disease or complications.

Seven additional studies have investigated the effect of maintenance or cyclic therapy with rifaximin on the risk of diverticulitis and chronic abdominal symptoms in patients with SUDD without a prior episode of diverticulitis.^{109–115} We did not include these studies in our assessment of rifaximin because the baseline risk of recurrence and the effect of therapy may differ in patients with SUDD when compared with those with a history of uncomplicated diverticulitis.

Question 10. Should Probiotics Rather Than No Therapy Be Used in Patients With a History of Acute Diverticulitis?

Key messages. We are uncertain whether probiotics compared with no therapy reduce the risk of recurrence of diverticulitis, diverticular complications, surgery, or abdominal pain in patients with a history of acute diverticulitis. (*Very-low quality of evidence*)

Effect estimates. We identified only one small trial evaluating the use of probiotics in patients with a history of diverticulitis (Table 11).¹¹⁶ In this study, 83 patients (63% female; mean age, 63 years) were randomized to receive a suspension of *Escherichia coli* plus *Proteus vulgaris* for 2 weeks every month within the first 3 months after the acute event or to placebo. Both groups also received at least 15 g of fiber daily. The results suggested that the use of probiotics might produce 120 fewer recurrences at 5 years per 1000 patients treated (95% CI from 175 fewer to 154 more; very low quality of evidence).

We found no trial evaluating the outcomes of diverticular complications, surgery, and abdominal pain in patients

Table 11. Question 10: Should Probiotics Rather Than No Therapy Be Used in Patients With a History of Acute Diverticulitis?

Outcomes/no. of participants (no. of studies)	Risk ratio (95% CI)	Anticipated absolute effects			Quality of the evidence (GRADE)	What happens
		Without probiotics	With probiotics ^a	Difference (95% CI)		
Recurrence (follow-up, 3 mo)/83 patients (1 study) ¹¹⁶	0.37 (0.08–1.81)	190 recurrences per 1000 patients at 5 y ^b	70 recurrences per 1000 patients at 5 y	120 fewer recurrences (from 175 fewer to 154 more per 1000 patients)	⊕⊕⊕⊕ Very low due to very serious imprecision and risk of bias ^{c–e}	The effect of probiotics is uncertain
Diverticular complications (follow-up, 12 mo)/105 patients (1 study) ¹¹⁷	0.30 (0.01–7.29)	34 complications per 1000 patients at 5 y ^b	10 complications per 1000 patients at 5 y	14 fewer complications (from 33 fewer to 214 more per 1000 patients)	⊕⊕⊕⊕ Very low due to very serious imprecision and indirectness ^{c–f}	The effect of probiotics is uncertain
Surgery (follow-up, 12 mo)/105 patients (1 study) ¹¹⁷	0.30 (0.01–7.29)	109 surgeries per 1000 patients at 5 y ^b	33 surgeries per 1000 patients at 5 y	76 fewer surgeries (from 108 fewer to 686 more per 1000 patients)	⊕⊕⊕⊕ Very low due to very serious imprecision and indirectness ^{c–f}	The effect of probiotics is uncertain
Chronic abdominal pain (follow-up, 12 mo)/105 patients (1 study) ¹¹⁷	0.32 (0.16–0.64)	460 patients with pain per 1000 at 1 y	147 patients with pain per 1000 at 1 y	313 fewer patients with pain (from 386 to 166 fewer per 1000 patients)	⊕⊕⊕⊕ Very low due to very serious imprecision and indirectness ^{c–f}	The effect of probiotics is uncertain

NOTE. Population: patients with a history of acute diverticulitis; setting: outpatient; intervention: probiotics; comparison: placebo.

^aSuspension of *Escherichia coli* plus *Proteus vulgaris* (1 trial) or *Lactobacillus casei* (1 trial).

^bBaseline risk estimated from a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

^cCIs include appreciable benefit or harm.

^dOnly a small number of events were observed.

^eUnblinded trial. The methods used to allocate participants are poorly described.

^fThe trial was conducted in patients with symptomatic uncomplicated diverticular disease.

with previous diverticulitis. However, we identified a trial testing the use of mesalamine (1.6 g/day for 10 days/month for 12 months), *Lactobacillus casei* (24 billion/day for 10 days/month for 12 months), or the combination against placebo in patients with SUDD.¹¹⁷ We extracted the data from the groups allocated to *Lactobacillus* (n = 55; 51% female; median age, 64 years) and placebo (n = 50; 40% female; median age, 60 years). The results suggested that the use of *Lactobacillus* would produce 14 fewer complications at 5 years per 1000 patients (95% CI from 33 fewer to 214 more; very low quality of evidence), 76 fewer surgeries at 5 years per 1000 patients (95% CI from 108 fewer to 686 more; very low quality of evidence), and 313 fewer patients with abdominal pain at 1 year per 1000 patients (95% CI from 386 to 166 fewer; very low quality of evidence).

Quality of the evidence. Both trials identified included a small number of patients and had few events; therefore, we rated down the quality of the evidence by 2 levels due to very serious imprecision. Additionally, for the outcome of recurrence, we rated down the quality of the evidence due to risk of bias because the trial by Dughera et al¹¹⁶ was not blinded and the methods used to allocate participants are poorly described. Finally, we rated down the quality of the evidence due to indirectness for the outcomes of diverticular complications, surgery, and abdominal pain given the use of indirect data from patients with symptomatic diverticular disease. We judged the overall quality of the evidence as very low.

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. Microbial dysbiosis is hypothesized to contribute to the pathogenesis of acute diverticulitis.¹¹⁸ Select probiotics may modify the gastrointestinal microbiota.¹¹⁹ We reviewed a single randomized controlled trial that aimed to determine whether nonpathogenic *Escherichia coli* and *Proteus vulgaris* would reduce the risk of recurrent acute diverticulitis.¹¹⁶ Participants randomized to these probiotics had a reduced risk of recurrence compared with those randomized to placebo during the 3 months of follow-up. The quality of this trial was very low. The sample size was small, the allocation methods were poorly described, and cross-sectional imaging was not used to confirm the diagnosis of incident or recurrent diverticulitis. Furthermore, episodes of initial diverticulitis were treated using nonstandard antibiotics, including rifaximin or ciprofloxacin alone.

We found no study assessing whether probiotics reduces the risk of diverticular complications, surgery, and abdominal pain. Therefore, we reviewed indirect and low-quality evidence from a single trial of probiotics in patients with SUDD. SUDD is a diagnosis given to patients with abdominal symptoms and diverticulosis without colitis or overt inflammation. The diagnosis does not require a history of acute diverticulitis.

The notion that we might therapeutically manipulate the gastrointestinal microbiota to prevent acute diverticulitis is intriguing. However, the gastrointestinal microbiota is remarkably complex and the relationship between the microbes and diverticulitis has not been defined. The

mechanisms of action of probiotic strains vary considerably. Some strains have the capacity to up-regulate anti-inflammatory factors, whereas others suppress proinflammatory factors or improve intestinal barrier function.¹¹⁹ Before rational therapeutic trials of probiotics can be performed, substantial groundwork needs to be performed to develop an understanding of the relationship between the microbiome and diverticulitis.

Question 11. Should Physical Activity Rather Than Regular Activity Be Encouraged in Patients With a History of Acute Diverticulitis?

Key messages. We are uncertain whether physical activity improves the risk of recurrence of diverticulitis, diverticular complications, surgery, or abdominal pain in patients with a history of acute diverticulitis. (**Very-low quality of evidence**)

Effect estimates. We found no study evaluating the effect of physical activity in patients with a history of acute diverticulitis. However, we identified a large population-based study of 47,288 patients between 45 and 75 years of age without previous diverticulitis, which compared the quintiles with more and less physical activity within the cohort (Table 12).¹²⁰ The results suggested that vigorous physical activity might decrease the risk of acute diverticulitis (adjusted risk ratio, 0.66; 95% CI, 0.51–0.86), but there was not a significant effect of nonvigorous physical activity (adjusted risk ratio, 0.96; 95% CI, 0.76–1.21). We estimated that vigorous physical activity would produce 65 fewer recurrences per 1000 patients at 5 years (95% CI from 93 to 27 fewer; very low quality of evidence), whereas nonvigorous physical activity would produce 8 events per 1000 patients at 5 years (95% CI from 46 fewer to 40 more; very low quality of evidence). Because the relative estimates came from a population with substantial differences from our target population, we rated down the quality of evidence by indirectness. We found no data regarding the effect of physical activity on diverticular complications, surgery, or chronic abdominal pain.

Quality of the evidence. For the outcome of recurrence, we rated the quality of the evidence as very low, given the use of indirect evidence to estimate the relative effect. We judged the overall quality of the evidence as very low.

Patients' values and preferences. We found no relevant data about patients' values and preferences.

Discussion. The sharp increase in the prevalence of diverticular disease throughout the 20th and early 21st centuries led to interest in potential lifestyle risk factors, including physical activity. Physical activity has a number of potential beneficial effects on the colon that could decrease the risk of diverticulitis, including increased colon transit rate, decreased colon pressures, and enhanced immune function.^{121,122}

In our review, we concluded that physical activity, in particular vigorous physical activity, may decrease the risk of recurrent diverticulitis in patients with a prior history of diverticular disease. However, the strength of our

Table 12. Question 11: Should Physical Activity Rather Than Regular Activity Be Encouraged in Patients With a History of Acute Diverticulitis?

Outcomes/no. of participants (no. of studies)	Risk ratio (95% CI)	Anticipated absolute effects			Quality of the evidence (GRADE)	What happens
		Without physical activity	With physical activity	Difference (95% CI)		
Recurrence (follow-up, 18 y)/47,288 patients (1 study) ¹²⁰	Vigorous: 0.66 ^a (0.51–0.86)	190 recurrences per 1000 patients at 5 y ^b	125 recurrences per 1000 patients at 5 y	65 fewer recurrences (from 93 to 27 fewer per 1000 patients)	⊕⊕⊕⊕ Very low due to indirectness ^c	The effect of physical activity is uncertain
	Nonvigorous: 0.96 ^a (0.76–1.21)	190 recurrences per 1000 patients at 5 y ^b	182 recurrences per 1000 patients at 5 y	8 fewer recurrences (from 46 fewer to 40 more per 1000 patients)		
Diverticular complications	—	No data	No data	No data	—	No data
Surgery	—	No data	No data	No data	—	No data
Chronic abdominal pain	—	No data	No data	No data	—	No data

NOTE. Population: patients with a history of acute diverticulitis; setting: outpatient; intervention: physical activity; comparison: regular activity.

^aRelative effect estimated from a cohort of 47,288 men without previous diverticulitis.¹²⁰

^bBaseline risk estimated from a cohort of 20,136 patients treated medically for a first episode of acute uncomplicated diverticulitis (mean follow-up, 5.5 years).⁴

^cWe rated down the quality of the evidence because the relative effect estimate comes from a population without previous diverticulitis.

conclusion is very limited because the risk estimates were calculated based on an observational study of patients with incident not recurrent diverticulitis.

The level of physical activity needed for risk reduction in diverticular disease may be higher than for other chronic diseases.¹²³ The cohort study used for the estimates in this review found that vigorous but not nonvigorous activity was significantly associated with a decreased risk of incident diverticulitis.¹²⁰ Running, the most common form of vigorous exercise, was the only specific activity to show a significant inverse relationship with diverticulitis after adjusting for other confounders, including other forms of vigorous activity (adjusted relative risk, 0.53; 95% CI, 0.32–0.88). Williams et al made similar conclusions in a study of runners 50 years of age or older who participated in the National Runners’ Health Study.¹²⁴ The risk of diverticulitis was inversely related to the number of miles run per week and race performance times (as a measure of cardiovascular fitness). However, in a prospective study in Sweden, leisure physical activity was not related to hospitalization for diverticular disease. In this study, physical activity was categorized into 3 levels, including sedentary, regular, and strenuous activity (at least 2 hours per week), but running was not specifically assessed.

Conclusions and Implications for Future Research

In this technical review, we addressed 11 key questions regarding the management of patients with acute uncomplicated diverticulitis and the prevention of recurrent

events. We evaluated the effect of each intervention on outcomes rated as critical or important by the guideline panel. We used the GRADE system to rate the quality of evidence and provided estimates of the absolute effect of each intervention to enable trade-offs between potential beneficial and harmful consequences. We also provided evidence regarding patient values and preferences when available.

We found the quality of the evidence regarding the management of acute diverticulitis or the prevention of recurrent diverticulitis to be universally low. Even in the setting of available randomized controlled trials evaluating the effect of antibiotics in acute diverticulitis and mesalazine for the prevention of recurrent events, we rated the evidence as low and moderate, respectively. In both cases, the number of study outcomes was small and therefore our estimates were imprecise. In addition, the study design in the antibiotics trial did not adequately reduce the risk of bias. Of the strategies evaluated for prevention of recurrent diverticulitis, we rated the evidence as very low for high-fiber diet, physical activity, use of rifaximin, use of probiotics, and surgical resection. In these cases, we used indirect evidence from studies of incident diverticulitis or from patients with SUDD due to the absence of studies of patients with a history of diverticulitis. In addition, data pertaining to diet, lifestyle, and use of aspirin were predominantly from studies of older men, potentially limiting the generalizability of our findings to other populations. We found only 2 small studies of elective colonic resection for prevention of recurrence and no study directly comparing conservative with surgical intervention in this setting.

Studies of conservative management after an initial attack were observational in design and did not account for recurrences managed in the outpatient setting. Results of an ongoing randomized trial evaluating medical versus surgical management are likely to provide important insights into this issue.⁶⁷ In this review, the only evidence rated as high quality related to complications of surgical, endoscopic, or medical interventions. In these instances, the risk of an intervention-related complication without the intervention is zero. Overall, it is important to note that the failure of this review to identify a clearly effective preventive measure for diverticulitis may reflect the dearth of evidence rather than a true lack of efficacy for the studied interventions.

There are many important questions regarding the management of diverticular disease that were beyond the scope of this guideline. The majority of adults older than 60 years of age have diverticulosis, but most will remain asymptomatic and fewer than 5% will develop diverticulitis.² Furthermore, the presence of diverticulosis is unknown in patients without prior imaging or lower endoscopy. Therefore, we focused this review on issues relevant to patients with a history of diverticulitis rather than those with asymptomatic diverticulosis. We further narrowed our review to 11 questions pertaining to uncomplicated and recurrent diverticulitis based on the perceived relevance to the target audience of gastroenterologists. We specifically did not assess data related to the management of complicated diverticulitis, which generally falls in the surgery realm and is covered in a recent American Society of Colon and Rectal Surgeons guideline and systematic review.^{10,60} Furthermore, we were unable to address SUDD within the constraints of this guideline. This broad topic lends itself to a separate guideline.

Despite considerable recent progress, this technical review illuminated significant gaps in our knowledge regarding the management of patients with a history of acute diverticulitis. Overall, we found surprisingly little literature on this important target population. Future studies of patients with a history of diverticulitis are warranted to better define the natural history of recurrence as well as risk factors and preventative interventions. We also noted potential confusion in the literature regarding patients with SUDD and those with a history of acute diverticulitis. For example, rifaximin has been studied as a preventive measure mainly in patients with SUDD without a documented history of acute diverticulitis.¹²⁵ In general, improved delineation of disease phenotypes will help elucidate efficacious interventions. For instance, patients with certain high-risk factors or multiple recurrent episodes of diverticulitis may be more likely to benefit from anti-inflammatory therapies but have not been the target of existing trials. Furthermore, a more sophisticated understanding of the pathoetiologic mechanisms underlying the development of diverticulitis is likely to uncover new avenues for treatment and prevention. Finally, for many of the questions addressed in this review, we found little to no data on outcomes determined to be critical or important. This was particularly true for patient values and preferences. Future studies should examine the impact of

management strategies on quality of life and other patient-reported outcomes. Recently, a quality of life instrument was developed and validated to evaluate persistent symptoms after an episode of diverticulitis.¹⁵

In summary, over the past decade, there has been a rapid expansion of the literature on acute diverticulitis. This technical review sought to evaluate and summarize the existing literature in a structured format to guide clinicians in the management of this disorder. However, for many management issues, the evidence remains uncertain or of low quality. In this setting, clinical decisions must balance potential risks and benefits as well as incorporate individual patient values and preferences. Ongoing studies of medical and surgical therapies for the treatment and prevention of acute diverticulitis promise to shed light on the management of this disease.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at <http://dx.doi.org/10.1053/j.gastro.2015.10.001>.

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Reprint requests

Address requests for reprints to: Chair, Clinical Guidelines Committee, AGA National Office, 4930 Del Ray Avenue, Bethesda, Maryland 20814. e-mail: msiedler@gastro.org; telephone: (301) 941-2618.

Conflicts of interest

All members were required to complete a disclosure statement. These statements are maintained at the American Gastroenterological Association (AGA) Institute headquarters in Bethesda, Maryland, and pertinent disclosures are published with the report. The authors disclose no conflicts.

Funding

Supported in part by the National Center for Advancing Translational Sciences, National Institutes of Health (1KL2TR001109), and the National Institute of Diabetes and Digestive and Kidney Diseases (R01DK084157 and R01DK101495).

Appendix 1. Search Strategies and Results

Question 1. Should antibiotics rather than no antibiotics be used in patients with acute uncomplicated diverticulitis confirmed by CT scan?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid

MEDLINE(R) In-Process & Other Non-Indexed Citations
August 22, 2014

Summary of search results:

Total no. retrieved	99
Screening (title and abstract)	99
Screening (full text)	3
Included	2
Inclusion criteria	
Population: patients with acute uncomplicated diverticulitis	
Intervention: antibiotics	
Comparison: no antibiotics/standard care	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7066
2	(diverticulitides or diverticulitis).ti,ab.	10,348
3	exp Anti-Bacterial Agents/ use mesz,cctr,coch,clhta	552,847
4	exp antibiotic agent/ use emez	937,359
5	(anti?bacterial or antibiotic* or bacteriocid*).ti,ab.	596,861
6	1 or 2	13,154
7	or/3-5	1,729,548
8	6 and 7	1881
9	limit 8 to (english language and yr="2009 -Current") [Limit not valid in CDSR; records were retained]	799
10	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,401
11	(Meta Analysis or Controlled Clinical Trial).pt.	225,337
12	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	105,713
13	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data syntheses* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	433,283
14	exp Randomized Controlled Trial/	732,740
15	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,629
16	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	431,595
17	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*).ti,ab.	2,321,254
18	or/10-17	3,177,057
19	9 and 18	146
20	remove duplicates from 19	99

Question 2. Should a colonoscopy be performed versus no colonoscopy after an episode of acute diverticulitis confirmed by CT scan?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	47
Screening (title and abstract)	47
Screening (full text)	3
Included	1
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: colonoscopy	
Comparison: no colonoscopy	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7066
2	(diverticulitides or diverticulitis).ti,ab.	10,348
3	1 or 2	13,154
4	exp Colonoscopy/	68,258
5	(colonoscop* or (colon adj endoscop)).ti,ab.	53,134
6	4 or 5	83,327
7	3 and 6	991
8	limit 7 to (english language and yr="2009 -Current") [Limit not valid in CDSR; records were retained]	454
9	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,401
10	(Meta Analysis or Controlled Clinical Trial).pt.	225,337
11	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	105,713
12	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	433,283
13	exp Randomized Controlled Trial/	732,740
14	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,629
15	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	431,595
16	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*).ti,ab.	2,321,254
17	or/9-16	3,177,057
18	8 and 17	65
19	remove duplicates from 18	47

Question 3. Should elective colonic resection be performed versus medical management after an episode of acute uncomplicated diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	20
Screening (title and abstract)	20
Screening (full text)	1
Included	1
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: colonic resection	
Comparison: medical management	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7066
2	(diverticulitides or diverticulitis).ti,ab.	10,348
3	1 or 2	13,154
4	exp Colectomy/ use mesz,cctr,coch,clhta	15,773
5	exp hemicolectomy/ use emez	5016
6	Hemi?colectom*.ti,ab.	6768
7	or/4-6	23,898
8	3 and 7	815
9	limit 8 to (english language and yr="2009 -Current") [Limit not valid in CDSR; records were retained]	264
10	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,401
11	(Meta Analysis or Controlled Clinical Trial).pt.	225,337
12	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	105,713
13	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	433,283
14	exp Randomized Controlled Trial/	732,740
15	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,629
16	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	431,595
17	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	2,321,254
18	or/10-17	3,177,057
19	9 and 18	28
20	remove duplicates from 19	20

Question 4. Should a high-fiber diet, rather than a regular diet, be advised in patients with a history of acute diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	31
Screening (title and abstract)	31
Screening (full text)	2
Included	2
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: high-fiber diet	
Comparison: regular diet	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7066
2	(diverticulitides or diverticulitis).ti,ab.	10,348
3	1 or 2	13,154
4	exp Dietary Fiber/	30,019
5	(fiber or fibre or wheat bran or roughage).ti,ab.	279,420
6	4 or 5	288,713
7	3 and 6	335
8	limit 7 to (english language and yr="2009 -Current") [Limit not valid in CDSR; records were retained]	105
9	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,401
10	(Meta Analysis or Controlled Clinical Trial).pt.	225,337
11	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	105,713
12	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	433,283
13	exp Randomized Controlled Trial/	732,740
14	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,629
15	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	431,595
16	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	2,321,254
17	or/9-16	3,177,057
18	8 and 17	46
19	remove duplicates from 18	31

Question 5. Should consumption of corn, nuts, and popcorn be avoided in patients with a history of acute diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	9
Screening (title and abstract)	9
Screening (full text)	0
Included	0
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: corn, nuts, or popcorn	
Comparison: regular diet	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7066
2	(diverticulitides or diverticulitis).ti,ab.	10,348
3	1 or 2	13,154
4	exp Seeds/ use mesz,cctr,coch,clhta	30,658
5	exp plant seed/ use emez	40,348
6	exp Nuts/ use mesz,cctr,coch,clhta	2200
7	exp Nut/ use emez	10,552
8	exp Zea mays/ use mesz,cctr,coch,clhta	21,642
9	exp maize/ use emez	21,983
10	(seed* or popcorn or nut*).ti,ab.	806,101
11	or/4-10	864,750
12	3 and 11	143
13	limit 12 to (english language and yr="2009 -Current") [Limit not valid in CDSR; records were retained]	50
14	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,401
15	(Meta Analysis or Controlled Clinical Trial).pt.	225,337
16	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	105,713
17	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	433,283
18	exp Randomized Controlled Trial/	732,740
19	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,629
20	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	431,595
21	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*).ti,ab.	2,321,254
22	or/14-21	3,177,057
23	13 and 22	12
24	remove duplicates from 23	9

Question 6. Should aspirin be avoided in patients with a history of acute diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	89
Screening (title and abstract)	89
Screening (full text)	0
Included	0
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: aspirin	
Comparison: no aspirin/placebo	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7066
2	(diverticulitides or diverticulitis).ti,ab.	10,348
3	1 or 2	13,154
4	exp Anti-Inflammatory Agents, Non-Steroidal/ use mesz,cctr,coch,clhta	172,223
5	exp nonsteroid antiinflammatory agent/ use emez	423,492
6	(non?steroidal adj2 anti-inflammator*).ti,ab.	27,603
7	(nsaid* or aspirin* or ASA or acetylsalicylic acid).ti,ab.	194,471
8	or/4-7	675,349
9	3 and 8	698
10	limit 9 to (english language and yr="2009 -Current") [Limit not valid in CDSR; records were retained]	390
11	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta (Meta Analysis or Controlled Clinical Trial).pt.	73,401
12	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	225,337
13	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	105,713
14	exp Randomized Controlled Trial/	433,283
15	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	732,740
16	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	351,629
17	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*).ti,ab.	431,595
18	or/11-18	2,321,254
19	10 and 19	3,177,057
20	remove duplicates from 20	108
21		89

Question 7. Should nonaspirin NSAIDs be avoided in patients with a history of acute diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	89
Screening (title and abstract)	89
Screening (full text)	0
Included	0
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: aspirin	
Comparison: no aspirin/placebo	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7066
2	(diverticulitides or diverticulitis).ti,ab.	10,348
3	1 or 2	13,154
4	exp Anti-Inflammatory Agents, Non-Steroidal/ use mesz,cctr,coch,clhta	172,223
5	exp nonsteroid antiinflammatory agent/ use emez	423,492
6	(non?steroidal adj2 anti-inflammator*).ti,ab.	27,603
7	(nsaid* or aspirin* or ASA or acetylsalicylic acid).ti,ab.	194,471
8	or/4-7	675,349
9	3 and 8	698
10	limit 9 to (english language and yr="2009 -Current") [Limit not valid in CDSR; records were retained]	390
11	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,401
12	(Meta Analysis or Controlled Clinical Trial).pt.	225,337
13	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	105,713
14	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	433,283
15	exp Randomized Controlled Trial/	732,740
16	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,629
17	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	431,595
18	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*).ti,ab.	2,321,254
19	or/11-18	3,177,057
20	10 and 19	108
21	remove duplicates from 20	89

Question 8. Should mesalamine rather than no therapy be used in patients with a history of acute uncomplicated diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	45
Screening (title and abstract)	45
Screening (full text)	8
Included	6
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: mesalamine	
Comparison: no mesalamine/placebo	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7066
2	(diverticulitides or diverticulitis).ti,ab.	10,348
3	1 or 2	13,154
4	exp Mesalamine/ use mesz,cctr,coch,clhta	3085
5	exp mesalazine/ use emez	12,486
6	(Mesalazine or mesalamine or 5-aminosalicylic acid or 5-ASA or Asacol or Pentasa or Salofalk or Mezavant or Canasa or Rowasa or Delzicol or Lialda or Apriso).ti,ab.	9290
7	or/4-6	18,120
8	3 and 7	225
9	limit 8 to english language [Limit not valid in CDSR; records were retained]	198
10	limit 9 to yr="2009-Current"	130
11	Meta-Analysis/ use coch,clhta,mesz or exp Technology Assessment, Biomedical/ use cctr,coch,clhta,mesz	60,311
12	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,401
13	(Meta Analysis or Controlled Clinical Trial).pt.	225,337
14	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	105,713
15	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	433,283
16	exp Randomized Controlled Trial/	732,740
17	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,629
18	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	431,595
19	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	2,321,254
20	or/12-19	3,177,057
21	10 and 20	58
22	remove duplicates from 21	45

Question 9. Should rifaximin rather than no therapy be used in patients with a history of acute uncomplicated diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	26
Screening (title and abstract)	26
Screening (full text)	4
Included	1
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: rifaximin	
Comparison: no rifaximin/placebo	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7085
2	(diverticulitides or diverticulitis).ti,ab.	10,376
3	1 or 2	13,187
4	exp Rifamycins/ use mesz,cctr,coch,clhta	18,507
5	exp rifaximin/ use emez	2578
6	(Rifomycin* or rifamycin* or rifaximin or Rifagut or Xifaxan or lumenax or Xifaxanta or Normix).ti,ab.	5371
7	or/4-6	23,525
8	3 and 7	140
9	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,649
10	(Meta Analysis or Controlled Clinical Trial).pt.	225,592
11	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	106,375
12	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	435,484
13	exp Randomized Controlled Trial/	734,357
14	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,846
15	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	433,077
16	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial)).ti,ab.	2,327,201
17	or/9-16	3,185,580
18	8 and 17	51
19	limit 18 to english language [Limit not valid in CDSR; records were retained]	49
20	limit 19 to yr="2009 -Current"	33
21	remove duplicates from 20	26

Question 10. Should probiotics rather than no therapy be used in patients with a history of acute diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	30
Screening (title and abstract)	30
Screening (full text)	3
Included	2
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: probiotics	
Comparison: no probiotics/placebo	
Design: systematic reviews or randomized trials	

Search strategy:

#	Searches
1	exp Diverticulitis/
2	(diverticulitides or diverticulitis).ti,ab.
3	1 or 2
4	exp Probiotics/ use mesz,cctr,coch,clhta
5	exp probiotic agent/ use emez
6	(probiotic* or lactobacilli or Lactobacillus or bifidobacteria or streptococci or streptococcus).ti,ab.
7	or/4-6
8	3 and 7
9	limit 8 to (english language and yr="2011 -Current") [Limit not valid in CDSR; records were retained]
10	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta
11	(Meta Analysis or Controlled Clinical Trial).pt.
12	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez
13	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.
14	exp Randomized Controlled Trial/
15	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta
16	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez
17	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*).ti,ab.
18	or/10-17
19	9 and 18
20	limit 19 to english language [Limit not valid in CDSR; records were retained]
21	limit 20 to yr="2009 -Current"
22	remove duplicates from 21

Question 11. Should physical activity rather than regular activity be encouraged in patients with a history of acute diverticulitis?

Search date: August 24, 2014

Databases searched: EBM Reviews - Cochrane Central Register of Controlled Trials July 2014, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to July 2014, EBM Reviews - Health Technology Assessment 3rd Quarter 2014, EMBASE 1980 to 2014 Week 34, Ovid MEDLINE(R) 1946 to August Week 2 2014, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 22, 2014

Summary of search results:

Total no. retrieved	9
Screening (title and abstract)	9
Screening (full text)	0
Included	0
Inclusion criteria	
Population: patients with a history of acute uncomplicated diverticulitis	
Intervention: physical activity	
Comparison: no physical activity	
Design: systematic reviews or randomized trials	

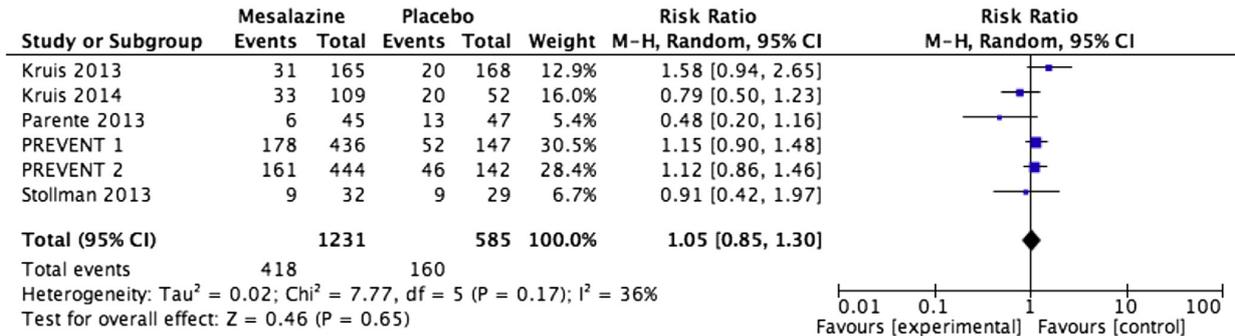
Search strategy:

#	Searches	Results
1	exp Diverticulitis/	7085
2	(diverticulitides or diverticulitis).ti,ab.	10,376
3	1 or 2	13,187
4	exp Motor Activity/ use mesz,cctr,coch,clhta	215,668
5	exp physical activity/ use emez	235,842
6	((activity or active or activities) adj2 (locomotor or physical* or motor)).ti,ab.	218,598
7	exercise*.ti,ab.	474,122
8	exp Physical Fitness/	51,992
9	exp fitness/ use emez	27,721
10	exp Life Style/	141,847
11	or/4-10	1,047,640
12	3 and 11	108
13	Meta-Analysis/ use mesz,cctr,coch,clhta or Meta-Analysis as Topic/ use mesz,cctr,coch,clhta or exp Technology Assessment, Biomedical/ use mesz,cctr,coch,clhta	73,649
14	(Meta Analysis or Controlled Clinical Trial).pt.	225,592
15	Meta Analysis/ use emez or "Meta Analysis (Topic)"/ use emez or Biomedical Technology Assessment/ use emez	106,375
16	(meta analy* or metaanaly* or pooled analysis or ((systematic* or methodologic*) adj3 (review* or overview*)) or published studies or published literature or hand search* or handsearch* or medline or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab.	435,484
17	exp Randomized Controlled Trial/	734,357
18	exp Random Allocation/ use mesz,cctr,coch,clhta or exp Double-Blind Method/ use mesz,cctr,coch,clhta or exp Control Groups/ use mesz,cctr,coch,clhta or exp Placebos/ use mesz,cctr,coch,clhta	351,846
19	exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	433,077
20	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial)).ti,ab.	2,327,201
21	or/13-20	3,185,580
22	12 and 21	13
23	limit 22 to english language [Limit not valid in CDSR; records were retained]	13
24	limit 23 to yr="2009 -Current"	10
25	remove duplicates from 24	9

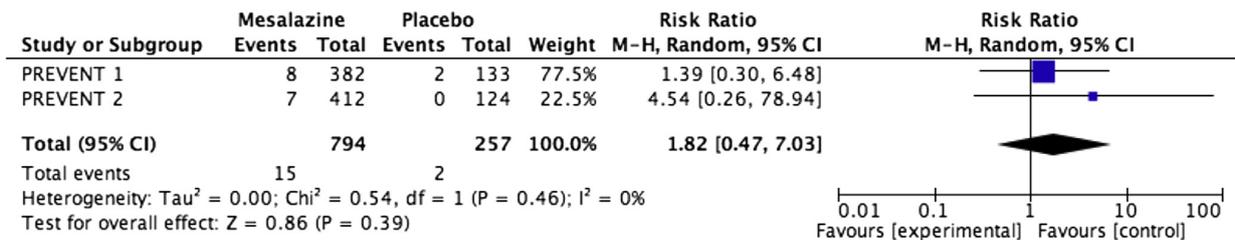
Appendix 2. Forest Plots

Question 8. Should mesalamine rather than no therapy be used in patients with a history of acute diverticulitis?

1. Recurrences



2. Surgery



3. Abdominal pain

